



John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963

12345678901

March 1, 2008



3767

Dear John Public:

Thank you for filling your prescription for HEART® (timon) at Hometown Pharmacy. As your pharmacy, we want to do everything we can to help you understand and manage your condition. That's why we'd like to offer you the **Hometown Pharmacy Patient Care Program**.

The **Hometown Pharmacy Patient Care Program** is a complimentary service designed to help you take your medication regularly, as directed by your doctor. This program may include:

- Important information about your condition.
- Tips to help you get the most out of your therapy with HEART.
- Timely updates and reminders regarding the status of your HEART prescription.

Please take a moment to read the information about HEART on the back of this page. If you have any questions about your HEART prescription, we are here for you!

We hope you find the provided information useful. However, if you do not wish to take advantage of the program, please call 1-800-555-1212 and enter **12345678901** when prompted, or check the box on the bottom of the back of this page and return the form in the envelope provided, whichever is most convenient.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

**What you need to know about HEART® (timon).**

- HEART helps reduce your risk of having a future heart attack or stroke, if you have had a recent heart attack, a recent stroke, or established peripheral arterial disease.
- HEART is designed to help keep platelets from sticking together and forming clots. This helps keep your blood flowing and helps reduce your risk of a future heart attack or stroke.
- Even though you may be feeling better, it's important to keep taking your medications, as prescribed by your doctor, including HEART, because you're still at risk.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

69-041024B

B1-D0178C

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Over Please

**Please see Important Information and enclosed Prescribing Information.**

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

## Understanding your condition and the benefits of taking HEART® (timon).

### Who should take HEART?

HEART is recommended daily for patients who have:

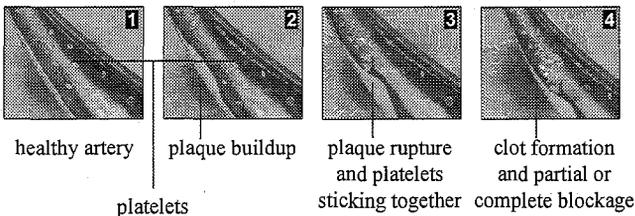
- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

HEART is also recommended in addition to aspirin for patients who have:

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack)

All of these conditions put you at increased risk of having a future heart attack or stroke.

### What led to your condition?



The easiest way to understand how your condition developed is to learn about what causes platelet clotting in the arteries. Platelet clots can reduce or completely block the flow of oxygen-rich blood to important parts of your body, like your heart, brain, or legs. Here's how this happens:

1. Healthy arteries are smooth and flexible, allowing oxygen-rich blood to flow through easily.
2. Over time, certain factors can cause fat, including cholesterol, to collect in the arterial walls. The cholesterol thickens and forms plaque, narrowing the arteries.

3. As blood flows through the narrowed artery, the plaque can rupture. This causes platelets in the blood to stick to the damaged area (similar to a scab on the skin) by clumping together and forming a clot (thrombus).
4. A clot can reduce or completely block the flow of blood through an artery. If a clot occurs in an artery that leads to the heart, the result can be unstable angina or a heart attack. If a clot forms in an artery leading to the brain, a stroke can occur. If a clot forms in an artery supplying the leg muscles, the result can be poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest.

### How HEART works.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why it's important to refill your HEART prescription before it runs out.

### How HEART should be taken.

HEART should be taken with or without food, exactly as your doctor has directed you. If you accidentally miss a day, do not double up on your medication, just continue your usual dose. If you have any questions about taking your medications, please consult your doctor or pharmacist. Always check with your doctor before stopping or starting any prescriptions or over-the-counter medications and dietary supplements.

**Please see enclosed Prescribing Information and Important Information on reverse side.**

PLW1.LDE P02 ZW478

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



**NOTE:** Complete this section only if you do NOT wish to participate in the **Hometown Pharmacy Patient Care Program.**

Check the box below, detach, and mail in the envelope provided.

I do not wish to participate in the **Hometown Pharmacy Patient Care Program.**

If you wish to inform us by phone, please call 1-800-555-1212 and enter **12345678901** when prompted.





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The **Hometown Pharmacy Patient Care Program** is a complimentary service designed to help you take your medication regularly, as directed by your doctor. This program may include:

- Important information about your condition.
- Tips to help you get the most out of your therapy with HEART.
- Timely updates and reminders regarding the status of your HEART prescription.

In fact, our records indicate that you are due for a HEART refill on **September 30, 2005. It's quick and easy to have your prescription refilled! Simply call (413) 555-1212** and enter your HEART prescription number: **1234567890** when prompted. Our automated system allows you to quickly place your order without having to speak with a pharmacy associate.

To start, please take a moment to read the information about HEART on the back of this page. If you have any questions about your HEART prescription, we are here for you! If you do not wish to take advantage of this program, check the box located on the back of this page and return the form in the envelope provided, or call the number at the bottom of the back page, whichever is most convenient.

Sincerely  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
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**What you need to know about HEART® (timon).**

- HEART helps reduce your risk of having a future heart attack or stroke, if you have had a recent heart attack, a recent stroke, or established peripheral arterial disease.
- HEART is designed to help keep platelets from sticking together and forming clots. This helps keep your blood flowing and helps reduce your risk of a future heart attack or stroke.
- Even though you may be feeling better, it's important to keep taking your medications, as prescribed by your doctor, including HEART, because you're still at risk.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

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B1-D0222C

**Please see Important Information and enclosed Prescribing Information.**

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

If you no longer wish to receive patient education mailings, please call 1-800-555-1212.

## Understanding your condition and the benefits of taking HEART® (timon).

### Who should take HEART?

HEART is recommended for patients who have:

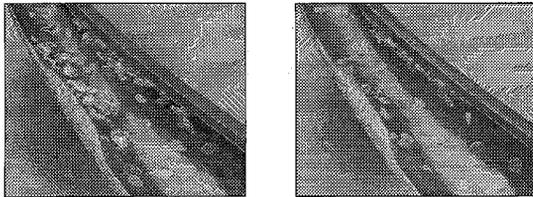
- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

### HEART is also recommended in addition to aspirin for patients who have:

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack).

All of these conditions put you at increased risk of having a future heart attack or stroke.

### What led to your condition?



The easiest way to understand how your condition developed is to learn about what causes platelet clotting in the arteries. Platelet clots can reduce or completely block the flow of oxygen-rich blood to important parts of your body, like your heart, brain, or legs. Here's how this happens:

1. Healthy arteries are smooth and flexible, allowing oxygen-rich blood to flow through easily.
2. Over time, certain factors can cause fat, including cholesterol, to collect in the arterial walls. The cholesterol thickens and forms plaque, narrowing the arteries.

3. As blood flows through the narrowed artery, the plaque can rupture. This causes platelets in the blood to stick to the damaged area (similar to a scab on the skin) by clumping together and forming a clot (thrombus).
4. A clot can reduce or completely block the flow of blood through an artery. If a clot occurs in an artery that leads to the heart, the result can be unstable angina or a heart attack. If a clot forms in an artery leading to the brain, a stroke can occur. If a clot forms in an artery supplying the leg muscles, the result can be poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest.

### How HEART works.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why it's important to refill your HEART prescription before it runs out.

### How HEART should be taken.

HEART should be taken with or without food, exactly as your doctor has directed you. If you accidentally miss a day, do not double up on your medication, just continue your usual dose. If you have any questions about taking your medications, please consult your doctor or pharmacist. Always check with your doctor before stopping or starting any prescriptions or over-the-counter medications and dietary supplements.

**Please see enclosed Prescribing Information and Important Information on reverse side.**

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



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I do not wish to participate in the **Hometown Pharmacy Patient Care Program**.

If you wish to inform us by phone, please call 1-800-555-1212 and enter 12345678901 when prompted.





John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963  
|||||||

12345678901

March 1, 2008

3767

Dear John Public:

We hope this letter finds you in good health. This letter is provided as part of the **Hometown Pharmacy Patient Care Program**, a complimentary service designed to help you take your medication regularly, as directed by your doctor, while also providing you with tips to help you get the most out of your prescription for HEART® (timon).

Remember, your doctor has prescribed HEART to help reduce your risk of a future heart attack or stroke. Part of our commitment to you as your pharmacy is to do everything we can to help make sure you have what you need to stay in good health—and our records show the refill on your HEART prescription is due on **September 30, 2005**.

**It's quick and easy to have your prescription refilled! Simply:**

- Call **(413) 555-1212**
- Enter your HEART prescription number **1234567890** when prompted.

Our automated system allows you to quickly place your refill order, without having to speak with a Pharmacy Associate. If your doctor has changed your prescription, please disregard this letter and follow your doctor's instructions.

Again, thank you for choosing Hometown Pharmacy. If you have any questions about your medication, please feel free to call or stop by the pharmacy. We look forward to seeing you soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

Over Please

**Why is HEART® (timon) important?**

You should know that HEART is an important part of your treatment. HEART helps keep platelets from sticking together and forming clots, which helps keep your blood flowing. If you have had a recent heart attack, a recent stroke, or established peripheral arterial disease, HEART can help reduce your risk of a future heart attack or stroke.

**Who should take HEART?**  
**HEART is recommended for patients who have:**

- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

**PLAVIX is also recommended in addition to aspirin for patients who have:**

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack).

All of these conditions put you at increased risk of having a future heart attack or stroke.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

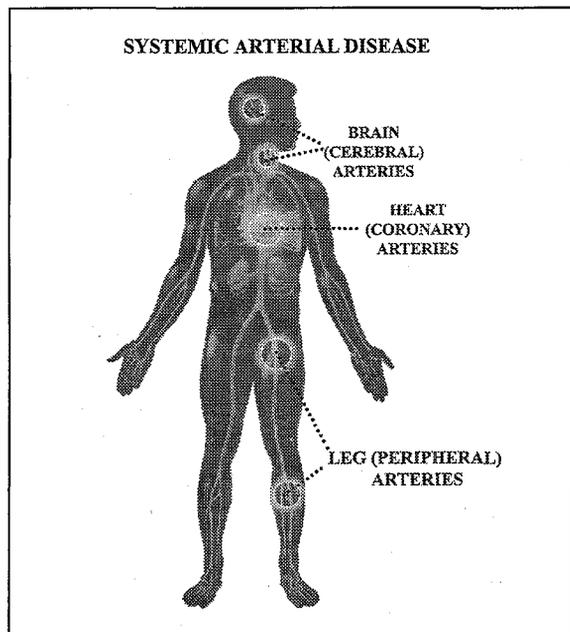
**Please see Important Information and enclosed Prescribing Information.**

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## Understanding your condition.

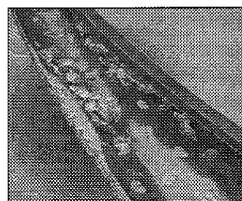
### Why you remain at increased risk of having a future heart attack or stroke.

- If you have had a heart attack, unstable angina, stroke or peripheral arterial disease, you are prone to platelet clotting.
- When platelets stick together and form clots in the arteries, they can reduce or block the flow of oxygen-rich blood to your heart or brain.
- This means you are at increased risk of having either a heart attack or a stroke.
- By helping to keep your blood flowing freely through the arteries, you can help reduce your risk.

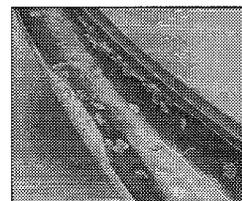


That's why you should talk to all of your doctors about staying on HEART® (timon). HEART helps keep platelets from sticking together and forming clots.

### How HEART® (timon) works.



Platelets can stick together and form clots.



HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor about staying on HEART.

### Other ways you can help protect yourself.

There are many things you can do to help reduce the risk of having a future heart attack or stroke. Taking HEART as prescribed by your doctor is one of them. There are additional risk factors you'll want to watch out for. They include:

- unhealthy diet
- smoking
- alcohol consumption
- high blood pressure
- high cholesterol
- being overweight

Be sure to talk to your doctor to make sure you're doing all you can to help reduce your risk of having a future heart attack or stroke. Naturally, this includes taking all your medications, including HEART, as prescribed. If you have any questions about taking your medication, please consult your doctor or pharmacist.

PLW1.LDE P02 ZW480

Please see Prescribing Information and enclosed Important Information on reverse side.

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March 1, 2008



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Dear John Public:

Greetings from Hometown Pharmacy. This letter is provided as part of the **Hometown Pharmacy Patient Care Program**, a complimentary service designed to help you take your medication regularly, as directed by your doctor. This program also provides you with tips to help you get the most out of your prescription for HEART® (timon).

We're writing you today because our records show the refill on your HEART prescription is due on **September 30, 2005**.

**It's quick and easy to have your prescription refilled! Simply:**

- Call (413) 555-1212
- Enter your HEART prescription number **1234567890** when prompted.

Our automated system allows you to quickly place your refill order, without having to speak with a Pharmacy Associate.

Remember, your doctor prescribed HEART to help protect you against a future heart attack or stroke. That's why it's important to continue taking HEART as prescribed. If your doctor has changed your prescription, please disregard this letter and follow your doctor's instructions.

Again, thank you for choosing Hometown Pharmacy. If you have any questions about your medication, please feel free to call or stop by the pharmacy. We look forward to seeing you soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

Over Please

**Why it's important for you to take HEART® (timon).**

Everyday you stay on HEART, you help stay protected against a future heart attack or stroke. In fact, if you have had a stroke or have poor circulation in the legs (peripheral arterial disease), HEART may be taken once daily, as prescribed by your doctor. If you've been diagnosed with heart-related chest pain (unstable angina) or a certain type of heart attack (non-ST-segment elevation heart attack, also known as non-Q-wave heart attack), the American Heart Association and the American College of Cardiology recommend HEART with aspirin for treatment for up to 9 months after diagnosis. That's why you should talk to your doctor about your progress and continue to take HEART as prescribed.

**Feeling better doesn't mean you're not at risk.** Sometimes people think that, after several months of treating their condition, they're healed. They feel better so they don't continue with their treatment. However, no matter how good you may feel, it's important to remember that:

- you remain at increased risk of having a future heart attack or stroke
- HEART helps you reduce this risk.

**So be sure to refill your HEART prescription before it runs out.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

**Please see Important Information and enclosed Prescribing Information.**

## Doing more to help prevent a future heart attack or stroke.

### Making lifestyle changes.

Because you're at increased risk of having a future heart attack or stroke, it is important to make certain lifestyle changes that can help you reduce that risk. Your doctor can tell you what changes would work the best for you, but here are some suggestions:

- Quit smoking—Smoking narrows and damages your blood vessels, which increases your risk of heart attack and stroke.
- Eat healthier foods—A diet that's low in saturated fat, sodium, and cholesterol can make a big difference in your health.
- Keep your blood pressure under control.
- Depending on your condition, some form of rehabilitation might be necessary. Talk to your doctor to find out if you would benefit from a rehabilitation program.
- Continue to take HEART® (timon) and other medications, as prescribed by your doctor.

### Coping with changes in your life.

When you have a condition that increases your risk of a future heart attack or stroke, some of the changes that take place may not be ones that you choose. It's important to understand that these changes are related to your condition. So talk to your doctor about what you can do to help manage them.

### They may include:

- Feelings such as anxiety, depression, anger, frustration, and/or fear.
- Problems with intimacy.
- A shift in parent/child relationships.

Just as you need time to adjust to your condition, your family and friends need time to adjust too. If you're having a hard time dealing with different emotions, talk to your doctor about counseling or support groups available in your area.

### Taking your medications.

Continuing to take HEART and all your medications exactly as prescribed by your doctor(s) is an important and positive way to help reduce your risk of a future heart attack or stroke. Always check with your doctor before stopping or starting any prescription or over-the-counter medication, and any dietary supplements.

Even though you may be feeling better, it's important to keep taking your medications, including HEART, as prescribed by your physician to increase your protection against a future heart attack or stroke.

PLW1.LDE P04 ZW482

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## Building a support network.

### Whom should you include in your support network?

Staying on a healthier path means doing more to take care of yourself and helping to protect yourself from a future heart attack or stroke. But you don't have to do it all alone. Many people in your life can help you stay protected. For example:

- Family
- Friends
- Neighbors
- Doctors
- Coworkers
- Local support groups
- Pharmacists
- Church or religious counselors.

One of the primary members of your support network is, of course, your doctor. That's why it's so important to partner with your doctor. Talk to your doctor about how you're feeling, ask questions, and discuss the progress you're making—good or bad—so your doctor can give you the best treatment possible. You should be comfortable about asking your doctor any questions you have regarding your condition, including whether you should renew your HEART® (timon) prescription before your current one runs out.

### The hardest part about getting help is knowing how to ask for it.

Some people have a hard time admitting they need help. But there's no reason to feel that way. In fact, it's very important to let the people in your life help you stay protected from a future heart attack or stroke, especially after you're feeling better. The more support you have, the more likely you'll be to continue making healthy choices that will help you reduce your risk of a future heart attack or stroke.

### Tips on getting the support you need.

Explain to the members of your support network when:

- you need emotional support
- you need physical support
- you want some personal space
- you want some company
- you want to do something for yourself
- you want help doing something.

### Where else can you find help?

#### American Heart Association

1-800-AHA-USA-1, [www.americanheart.org](http://www.americanheart.org)

#### Mended Hearts

1-888-HEART99, [www.mendedhearts.org](http://www.mendedhearts.org)

#### American Stroke Association

1-888-4-STROKE, [www.strokeassociation.org](http://www.strokeassociation.org)

#### National Stroke Association

1-800-STROKES, [www.stroke.org](http://www.stroke.org)

#### Vascular Disease Foundation

1-866-PADINFO, [www.VDF.org](http://www.VDF.org)

PLW1.LDE P06 ZW484

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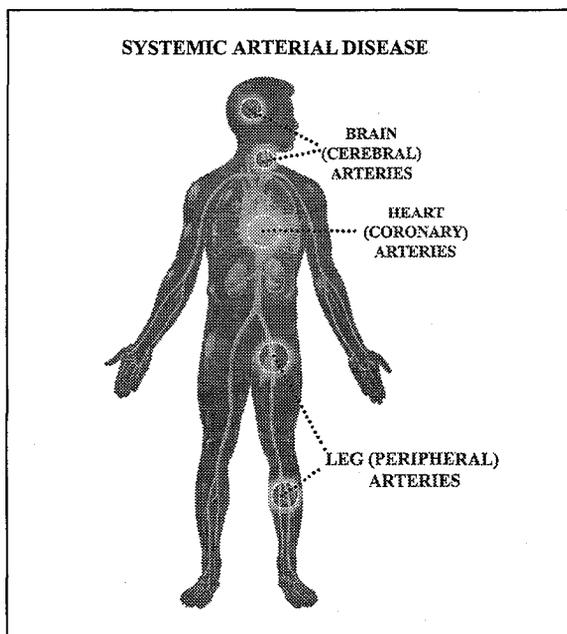


## Understanding your condition.

### Why HEART® (timon) is important.

Because you're at increased risk of having a heart attack or stroke, you should know that HEART is an important part of your treatment. Continuing to take HEART can help reduce your risk of a future heart attack or stroke.

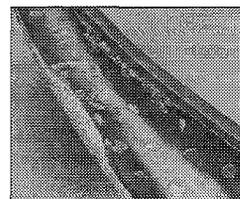
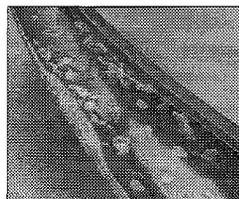
### Why you remain at increased risk of having a future heart attack or stroke.



- If you have had a heart attack or stroke or have unstable angina or peripheral arterial disease (PAD), you are prone to platelet clotting.
- When platelets stick together and form clots in the arteries, they can reduce or block the flow of oxygen-rich blood to your heart or brain.
- This means you are at increased risk of having either a heart attack or a stroke.
- By helping to keep your blood flowing freely through the arteries, you can help reduce your risk.

It's important for you to talk to your doctor about staying on HEART.

### How HEART works.



Platelets can stick together and form clots.

HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor about renewing your HEART prescription before your current one runs out.

### Other ways you can help protect yourself.

There are many things you can do to reduce the risk of having a future heart attack or stroke. Taking HEART as prescribed by your doctor is one of them. There are additional risk factors you'll want to watch out for. They include:

- unhealthy diet
- smoking
- alcohol consumption
- high blood pressure
- high cholesterol
- being overweight

Talk to your doctor to make sure you're doing all you can to help reduce your risk of having a future heart attack or stroke. Naturally, this includes taking all your medications, including HEART, as prescribed.

PLW1.LDE P08 ZW486

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**It's quick and easy to have your prescription refilled! Simply:**

- Call (413) 555-1212
- Enter your HEART prescription number 1234567890 when prompted.

Our automated system allows you to quickly place your refill order, without having to speak with a Pharmacy Associate.

It's important to remember that you're at increased risk of having a future heart attack or stroke. Your doctor has prescribed HEART to help you reduce this risk. That's why it's important for you to make an appointment with your doctor as soon as possible to talk about your progress and to ask about renewing your HEART prescription.

**Remember, if your doctor wants you to keep taking HEART, you will need to get a new prescription.**

If you have already picked up your new prescription, or if your doctor has changed your treatment, please disregard this letter.

Please take a few moments to read the information in the side bar to the right and on the back of this letter. It contains important tips and advice that can help you take an active role in your health care and reduce your risk of a future heart attack or stroke.

Thank you for choosing Hometown Pharmacy. We hope you are experiencing good health and we look forward to seeing you very soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

**Please see Important Information and enclosed Prescribing Information.**

**The importance of HEART® (timon)**

If you have had a recent heart attack, a recent stroke, or established peripheral arterial disease, it's important to remember that:

- your risk never goes away
- you should talk to all of your doctors about staying on HEART.

**You may feel better, but that doesn't mean you're not at risk.**

It's important to remember that, no matter how good you may feel, you're still at increased risk of having a future heart attack or stroke.

**How HEART works.**

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. So be sure to talk to your doctor about renewing your HEART prescription before it runs out.

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

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PLW1.LDE P09 MK3767\_1593\_11\_400\_400 ZW487

B1-D0182C

Over Please

## Are you doing all you can to help reduce your risk of a future heart attack or stroke?

### Discuss your progress and how you're feeling with your doctor.

If you have had a recent heart attack, a recent stroke, or established peripheral arterial disease, you are at increased risk of having a future heart attack or stroke. Getting the right information can make a big difference in your recovery or ongoing treatment. So be sure to keep your doctor informed about any changes in the way you're feeling or concerns you may have about your current treatment. Remember, HEART® (timon) starts working soon after you start taking it, and it will help protect you from a future heart attack or stroke. Your doctor is crucial to figuring out what's right for you—including why it's important to stay on HEART.

### Here are some questions to ask your doctor.

- Should I continue to take HEART?
- Once I've completed my HEART prescription, will I still be at risk for a future heart attack or stroke?
- What are the benefits of staying on HEART?

### How long should you stay on HEART?

HEART helps you stay protected against a future heart attack or stroke. That's why you should talk to your doctor about renewing your HEART prescription. Only your doctor can tell you if staying on HEART is right for you.

### Taking an active role in your health care.

If you make certain lifestyle changes, you can help reduce your risk of having a future heart attack or stroke. Your doctor can tell you what changes would work best for you. In the meantime, here are some suggestions:

- Quit smoking—Smoking narrows and damages your blood vessels, which increases your risk of heart attack and stroke.
- Eat healthier foods—A diet that's low in saturated fat, sodium, and cholesterol can make a big difference in your health.
- Keep your blood pressure under control.
- Depending on your condition, some form of rehabilitation might be necessary. Talk to your doctor to find out if you would benefit from a rehabilitation program.
- Continue to take HEART and other medications, as prescribed by your doctor.

PLW1.LDE P10 ZW488

**Please see enclosed Prescribing Information and Important Information on reverse side.**

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

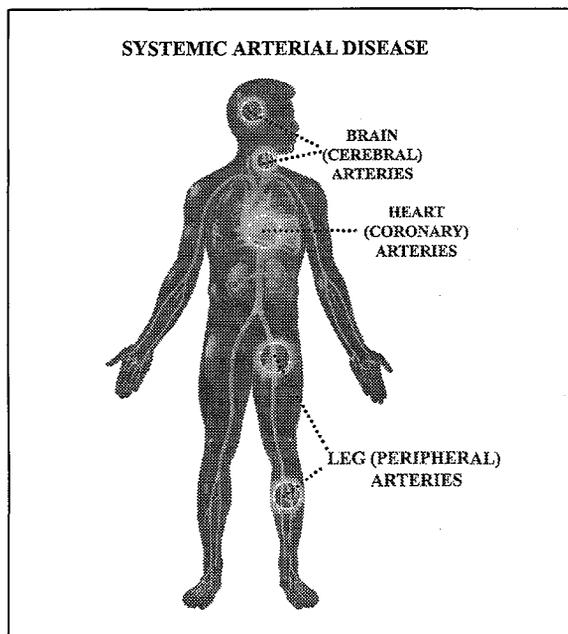
The educational information contained in this letter is offered to supplement your healthcare professional's advice, not replace it. Always follow your healthcare professional's instructions.



# Reducing your risk of a future heart attack or stroke.

Because you're at increased risk of having a future heart attack or stroke, you need to take precautions to help reduce your risk. Talk to your doctor to find out what more you can do to help stay protected. This may include staying on HEART® (timon).

## Why you remain at increased risk of having a future heart attack or stroke.



- If you have had a heart attack, unstable angina, stroke or peripheral arterial disease, you are at increased risk of platelet clotting.
- When platelets stick together and form clots in the arteries, they can reduce or block the flow of oxygen-rich blood to your heart or brain.
- This means you are at increased risk of having either a heart attack or a stroke.
- By helping to keep your blood flowing freely through the arteries, you can help reduce this risk.

That's why you should talk to your doctor about staying on HEART. Continuing to take HEART helps keep platelets from sticking together and forming clots.

PLW1.LDE P12 ZW490

## Who should take HEART® (timon).

HEART is recommended for patients who have:

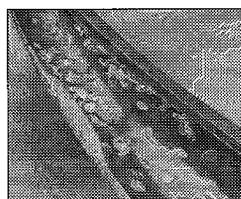
- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as a condition called peripheral arterial disease, or PAD).

HEART is also recommended in addition to aspirin for patients who have:

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack)

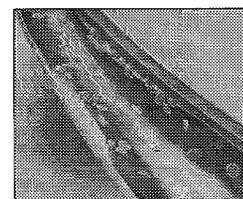
All of these conditions put you at increased risk of having a future heart attack or stroke.

## How HEART works.



Without PLAVIX

Platelets can stick together and form clots.



With PLAVIX

HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to all your doctors about staying on HEART.

## Talk to your doctor about staying on HEART.

Remember, your doctor is the most important source of information regarding your health. So be sure to talk to all of your doctors about any changes in the way you're feeling, as well as what medications you're on. If you have any questions about your current treatment, including why you should stay on HEART, don't hesitate to talk to your doctor.

Please see enclosed Prescribing Information and Important Information on reverse side.

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



## Are you doing all you can to reduce your risk of a future heart attack or stroke?

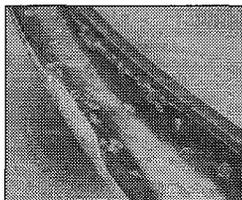
### Feeling better doesn't mean you are fully recovered.

After a month or more of treatment, some people feel they have fully recovered and may stop taking their medication. But you should know that once you're at increased risk of having a future heart attack or stroke, your risk never goes away. So talk to all your doctors about whether you should continue to take HEART® (timon) to help reduce your risk of a future heart attack or stroke.

### How HEART works.



Platelets can stick together and form clots.



HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor about staying on HEART.

### Talk to your doctor about the progress you're making and about staying on HEART® (timon).

It's important to keep an open dialogue with your doctor. Make a list of all the medications you're taking (prescription and over-the-counter) and share it with all of your health-care providers. Always check with your doctor before stopping or starting any prescription or over-the-counter medication, and dietary supplements.

### Here are some questions you may want to ask your doctor:

- Should I continue to take HEART?
- Once I've completed my HEART prescription, will I still be at risk for a future heart attack or stroke?
- What are the benefits of taking HEART?

**Remember, it's important to talk to your doctor about renewing your HEART prescription to continue to help reduce your risk of future heart attack or stroke.**

PLW1.LDE P14 ZW492

**Please see enclosed Prescribing Information and Important Information on reverse side.**

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963

12345678901

March 1, 2008



3767

Dear John Public:

Thank you for filling your prescription for HEART® (timon) at Hometown Pharmacy. As your pharmacy, we are here to help make sure that you have the information you need to help you stay in good health. That's why we want to let you know that our records indicate that your prescription for HEART is about to run out. You should also know that there are no refills left on this prescription.

It's important to know that if you have been hospitalized with heart-related chest pain (unstable angina), or a certain type of heart attack (non—Q—wave heart attack), conditions your doctor may refer to as acute coronary syndrome or ACS, you are at increased risk of having a future heart attack or stroke.

The same is true if you have had a recent heart attack or stroke. One of the things you can do to help reduce your risk is continue to take HEART according to the directions from your doctor. Talk to your doctor about renewing your HEART prescription.

**If your doctor wants you to keep taking HEART, you'll need to get a new prescription now.**

We'd like to share some important information with you about HEART. Please take a moment to look it over. It contains facts that will give you a better understanding of how HEART works. We hope you find it useful.

Again, thank you for choosing Hometown Pharmacy. If you have any questions about your medication, please feel free to call or stop by the pharmacy. We look forward to seeing you soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Turners Falls, MA 01301  
(413) 555-1212

Please see Important Information and enclosed

PLW1.LDE P15 MK3767\_1593\_11\_400\_400 ZW495

**Who should take HEART® (timon)?**

HEART is recommended daily for patients who have:

- had a heart attack
- had a stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease or PAD)

HEART is also recommended in addition to aspirin for patients who have:

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack)

All of these conditions put you at increased risk of having a future heart attack or stroke.

HEART helps reduce this risk.

**Remember to talk to your doctor about renewing your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

69-041024A

B1-H0133

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

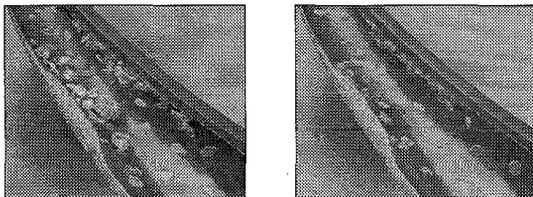
Over Please

## Understanding your condition and the benefits of taking HEART® (timon).

### How blood clots are formed.

Clots are a natural defense mechanism that prevent excessive bleeding. Clots are formed when platelets in your blood stick together. The resulting clot in an artery can reduce or completely stop the flow of blood to important parts of the body like the heart, brain or legs.

### How HEART works:



HEART is proven to help keep platelets in the blood from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor to find out if staying on HEART is right for you.

### Why it's important for you to stay on HEART.

Every day you take HEART, you help stay protected against a future heart attack or stroke. In fact, according to the American Heart Association and the American College of Cardiology, HEART is recommended with aspirin for treatment for up to 9 months after being diagnosed with heart-related chest pain (unstable angina) or a certain type of heart attack (non-ST-segment elevation heart attack, also known as non-Q-wave heart attack). That's why you should talk to your doctor about renewing your HEART prescription before your current one runs out. Remember, you and your doctor are partners in your health care.

### Feeling better doesn't mean you are fully recovered.

After a month or more of treatment, some people may feel they have fully recovered and may stop taking their medication. But you should know that once you're at increased risk of having a future heart attack or stroke, your risk never goes away. So talk to your doctor about whether you should continue to take HEART to help reduce your risk of a future heart attack or stroke.

### Here are some questions you may want to ask your doctor:

- Should I continue to take HEART?
- Once I've completed my HEART prescription, will I still be at risk for a future heart attack or stroke?
- What are the long-term benefits of staying on HEART?

It's important to keep an open dialogue with your doctor. Make a list of all the medications you're taking (prescription and over-the-counter) and share it with all of your health-care providers. Always check with your doctor before stopping or starting any prescription or over-the-counter medication, or dietary supplements.

If you have any questions about taking your medication, please consult your doctor or pharmacist.

**Please see enclosed Prescribing Information and Important Information on reverse side.**

PLW1.LDE P16 ZW496

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963

12345678901

March 1, 2008



3767

Dear John Public:

Thank you for filling your prescription for HEART® (timon) at Hometown Pharmacy. As your pharmacy, we want to do everything we can to help you understand and manage your condition. That's why we'd like to offer you the **Hometown Pharmacy Patient Care Program**.

The **Hometown Pharmacy Patient Care Program** is a complimentary service designed to help you take your medication regularly, as directed by your doctor. This program may include:

- Important information about your condition.
- Tips to help you get the most out of your therapy with HEART.
- Timely updates and reminders regarding the status of your HEART prescription.

Please take a moment to read the information about HEART on the back of this page. If you have any questions about your HEART prescription, we are here for you!

We hope you find the provided information useful. However, if you do not wish to take advantage of the program, please call 1-800-555-1212 and enter **12345678901** when prompted, or check the box on the bottom of the back of this page and return the form in the envelope provided, whichever is most convenient.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

**What you need to know about HEART® (timon).**

- HEART helps reduce your risk of having a future heart attack or stroke, if you have had a recent heart attack, a recent stroke, or established peripheral arterial disease.
- HEART is designed to help keep platelets from sticking together and forming clots. This helps keep your blood flowing and helps reduce your risk of a future heart attack or stroke.
- Even though you may be feeling better, it's important to keep taking your medications, as prescribed by your doctor, including HEART, because you're still at risk.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

69-041024B

B1-D0178C

PLW1.LDE P01 MK3767\_1593\_11\_400\_400 ZW477

Over Please

**Please see Important Information and enclosed Prescribing Information.**

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

If you no longer wish to receive patient education mailings, please call 1-800-555-1212.

## Understanding your condition and the benefits of taking HEART® (timon).

### Who should take HEART?

#### HEART is recommended daily for patients who have:

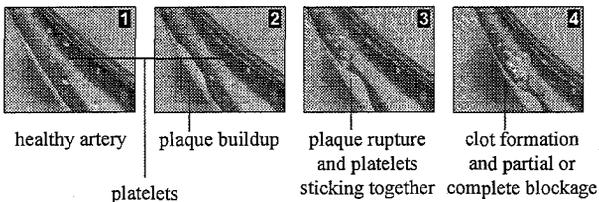
- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

#### HEART is also recommended in addition to aspirin for patients who have:

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack)

All of these conditions put you at increased risk of having a future heart attack or stroke.

### What led to your condition?



The easiest way to understand how your condition developed is to learn about what causes platelet clotting in the arteries. Platelet clots can reduce or completely block the flow of oxygen-rich blood to important parts of your body, like your heart, brain, or legs. Here's how this happens:

1. Healthy arteries are smooth and flexible, allowing oxygen-rich blood to flow through easily.
2. Over time, certain factors can cause fat, including cholesterol, to collect in the arterial walls. The cholesterol thickens and forms plaque, narrowing the arteries.

3. As blood flows through the narrowed artery, the plaque can rupture. This causes platelets in the blood to stick to the damaged area (similar to a scab on the skin) by clumping together and forming a clot (thrombus).
4. A clot can reduce or completely block the flow of blood through an artery. If a clot occurs in an artery that leads to the heart, the result can be unstable angina or a heart attack. If a clot forms in an artery leading to the brain, a stroke can occur. If a clot forms in an artery supplying the leg muscles, the result can be poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest.

### How HEART works.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why it's important to refill your HEART prescription before it runs out.

### How HEART should be taken.

HEART should be taken with or without food, exactly as your doctor has directed you. If you accidentally miss a day, do not double up on your medication, just continue your usual dose. If you have any questions about taking your medications, please consult your doctor or pharmacist. Always check with your doctor before stopping or starting any prescriptions or over-the-counter medications and dietary supplements.

**Please see enclosed Prescribing Information and Important Information on reverse side.**

PLW1.LDE P02 ZW478

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



**NOTE:** Complete this section only if you do NOT wish to participate in the **Hometown Pharmacy Patient Care Program.**

Check the box below, detach, and mail in the envelope provided.

I do not wish to participate in the **Hometown Pharmacy Patient Care Program.**

If you wish to inform us by phone, please call 1-800-555-1212 and enter **12345678901** when prompted.





John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963

12345678901

March 1, 2008



3767

Dear John Public:

Thank you for filling your prescription for HEART® (timon) at Hometown Pharmacy. As your pharmacy, we want to do everything we can to help you understand and manage your condition. That's why we'd like to offer you the **Hometown Pharmacy Patient Care Program**.

The **Hometown Pharmacy Patient Care Program** is a complimentary service designed to help you take your medication regularly, as directed by your doctor. This program may include:

- Important information about your condition.
- Tips to help you get the most out of your therapy with HEART.
- Timely updates and reminders regarding the status of your HEART prescription.

In fact, our records indicate that you are due for a HEART refill on **September 30, 2005. It's quick and easy to have your prescription refilled! Simply call (413) 555-1212 and enter your HEART prescription number: 1234567890** when prompted. Our automated system allows you to quickly place your order without having to speak with a pharmacy associate.

To start, please take a moment to read the information about HEART on the back of this page. If you have any questions about your HEART prescription, we are here for you! If you do not wish to take advantage of this program, check the box located on the back of this page and return the form in the envelope provided, or call the number at the bottom of the back page, whichever is most convenient.

Sincerely  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

Over Please

**What you need to know about HEART® (timon).**

- HEART helps reduce your risk of having a future heart attack or stroke, if you have had a recent heart attack, a recent stroke, or established peripheral arterial disease.
- HEART is designed to help keep platelets from sticking together and forming clots. This helps keep your blood flowing and helps reduce your risk of a future heart attack or stroke.
- Even though you may be feeling better, it's important to keep taking your medications, as prescribed by your doctor, including HEART, because you're still at risk.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

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PLW1.LDE P03 MK3767\_1593\_11\_400\_400 ZW493

**Please see Important Information and enclosed Prescribing Information.**

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

If you no longer wish to receive patient education mailings, please call 1-800-555-1212.

## Understanding your condition and the benefits of taking HEART® (timon).

### Who should take HEART?

#### HEART is recommended for patients who have:

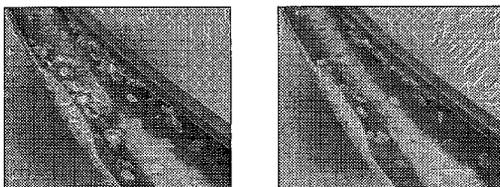
- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

#### HEART is also recommended in addition to aspirin for patients who have:

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack).

All of these conditions put you at increased risk of having a future heart attack or stroke.

### What led to your condition?



The easiest way to understand how your condition developed is to learn about what causes platelet clotting in the arteries. Platelet clots can reduce or completely block the flow of oxygen-rich blood to important parts of your body, like your heart, brain, or legs. Here's how this happens:

1. Healthy arteries are smooth and flexible, allowing oxygen-rich blood to flow through easily.
2. Over time, certain factors can cause fat, including cholesterol, to collect in the arterial walls. The cholesterol thickens and forms plaque, narrowing the arteries.

3. As blood flows through the narrowed artery, the plaque can rupture. This causes platelets in the blood to stick to the damaged area (similar to a scab on the skin) by clumping together and forming a clot (thrombus).
4. A clot can reduce or completely block the flow of blood through an artery. If a clot occurs in an artery that leads to the heart, the result can be unstable angina or a heart attack. If a clot forms in an artery leading to the brain, a stroke can occur. If a clot forms in an artery supplying the leg muscles, the result can be poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest.

### How HEART works.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why it's important to refill your HEART prescription before it runs out.

### How HEART should be taken.

HEART should be taken with or without food, exactly as your doctor has directed you. If you accidentally miss a day, do not double up on your medication, just continue your usual dose. If you have any questions about taking your medications, please consult your doctor or pharmacist. Always check with your doctor before stopping or starting any prescriptions or over-the-counter medications and dietary supplements.

**Please see enclosed Prescribing Information and Important Information on reverse side.**

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.



**NOTE:** Complete this section only if you do NOT wish to participate in the **Hometown Pharmacy Patient Care Program**. Check the box below, detach and mail in the envelope provided.

I do not wish to participate in the **Hometown Pharmacy Patient Care Program**.

If you wish to inform us by phone, please call 1-800-555-1212 and enter 12345678901 when prompted.





John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963

12345678901

March 1, 2008

|||||.....|||||.....|||||.....|||||.....|||||.....

3767

Dear John Public:

We hope this letter finds you in good health. This letter is provided as part of the **Hometown Pharmacy Patient Care Program**, a complimentary service designed to help you take your medication regularly, as directed by your doctor, while also providing you with tips to help you get the most out of your prescription for HEART® (timon).

Remember, your doctor has prescribed HEART to help reduce your risk of a future heart attack or stroke. Part of our commitment to you as your pharmacy is to do everything we can to help make sure you have what you need to stay in good health—and our records show the refill on your HEART prescription is due on **September 30, 2005**.

**It's quick and easy to have your prescription refilled! Simply:**

- Call **(413) 555-1212**
- Enter your HEART prescription number **1234567890** when prompted.

Our automated system allows you to quickly place your refill order, without having to speak with a Pharmacy Associate. If your doctor has changed your prescription, please disregard this letter and follow your doctor's instructions.

Again, thank you for choosing Hometown Pharmacy. If you have any questions about your medication, please feel free to call or stop by the pharmacy. We look forward to seeing you soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

Over Please

**Please see Important Information and enclosed Prescribing Information.**

**Why is HEART® (timon) important?**

You should know that HEART is an important part of your treatment. HEART helps keep platelets from sticking together and forming clots, which helps keep your blood flowing. If you have had a recent heart attack, a recent stroke, or established peripheral arterial disease, HEART can help reduce your risk of a future heart attack or stroke.

**Who should take HEART?**

**HEART is recommended for patients who have:**

- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

**PLAVIX is also recommended in addition to aspirin for patients who have:**

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q-wave heart attack).

All of these conditions put you at increased risk of having a future heart attack or stroke.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

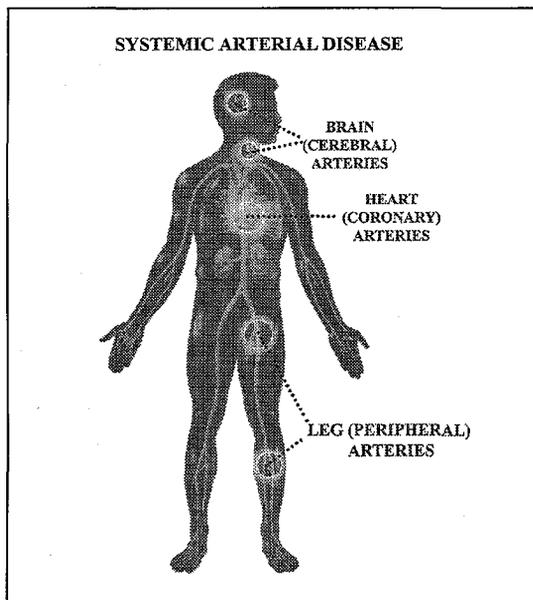
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B1-D0179C

## Understanding your condition.

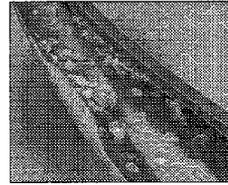
### Why you remain at increased risk of having a future heart attack or stroke.

- If you have had a heart attack, unstable angina, stroke or peripheral arterial disease, you are prone to platelet clotting.
- When platelets stick together and form clots in the arteries, they can reduce or block the flow of oxygen-rich blood to your heart or brain.
- This means you are at increased risk of having either a heart attack or a stroke.
- By helping to keep your blood flowing freely through the arteries, you can help reduce your risk.

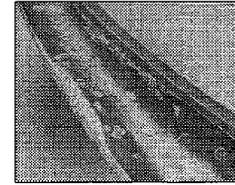


That's why you should talk to all of your doctors about staying on HEART® (timon). HEART helps keep platelets from sticking together and forming clots.

### How HEART® (timon) works.



Platelets can stick together and form clots.



HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor about staying on HEART.

### Other ways you can help protect yourself.

There are many things you can do to help reduce the risk of having a future heart attack or stroke. Taking HEART as prescribed by your doctor is one of them. There are additional risk factors you'll want to watch out for. They include:

- unhealthy diet
- high blood pressure
- smoking
- high cholesterol
- alcohol consumption
- being overweight

Be sure to talk to your doctor to make sure you're doing all you can to help reduce your risk of having a future heart attack or stroke. Naturally, this includes taking all your medications, including HEART, as prescribed. If you have any questions about taking your medication, please consult your doctor or pharmacist.

PLW1.LDE P02 ZW480

**Please see Prescribing Information and enclosed Important Information on reverse side.**

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## Doing more to help prevent a future heart attack or stroke.

### Making lifestyle changes.

Because you're at increased risk of having a future heart attack or stroke, it is important to make certain lifestyle changes that can help you reduce that risk. Your doctor can tell you what changes would work the best for you, but here are some suggestions:

- Quit smoking—Smoking narrows and damages your blood vessels, which increases your risk of heart attack and stroke.
- Eat healthier foods—A diet that's low in saturated fat, sodium, and cholesterol can make a big difference in your health.
- Keep your blood pressure under control.
- Depending on your condition, some form of rehabilitation might be necessary. Talk to your doctor to find out if you would benefit from a rehabilitation program.
- Continue to take HEART<sup>®</sup> (timon) and other medications, as prescribed by your doctor.

### Coping with changes in your life.

When you have a condition that increases your risk of a future heart attack or stroke, some of the changes that take place may not be ones that you choose. It's important to understand that these changes are related to your condition. So talk to your doctor about what you can do to help manage them.

### They may include:

- Feelings such as anxiety, depression, anger, frustration, and/or fear.
- Problems with intimacy.
- A shift in parent/child relationships.

Just as you need time to adjust to your condition, your family and friends need time to adjust too. If you're having a hard time dealing with different emotions, talk to your doctor about counseling or support groups available in your area.

### Taking your medications.

Continuing to take HEART and all your medications exactly as prescribed by your doctor(s) is an important and positive way to help reduce your risk of a future heart attack or stroke. Always check with your doctor before stopping or starting any prescription or over-the-counter medication, and any dietary supplements.

Even though you may be feeling better, it's important to keep taking your medications, including HEART, as prescribed by your physician to increase your protection against a future heart attack or stroke.

PLW1.LDE P04 ZW482

**Please see enclosed Prescribing Information and Important Information on reverse side.**

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## Building a support network.

### Whom should you include in your support network?

Staying on a healthier path means doing more to take care of yourself and helping to protect yourself from a future heart attack or stroke. But you don't have to do it all alone. Many people in your life can help you stay protected. For example:

- Family
- Friends
- Neighbors
- Doctors
- Coworkers
- Local support groups
- Pharmacists
- Church or religious counselors.

One of the primary members of your support network is, of course, your doctor. That's why it's so important to partner with your doctor. Talk to your doctor about how you're feeling, ask questions, and discuss the progress you're making—good or bad—so your doctor can give you the best treatment possible. You should be comfortable about asking your doctor any questions you have regarding your condition, including whether you should renew your HEART® (timon) prescription before your current one runs out.

### The hardest part about getting help is knowing how to ask for it.

Some people have a hard time admitting they need help. But there's no reason to feel that way. In fact, it's very important to let the people in your life help you stay protected from a future heart attack or stroke, especially after you're feeling better. The more support you have, the more likely you'll be to continue making healthy choices that will help you reduce your risk of a future heart attack or stroke.

### Tips on getting the support you need.

Explain to the members of your support network when:

- you need emotional support
- you need physical support
- you want some personal space
- you want some company
- you want to do something for yourself
- you want help doing something.

### Where else can you find help?

#### American Heart Association

1-800-AHA-USA-1, [www.americanheart.org](http://www.americanheart.org)

#### Mended Hearts

1-888-HEART99, [www.mendedhearts.org](http://www.mendedhearts.org)

#### American Stroke Association

1-888-4-STROKE, [www.strokeassociation.org](http://www.strokeassociation.org)

#### National Stroke Association

1-800-STROKES, [www.stroke.org](http://www.stroke.org)

#### Vascular Disease Foundation

1-866-PADINFO, [www.VDF.org](http://www.VDF.org)

PLW1.LDE P06 ZW484

Please see enclosed Prescribing Information and Important Information on reverse side.

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John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963  
|||.....|||..|||..|||.....|||..|||.....|||..|||

12345678901

March 1, 2008

3767

Dear John Public:

We want to thank you for filling your prescription for HEART® (timon) at Hometown Pharmacy and to let you know that our records show that the refill on your current HEART prescription is due on **September 30, 2005**.

**It's quick and easy to have your prescription refilled! Simply:**

- Call (413) 555-1212
- Enter your HEART prescription number **1234567890** when prompted.

Our automated system allows you to quickly place your refill order, without having to speak with a Pharmacy Associate.

Your doctor prescribed HEART to help reduce your risk of a future heart attack or stroke. Be sure to talk to all your doctors about staying on HEART to help reduce this risk.

Part of our commitment as your pharmacy is to provide you with information to help you stay in good health. This letter is provided as part of the **Hometown Pharmacy Patient Care Program**, a complimentary service designed to help you take your medication regularly, as directed by your doctor, while also providing you with tips to help you get the most out of your prescription for HEART. We hope you find the information provided useful.

Even though you may still have some refills left on your prescription, talk to your doctor about the progress you're making with HEART and to find out about continuing on HEART.

If your doctor has changed your prescription, please disregard this letter and follow your doctor's instructions.

We wish you good health and look forward to seeing you very soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

**Who should take HEART® (timon)?**

**HEART is recommended for patients who have:**

- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as peripheral arterial disease, or PAD).

**HEART is also recommended in addition to aspirin for patients who have:**

- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack).

All of these conditions put you at increased risk of having a future heart attack or stroke.

**Be sure to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

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B1-D0189C

PLW1.LDE P07 MK3767\_1593\_11\_400\_400 ZW485

Over Please

**Please see Important Information and enclosed Prescribing Information.**

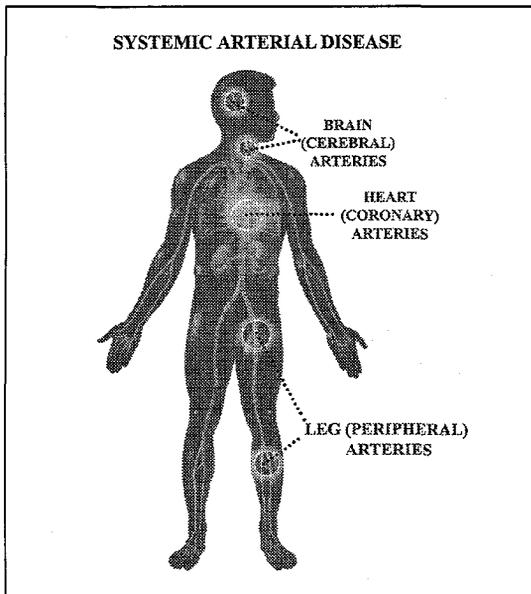
If you no longer wish to receive patient education mailings, please call 1-800-555-1212.

## Understanding your condition.

### Why HEART® (timon) is important.

Because you're at increased risk of having a heart attack or stroke, you should know that HEART is an important part of your treatment. Continuing to take HEART can help reduce your risk of a future heart attack or stroke.

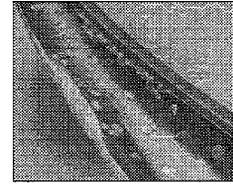
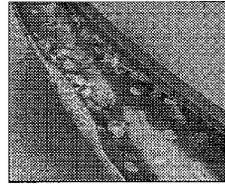
### Why you remain at increased risk of having a future heart attack or stroke.



- If you have had a heart attack or stroke or have unstable angina or peripheral arterial disease (PAD), you are prone to platelet clotting.
- When platelets stick together and form clots in the arteries, they can reduce or block the flow of oxygen-rich blood to your heart or brain.
- This means you are at increased risk of having either a heart attack or a stroke.
- By helping to keep your blood flowing freely through the arteries, you can help reduce your risk.

It's important for you to talk to your doctor about staying on HEART.

### How HEART works.



Platelets can stick together and form clots.

HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor about renewing your HEART prescription before your current one runs out.

### Other ways you can help protect yourself.

There are many things you can do to reduce the risk of having a future heart attack or stroke. Taking HEART as prescribed by your doctor is one of them. There are additional risk factors you'll want to watch out for. They include:

- unhealthy diet
- smoking
- alcohol consumption
- high blood pressure
- high cholesterol
- being overweight

Talk to your doctor to make sure you're doing all you can to help reduce your risk of having a future heart attack or stroke. Naturally, this includes taking all your medications, including HEART, as prescribed.

PLW1.LDE P08 ZW486

Please see enclosed Prescribing Information and Important Information on reverse side.

Funding for this program is provided by Pharma, the maker of HEART. The confidentiality of your personal information is important to us. No individually identifiable information about you, your medication or health condition has been or will be shared with the supporters of this program.

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## Are you doing all you can to help reduce your risk of a future heart attack or stroke?

### Discuss your progress and how you're feeling with your doctor.

If you have had a recent heart attack, a recent stroke, or established peripheral arterial disease, you are at increased risk of having a future heart attack or stroke. Getting the right information can make a big difference in your recovery or ongoing treatment. So be sure to keep your doctor informed about any changes in the way you're feeling or concerns you may have about your current treatment. Remember, HEART® (timon) starts working soon after you start taking it, and it will help protect you from a future heart attack or stroke. Your doctor is crucial to figuring out what's right for you—including why it's important to stay on HEART.

### Here are some questions to ask your doctor.

- Should I continue to take HEART?
- Once I've completed my HEART prescription, will I still be at risk for a future heart attack or stroke?
- What are the benefits of staying on HEART?

### How long should you stay on HEART?

HEART helps you stay protected against a future heart attack or stroke. That's why you should talk to your doctor about renewing your HEART prescription. Only your doctor can tell you if staying on HEART is right for you.

### Taking an active role in your health care.

If you make certain lifestyle changes, you can help reduce your risk of having a future heart attack or stroke. Your doctor can tell you what changes would work best for you. In the meantime, here are some suggestions:

- Quit smoking—Smoking narrows and damages your blood vessels, which increases your risk of heart attack and stroke.
- Eat healthier foods—A diet that's low in saturated fat, sodium, and cholesterol can make a big difference in your health.
- Keep your blood pressure under control.
- Depending on your condition, some form of rehabilitation might be necessary. Talk to your doctor to find out if you would benefit from a rehabilitation program.
- Continue to take HEART and other medications, as prescribed by your doctor.

PLW1.LDE P10 ZW488

**Please see enclosed Prescribing Information and Important Information on reverse side.**

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John Public  
10 Mowhawk Trail  
Turners Falls, MA 01376-1963

12345678901

March 1, 2008



3767

Dear John Public:

We hope all is going well with you and that you're in good health. We at Hometown Pharmacy want to do what we can to help you get the most out of your HEART® (chemical name) prescription. That's why we want you to know that, according to our records, your prescription for HEART was due on **September 30, 2005**. So we urge you to come in or call to refill your prescription as soon as possible.

**It's quick and easy to have your prescription refilled! Simply:**

- Call **(413) 555-1212**
- Enter your HEART prescription number **1234567890** when prompted.

Our automated system allows you to quickly place your refill order, without having to speak with a Pharmacy Associate.

This letter is provided as part of the **Hometown Pharmacy Patient Care Program**, a complimentary service designed to help you take your medication regularly, as directed by your doctor, while also providing you with tips to help you get the most out of your prescription for HEART. We hope you find the information provided useful.

It's important to remember that if you have had a recent heart attack, a recent stroke, or established peripheral arterial disease, you're at increased risk of having a future heart attack or stroke. To help you reduce this risk, your doctor prescribed HEART. So it's important for you to talk to all your doctors about what you can do to help reduce your risk of a future heart attack or stroke.

If your doctor has changed your prescription, or if you have already had this prescription filled, please disregard this letter.

Of course, if you have any questions about your medication, please feel free to call or stop by the pharmacy. Thank you for choosing Hometown Pharmacy. We look forward to seeing you soon.

Sincerely,  
Valmore Dion, Pharmacist  
Hometown Plaza, 1000 West School St.  
Greenfield, MA 01301  
(413) 555-1212

**The importance of staying on HEART® (timon).**

**Feeling better doesn't mean you're not at risk.**

Sometimes people think that after a month or so of treating their recent heart attack, recent stroke, or established peripheral arterial disease, they're no longer at risk of a future heart attack or stroke. However, no matter how good you may feel, it's important to remember that:

- you remain at increased risk of having a future heart attack or stroke
- HEART, as your doctor prescribes, helps you reduce this risk.

**Remember to refill your HEART prescription.**

**Important Information:** If you have a medical condition that causes bleeding, such as stomach ulcer, you shouldn't use HEART. The risk of bleeding may increase with HEART, and when you take HEART with certain other medicines, including aspirin. Review your medicines with your doctor to minimize this risk. Additional rare but serious side effects could occur.

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Over Please

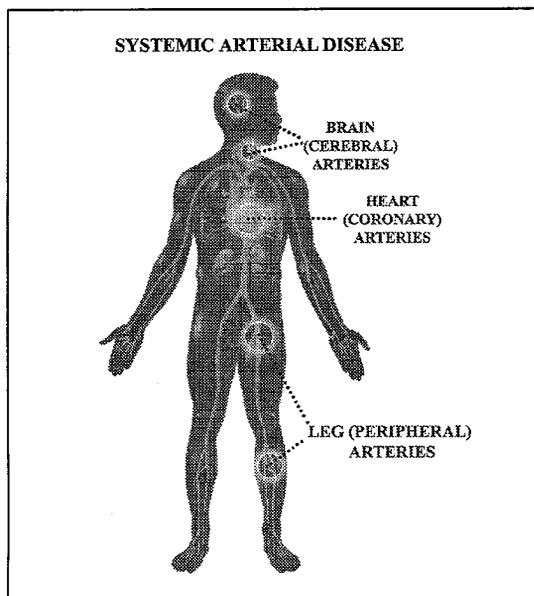
**Please see Important Information and enclosed Prescribing Information.**

If you no longer wish to receive patient education mailings, please call 1-800-555-1212.

## Reducing your risk of a future heart attack or stroke.

Because you're at increased risk of having a future heart attack or stroke, you need to take precautions to help reduce your risk. Talk to your doctor to find out what more you can do to help stay protected. This may include staying on HEART® (timon).

### Why you remain at increased risk of having a future heart attack or stroke.



- If you have had a heart attack, unstable angina, stroke or peripheral arterial disease, you are at increased risk of platelet clotting.
- When platelets stick together and form clots in the arteries, they can reduce or block the flow of oxygen-rich blood to your heart or brain.
- This means you are at increased risk of having either a heart attack or a stroke.
- By helping to keep your blood flowing freely through the arteries, you can help reduce this risk.

That's why you should talk to your doctor about staying on HEART. Continuing to take HEART helps keep platelets from sticking together and forming clots.

PLW1.LDE P12 ZW490

### Who should take HEART® (timon).

HEART is recommended for patients who have:

- had a recent heart attack
- had a recent stroke
- poor circulation in the legs that may cause pain during exercise, such as walking, and may be relieved by rest (known as a condition called peripheral arterial disease, or PAD).

HEART is also recommended in addition to aspirin for patients who have:

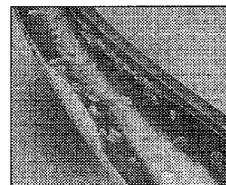
- had heart-related chest pain (unstable angina)
- had a certain type of heart attack (non—Q—wave heart attack)

All of these conditions put you at increased risk of having a future heart attack or stroke.

### How HEART works.



Without PLAVIX



With PLAVIX

Platelets can stick together and form clots.

HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to all your doctors about staying on HEART.

### Talk to your doctor about staying on HEART.

Remember, your doctor is the most important source of information regarding your health. So be sure to talk to all of your doctors about any changes in the way you're feeling, as well as what medications you're on. If you have any questions about your current treatment, including why you should stay on HEART, don't hesitate to talk to your doctor.

Please see enclosed Prescribing Information and Important Information on reverse side.

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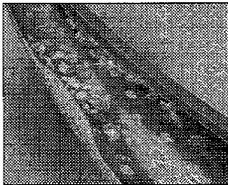


## Are you doing all you can to reduce your risk of a future heart attack or stroke?

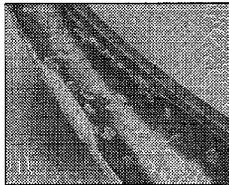
### Feeling better doesn't mean you are fully recovered.

After a month or more of treatment, some people feel they have fully recovered and may stop taking their medication. But you should know that once you're at increased risk of having a future heart attack or stroke, your risk never goes away. So talk to all your doctors about whether you should continue to take HEART® (timon) to help reduce your risk of a future heart attack or stroke.

### How HEART works.



Platelets can stick together and form clots.



HEART helps keep platelets from sticking together.

HEART is proven to help keep platelets from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor about staying on HEART.

### Talk to your doctor about the progress you're making and about staying on HEART® (timon).

It's important to keep an open dialogue with your doctor. Make a list of all the medications you're taking (prescription and over-the-counter) and share it with all of your health-care providers. Always check with your doctor before stopping or starting any prescription or over-the-counter medication, and dietary supplements.

### Here are some questions you may want to ask your doctor:

- Should I continue to take HEART?
- Once I've completed my HEART prescription, will I still be at risk for a future heart attack or stroke?
- What are the benefits of taking HEART?

**Remember, it's important to talk to your doctor about renewing your HEART prescription to continue to help reduce your risk of future heart attack or stroke.**

PLW1.LDE P14 ZW492

**Please see enclosed Prescribing Information and Important Information on reverse side.**

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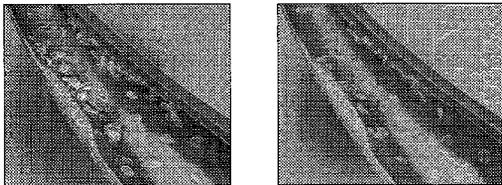


## Understanding your condition and the benefits of taking HEART® (timon).

### How blood clots are formed.

Clots are a natural defense mechanism that prevent excessive bleeding. Clots are formed when platelets in your blood stick together. The resulting clot in an artery can reduce or completely stop the flow of blood to important parts of the body like the heart, brain or legs.

### How HEART works:



HEART is proven to help keep platelets in the blood from sticking together and forming clots, which helps keep your blood flowing. This, in turn, helps protect you from a future heart attack or stroke. That's why you should talk to your doctor to find out if staying on HEART is right for you.

### Why it's important for you to stay on HEART.

Every day you take HEART, you help stay protected against a future heart attack or stroke. In fact, according to the American Heart Association and the American College of Cardiology, HEART is recommended with aspirin for treatment for up to 9 months after being diagnosed with heart-related chest pain (unstable angina) or a certain type of heart attack (non-ST-segment elevation heart attack, also known as non-Q-wave heart attack). That's why you should talk to your doctor about renewing your HEART prescription before your current one runs out. Remember, you and your doctor are partners in your health care.

### Feeling better doesn't mean you are fully recovered.

After a month or more of treatment, some people may feel they have fully recovered and may stop taking their medication. But you should know that once you're at increased risk of having a future heart attack or stroke, your risk never goes away. So talk to your doctor about whether you should continue to take HEART to help reduce your risk of a future heart attack or stroke.

### Here are some questions you may want to ask your doctor:

- Should I continue to take HEART?
- Once I've completed my HEART prescription, will I still be at risk for a future heart attack or stroke?
- What are the long-term benefits of staying on HEART?

It's important to keep an open dialogue with your doctor. Make a list of all the medications you're taking (prescription and over-the-counter) and share it with all of your health-care providers. Always check with your doctor before stopping or starting any prescription or over-the-counter medication, or dietary supplements.

If you have any questions about taking your medication, please consult your doctor or pharmacist.

**Please see enclosed Prescribing Information and Important Information on reverse side.**

PLW1.LDE P16 ZW496

The educational information contained in this letter is offered to supplement your healthcare professional's advice, not to replace it. Always follow your healthcare professional's instructions.

Adheris Testimony -- Board of Pharmacy meeting -- 4/11/08

I am Dan Rubin, the CEO of Adheris, and I am appreciative of the opportunity to provide comment in support of Senate Bill 1096.

Adheris partners with retail pharmacies to help them run educational programs that inform patients about the medications that their doctors have prescribed and to encourage them to maintain the course of therapy that their doctor has selected. The communications provided to patients are always reviewed and approved by the pharmacist prior to being sent.

Let me say at the outset that SB1096 is not about marketing or switching drugs. It is about supporting the prescription as written by the doctor and helping patients understand their medications and how to take them. This bill specifically prohibits marketing or switching patients to a different therapy.

There are several points that I hope you will keep in mind as you evaluate SB 1096:

First, a large proportion of patients -- at least half -- do not take their medications as prescribed by their physicians, which leads to poor health outcomes for the patient and unnecessary medical expenses for the health care system. There is a large body of evidence testifying to the breadth, depth and consequences of the problem of poor patient adherence to therapy.

Second, the management of chronic health conditions is a major challenge today, and it is critically important to provide reinforcement and education not just at the point of diagnosis or dispensing, but on an ongoing basis. Patients often live with their conditions for months or years, and providing timely reinforcement and education has been proven to lead to better health outcomes.

Third, programs which provide education and reminder messaging about prescribed therapy are defined as treatment by the federal HIPAA guidelines, and with the sole exception of CA, these programs are offered for several dozen medications in 49 states – but only a handful of products are supported in CA today. The list of programs that are not being offered to CA citizens include programs for a wide range of conditions that include diabetes, asthma, hypertension, high cholesterol, cancer, stroke prevention, epilepsy, multiple sclerosis, osteoporosis, COPD, and glaucoma. SB 1096 would allow Californians to receive valuable information about their medications, leading to better health outcomes.

Fourth, CA law already allows health care providers and their contractors or using HIPAA terms, business associates, to use a patient's medical information to "provide health care services to the patient". The central objective of Senate Bill 1096 is to make it clear that a "written communication mailed to a patient by a pharmacy about a drug that the patient has already been prescribed shall be deemed as a "health care service".

Fifth, beyond the fact that SB 1096 would only allow communications about a prescription medication that has already been prescribed by a licensed health care professional, these communications would only be permitted if a number of other requirements are met, including the assurance that no other pharmaceutical products are mentioned in the communication (i.e. no marketing or promotion of drug switching), that the information is accurate, balanced and consistent with the FDA approved product labeling, that the privacy and confidentiality of the patient's health information is protected, that convenient opt out mechanisms are prominently displayed on the communication, and that there is clear disclosure if there is any sponsorship by a third party. While all of these provisions are included in SB 1096, I would like to emphasize that there is nothing in this bill that extends in any way the circumstances under which a patient's information can be disclosed to any other party.

Finally, we know that a number of parties have offered the view that these types of communication programs could interfere with the patient – physician relationship. We could not disagree more strongly, since the messaging that SB 1096 would allow only pertains to a medication that has already been prescribed by the physician and dispensed by the pharmacist. SB 1096 would not allow the mention of any other prescription products. We recognize and accept that physicians sometimes change a patient's drug regimen, and as a practice, Adheris programs routinely includes a statement that the patient should follow the direction of their doctor if they have any questions or their medication has been changed. We would be very receptive to an amendment that all communications should include language to that effect .

I thank you for your attention and hope that you will join the numerous organizations which have supported this bill, which include:

- National Consumers League
- Mental Health Association in CA
- Alliance for Better Medicine
- National Association of Cancer Patients
- Charles Drew University of Medicine and Science
- Los Angeles Society of Allergy, Asthma, and Clinical Immunology

to name a few.

Thank you again for your time.

# Pharmacist Intervention to Improve Medication Adherence in Heart Failure

## A Randomized Trial

Michael D. Murray, PharmD, MPH; James Young, PharmD; Shawn Hoke, BA; Wanzhu Tu, PhD; Michael Weiner, MD, MPH; Daniel Morrow, PhD; Kevin T. Stroupe, PhD; Jingwei Wu, MS; Daniel Clark, PhD; Faye Smith, MA; Irimina Gradus-Pizlo, MD; Morris Weinberger, PhD; and D. Craig Brater, MD

**Background:** Patients with heart failure who take several prescription medications sometimes have poor adherence to their treatment regimens. Few interventions designed to improve adherence to therapy have been rigorously tested.

**Objective:** To determine whether a pharmacist intervention improves medication adherence and health outcomes compared with usual care for low-income patients with heart failure.

**Design:** Randomized, controlled trial conducted from February 2001 to June 2004.

**Setting:** University-affiliated, inner-city, ambulatory care practice.

**Patients:** 314 low-income patients 50 years of age or older with heart failure confirmed by their primary care physician.

**Intervention:** Patients were randomly assigned to intervention (39% [ $n = 122$ ]) or usual care (61% [ $n = 192$ ]) groups and were followed for 12 months. A pharmacist provided a 9-month multi-level intervention, with a 3-month poststudy phase. An interdisciplinary team of investigators designed the intervention to support medication management by patients who have low health literacy and limited resources.

**Measurements:** Primary outcomes were adherence, as measured by using electronic prescription monitors, and exacerbations requiring emergency department care or hospital admission. Secondary outcomes included health-related quality of life, patient satisfaction with pharmacy services, and total direct costs.

**Results:** During the 9-month intervention period, medication adherence was 67.9% and 78.8% in the usual care and intervention

groups, respectively (difference, 10.9 percentage points [95% CI, 5.0 to 16.7 percentage points]). However, these salutary effects dissipated in the 3-month postintervention follow-up period, in which adherence was 66.7% and 70.6%, respectively (difference, 3.9 percentage points [CI, -5.9 to 6.5 percentage points]). Medications were taken on schedule 47.2% of the time in the usual care group and 53.1% of the time in the intervention group (difference, 5.9 percentage points [CI, 0.4 to 11.5 percentage points]), but this effect also dissipated at the end of the intervention (48.9% vs. 48.6%, respectively; difference, 0.3 percentage point [CI, -5.9 to 6.5 percentage points]). Emergency department visits and hospital admissions were 19.4% less (incidence rate ratio, 0.82 [CI, 0.73 to 0.93]) and annual direct health care costs were lower (\$-2960 [CI, \$-7603 to \$1338]) in the intervention group.

**Limitations:** Because electronic monitors were used to ascertain adherence, patients were not permitted to use medication container adherence aids. The intervention involved 1 pharmacist and a single study site that served a large, indigent, inner-city population of patients. Because the intervention had several components, intervention effects could not be attributed to a single component.

**Conclusions:** A pharmacist intervention for outpatients with heart failure can improve adherence to cardiovascular medications and decrease health care use and costs, but the benefit probably requires constant intervention because the effect dissipates when the intervention ceases.

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In the United States, 5 million people have heart failure, with total health care costs exceeding \$29 billion (1). These costs are largely derived from expensive exacerbations that require emergency visits and hospitalizations (1, 2). Regularly administered cardiovascular medications may preserve cardiac function, improve quality of life, and reduce risk for costly exacerbations. However, patients sometimes do not adhere to prescribed instructions and have poor outcomes (3-5). Researchers have estimated that approximately 50% of patients with chronic illnesses do not take their medications as prescribed (6). Reasons for non-adherence include lack of patient knowledge, skills, and support to appropriately self-manage complicated medication regimens (7, 8).

Although chronic disease management programs abound, few studies have rigorously tested interventions aimed at improving patient adherence to prescribed medications and their effect on health outcomes (9, 10). We con-

ducted a randomized clinical trial to assess the effect of a pharmacist intervention on patients who are socioeconomically disadvantaged and medically vulnerable. We hypothesized that the intervention would improve adherence to heart failure medications, reduce exacerbations requiring emergency department visits or hospitalization, improve disease-specific quality of life, increase patient satisfaction, and reduce health care costs.

See also:

### Print

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### Web-Only

Appendix Tables

Conversion of figure and tables into slides

## METHODS

### Design Overview

The methods for our randomized trial are described elsewhere (11–13). We recruited patients from the general medicine and cardiology practices of Wishard Health Services, Indianapolis, Indiana, which serves socioeconomically disadvantaged and medically vulnerable patients. The study was conducted from February 2001 to June 2004. Patients took part in the study for 12 months and received 9 months of active intervention by the pharmacist or usual care followed by 3 months of postintervention assessment. Patients in the usual care and intervention groups visited the same pharmacy location, but the intervention pharmacist was instructed to have no contact with patients in the usual care group. The institutional review boards of Indiana University–Purdue University and the University of North Carolina at Chapel Hill approved this study.

### Setting and Patients

Indiana University Medical Group, Indianapolis, is an academic primary care group practice composed of primary and specialty care clinics affiliated with Wishard Health Services. Faculty physicians, residents, and nurse practitioners provide care to 13 000 adults (mean age, 57 years [SD, 15]; 60% women; 50% African American). Annually, these patients make approximately 50 000 visits to practices, 72 000 visits to emergency departments, and 135 000 visits to pharmacies and have 16 000 hospitalizations. We recruited patients from 4 identical general medicine practices, 1 cardiology practice, and Wishard Memorial Hospital. Practices met in half-day sessions per week that were attended by 2 or 3 faculty members and 3 to 5 residents or fellows from each practice. Faculty physicians practiced 1 to 5 half-days per week, whereas fellows practiced 1 to 2 half-days per week and residents attended the practice 1 half-day per week.

Outpatients of Wishard Health Services fill their prescriptions at central or decentralized outpatient pharmacies located at the ambulatory care center or at 1 of several satellite pharmacies stationed at neighborhood clinics. Fully stocked decentralized pharmacies serviced all study patients. From February 2001 to January 2003, the study pharmacy was located in a building adjacent to the ambulatory care center. From February 2003 to June 2004, the study pharmacy was moved to a space adjacent to the general medicine practices in the ambulatory care center. Two pharmacists and 1 technician were stationed at the pharmacy. The study pharmacist was instructed to service patients in the intervention group only, and a second pharmacist serviced patients in the usual care group and filled prescriptions to be delivered to patients at outlying clinics. The technician filled prescriptions and read electronic adherence monitors.

Weekly lists of eligible patients were created by using the Regenstrief Medical Record System (Regenstrief Institute, Indianapolis, Indiana) (14, 15). We invited clinically

### Context

Patients sometimes have difficulty following complicated treatment regimens.

### Contribution

In this trial, 314 low-income patients with congestive heart failure were randomly assigned to a pharmacist intervention or usual care. The pharmacist assessed patient knowledge and provided instructions about medication use. During the 9-month intervention, patients in the intervention group had greater medication adherence than patients in the usual care group (79% vs. 68%). These differences dissipated within 3 months of stopping the intervention. Patients in the intervention group also had fewer exacerbations resulting in emergency department visits or hospitalizations than patients in the usual care group.

### Implication

Ongoing educational intervention by a pharmacist can improve medication adherence and outcomes in patients with heart failure.

—The Editors

stable patients from general internal medicine practices, a cardiology clinic, and Wishard Memorial Hospital (at discharge) to participate in the study. Of 3034 patients with a diagnosis of heart failure, 1512 met criteria for enrollment. Patients were eligible if they were 50 years of age or older; planned to receive all of their care, including prescribed medications, at Wishard Health Services; had a diagnosis of heart failure confirmed by their primary care physician; regularly used at least 1 cardiovascular medication for heart failure (angiotensin-converting enzyme [ACE] inhibitor or angiotensin-receptor blocker,  $\beta$ -adrenergic antagonist, diuretic, digoxin, or aldosterone antagonist); were not using or were not planning to use a medication container adherence aid (for example, a pill box); had access to a working telephone; and could hear within the range of normal conversation. We excluded patients with dementia. Patients received their prescription medications through state and local assistance plans at no cost. Thus, cost of medicines was not a deterrent to adherence.

### Randomization

A trained interviewer conducted a baseline interview at enrollment. Interviewers were blinded to patients' study status and played no role in the delivery of the intervention. Interviewers contacted a centralized data manager at the end of each interview to determine the patient's study assignment, which was otherwise concealed. We randomly assigned patients, without blocking or stratification, to receive the pharmacy intervention or usual care by using a univariate discrete distribution from the IMSL Fortran library's subroutine RNGDA pseudorandom number gener-

ator (Absoft Corp., Rochester Hills, Michigan) (16). We randomly assigned more patients to the usual care group so that this group could also be a prospective cohort for studying risk factors associated with the clinical deterioration of heart failure. Of the 314 patients included in the study, 229 were recruited from the general internal medicine practices, 15 from the cardiology clinic, and 70 on discharge from the Wishard Memorial Hospital. The numbers of patients assigned to the intervention and usual care groups did not differ by recruitment site ( $P = 0.83$ ).

### Intervention

A pharmacist delivered the intervention by using a protocol (Appendix Table 1, available at [www.annals.org](http://www.annals.org)) that included a baseline medication history of all prescription and over-the-counter drugs and dietary supplements taken by patients, which patients brought with them to the baseline interview, and the results of an assessment of patient medication knowledge and skills (7, 8). The pharmacist dispensed enough of the patient's medications to last approximately 2 months.

When medications were dispensed, the pharmacist provided patient-centered verbal instructions and written materials about the medications (11, 13, 17) by using a schema for instruction that has been tested (18, 19). We assigned each medication category an icon (for example, the icon for ACE inhibitors was a red ace of hearts). The same icon appeared on the container label and lid and on the written patient instructions. Written instructions were aimed at patients with low health literacy and contained an easy-to-follow timeline to remind patients when to take their medications (13).

The pharmacist monitored patients' medication use, health care encounters, body weight, and other relevant data by using a study database (20, 21). Information about patients was communicated as needed to clinic nurses and primary care physicians by face-to-face visits, telephone, paging (physician only), and e-mail (physician only). Technicians supported the pharmacist's dispensing efforts within the pharmacy throughout the study. We incorporated costs therein into the economic analysis. Pharmacists serviced patients in the usual care group who were not associated with the intervention or the study.

An interdisciplinary team of investigators that included pharmacists with advanced training in patient education and cardiovascular pharmacotherapy, a geriatrician, a cardiologist with expertise in heart failure, a behavioral scientist, and a cognitive psychologist trained the intervention pharmacist. The intervention pharmacist also studied guidelines for treating heart failure (22), key concepts in the pharmaceutical care of older adults, communication techniques, and the pharmacotherapy of the cardiovascular drugs for heart failure. All pharmacists at Wishard Health Services were aware of the study and were instructed on

how to handle and redirect intervention patients who inadvertently arrived at their pharmacy.

### Usual Care

Patients in the usual care group were aware of the purpose of the study, and their primary care physicians approved their participation. They received their prescription services from pharmacists who rotated through the study pharmacy. These pharmacists had not received the specialized training provided by the interdisciplinary team to the intervention pharmacist and did not have access to the patient-centered study materials. Aside from an initial medication history taken by the intervention pharmacist before randomization, patients in the usual care group were to have no further contact with the intervention pharmacist. Nonetheless, during the busiest times, patients in the intervention and usual care groups may have been in the pharmacy at the same time.

### Outcomes and Measurements

The primary study outcomes were medication adherence tracked by using electronic monitors and clinical exacerbations that required visits to the emergency department or hospitalization. Medication adherence was assessed by electronic monitoring using Medication Event Monitoring System (MEMS) V prescription container lids (AARDEX Ltd., Zug, Switzerland). All prescribed cardiovascular medications were dispensed with MEMS lids that recorded the time and date of each opening and closing onto a digital chip. The same icon was used on the container body and lid to ensure that patients placed the lid on the correct prescription container throughout the study. We used data retrieved from the lids to compute taking adherence and scheduling adherence. Taking adherence is the percentage of prescribed medication taken and measures deviation from the physician's prescription. Scheduling adherence measures the day-to-day deviation in the timing of administration. A medication prescribed for once-daily administration would need to be administered within 2.4 hours of the previous dose (usually taken the preceding day), whereas medications prescribed for twice-daily administration would need to be administered within 1.2 hours of the previous dose (usually taken the preceding day or the same day). Scheduling adherence, as we computed it, measures the reliability or consistency of dosing over time (23, 24).

We measured refill adherence as the medication possession ratio (supplies of medications received relative to amount prescribed) by using prescription records from the Regenstrief Medical Record System (25, 26). We computed results for 1 year, incorporating the 9-month intervention period and the 3-month postintervention period. Because the calculation of refill adherence requires at least 2 refills and patients came for refills at approximately 2-month intervals, we could not compute the refill adherence for the 3-month postintervention period separately. Considering the carry-over effect (to the next refill) of the

intervention that stopped at 9 months, the intervention effect on medication supplies would extend to 11 to 12 months. Hence, we believe that the 12-month period adequately reflects the effect of the intervention. We determined self-reported adherence for the previous month at baseline and 9 months by using validated questionnaires (27, 28). Using these questionnaire scores, we computed a composite score of self-reported adherence (30).

We assessed exacerbations by using hospital admission data from emergency department visits. We extracted data for heart failure-specific, all cardiovascular, and all-cause reasons for emergency visits and hospitalizations; these were adjudicated by a registered nurse abstractor who used a previously validated method (30), from the Regenstrief Medical Record System.

Secondary outcomes included health-related quality of life, satisfaction with pharmacy services, and total direct health care costs. We analyzed disease-specific quality of life by using the Chronic Heart Failure Questionnaire (31), which performs well in the clinical setting of our study (32, 33). This validated questionnaire has 4 dimensions: fatigue, dyspnea, emotion, and mastery. We averaged the scores on each scale, ranging from 1 (worst function) to 7 (best function), across items within each dimension. We assessed satisfaction with pharmacy services by using an internally developed and validated 12-item instrument (Cronbach  $\alpha$  level = 0.91). We measured direct health care costs by using fixed and variable intervention costs (26). Fixed costs included training of the intervention pharmacist, material development, programming, and equipment. Variable costs included time spent by the pharmacist delivering the intervention, time spent by physicians speaking with the pharmacist about patients in the intervention group, and costs of written materials. We measured time spent by pharmacists by directly observing them servicing patients at random 3- to 4-hour intervals.

#### Follow-up Procedures

After study enrollment and baseline interviews, patients returned for interviews at 3, 6, 9, and 12 months. We conducted monthly telephone surveys to collect data on health-related quality of life; ascertain problems associated with electronic monitoring of medication containers and new uses of medication aids, such as pill containers; determine the occurrence of health care use or new prescriptions outside of the study site; and verify address, income, and transportation information. We assessed interviewer blinding by using a computerized closeout protocol at the end of each interview that required interviewers to guess whether each patient was in the intervention or usual care group. The mean ability of the interviewers to correctly guess patients' group assignment was 49% (50% would be predicted if guessing by chance). We determined that the time spent interviewing was similar between intervention and usual care groups for in-person interviews ( $P = 0.33$ ) and telephone interviews ( $P = 0.45$ ).

Patients visited the pharmacy primarily to refill prescriptions. However, patients in the intervention group were encouraged to call or visit the pharmacist for assistance or questions involving their medications. We collected adverse drug event and medication error data by using a program developed for a separate study (34, 35). This program used coded and text data available in the Regenstrief Medical Record System to identify commonly occurring adverse events and medication errors in outpatients. Relevant events included ACE inhibitor-related allergy or cough, toxic serum digoxin concentrations, or use of nonsteroidal anti-inflammatory drugs in persons with high serum potassium concentrations or renal insufficiency. A data safety and monitoring board was kept apprised of all study activities through the receipt of monthly meeting minutes and 3 formal reports.

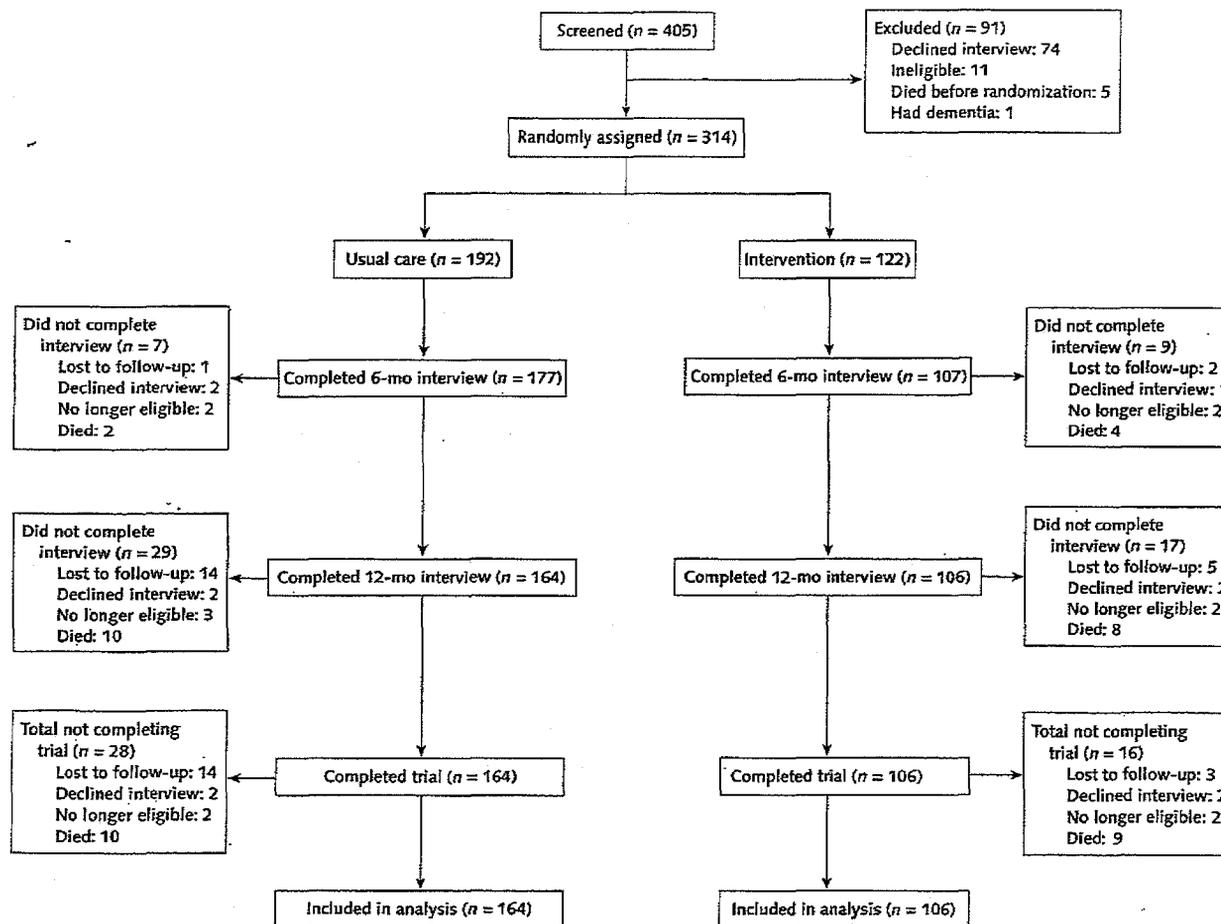
#### Statistical Analysis

We estimated that a sample size of at least 100 patients in each group would provide 94% power to detect a 10% difference in means for medication adherence by using a  $t$ -test with a 2-sided  $\alpha$  level of 0.05 and assuming a 20% SD. For acute exacerbations, we used a 2-sided log-rank test with proportional events of 0.1 and 0.3 in the intervention and usual care groups, respectively, to estimate that a sample size of 100 patients per group would provide 93% power, when the  $\alpha$  level is set at 0.05 and the hazard ratio is constant at 3.38.

We made between-group comparisons by using  $t$ -tests or the 2-sample Wilcoxon test for continuous variables and chi-square tests for categorical variables. For medication adherence, we compared overall and drug category-specific taking and scheduling adherences. Using data from the MEMS lids, we assessed taking and scheduling adherence, the values of which may range from 0% to 100%. We imputed the data that were missing because of lost medication container lids by using a regression imputation method. We generated 5 imputed MEMS adherence data sets by using SAS PROC MI (SAS Institute, Inc., Cary, North Carolina) from the regression imputation models on the basis of self-reported adherence at baseline and group assignment. We then combined point estimates of the treatment effect from the imputed data sets to achieve valid point and CI estimates by using SAS PROC MIANALYZE (36). Herein, we imputed the overall taking and scheduling adherence outcomes. We did not impute adherence to individual drug classes because patients did not take each medication and we could not justify imputing patients' adherence to medications that were not prescribed. To assess the robustness of the study findings in the presence of missing MEMS adherence measurements, we conducted sensitivity analyses by using 9 scenarios of varying levels of adherence for individuals in the 2 groups who did not complete the trial (Appendix Table 2, available at [www.annals.org](http://www.annals.org)).

Clinical exacerbations were characterized by emer-

Figure. Study flow diagram.



gency department visits and hospitalizations. We analyzed the type-specific and overall counts of emergency department visits and hospital admissions by using log-linear regression models that were based on Poisson or negative binomial distributions. To accommodate unequal durations of follow-up, we incorporated the logarithmic duration of follow-up into the log-linear model as an offset parameter. We obtained regression parameters and SEs from the final models. We calculated the incidence rate ratio by exponentiating the parameter estimates. We performed the analysis by using SAS PROC GENMOD, version 9.1. We analyzed changes from baseline for disease-specific quality of life and satisfaction with pharmacy services by using a paired *t*-test. We calculated direct health care costs in 2003 U.S. dollars for the intervention and usual care groups and estimated the between-group difference in costs. To compute the 95% CI around the difference in costs, we used a nonparametric, bias-corrected, accelerated bootstrap approach because of the skewed nature of cost data (37).

To determine whether unintended negative consequences of the intervention were evident, we analyzed the composite of adverse drug events and medication errors. We used the chi-square test to test the hypotheses that the adverse events and errors among patients were independent of group assignment. We also used the method of Krishnamoorthy and Thomson to directly compare rates of these events (38).

**Role of the Funding Source**

The National Institutes of Health partly funded the study. The funding source had no role in the study design or intervention, recruitment of patients, data collection, analysis, or interpretation of the results, writing of the manuscript, or decision to submit the manuscript for publication.

**RESULTS**

The Figure shows the flow of patients through the study. Compared with all potentially eligible patients (*n* =

1512), the 314 patients enrolled in the study were younger (63 vs. 67 years;  $P < 0.001$ ) and were more likely to be women (67% vs. 59%;  $P = 0.009$ ). At baseline, however, patients were otherwise similar to the total population of patients with heart failure ( $n = 3034$ ; mean age, 60 years), of whom 66% were women. Randomization resulted in well-balanced groups (Table 1), except that more patients in the usual care group than the intervention group had a history of coronary artery disease (76% vs. 63%). Follow-up rates were similar in the intervention (87%) and usual care (85%) groups.

The pharmacist dispensed 1004 electronic monitor lids on cardiovascular medication containers. Of the 404 lids dispensed to patients in the intervention group (a mean of 3.3 lids per patient), 330 lids were returned by closeout (81.7%). Of the 600 lids dispensed to patients in the usual care group (a mean of 3.1 lids per patient), 472 lids were returned by closeout (78.7%). The difference in lid returns between groups was not significant ( $P = 0.22$ ). Furthermore, the results of the sensitivity analyses to determine the effect of missing data from lost lids and patient withdrawals indicated that our results were robust to the varying levels of adherence for individuals with missing data (Appendix Table 2, available at [www.annals.org](http://www.annals.org)).

The pharmacist logged 5588 activities. The most common of these were educating patients about their medications, resolving medication problems, reinforcing physicians' instructions to patients about prescribed medications, reminding patients of the importance of adherence and obtaining refills, communicating with physicians, and encouraging important patient lifestyle changes (such as stopping smoking and dietary sodium discretion).

### Medication Adherence

Overall taking adherence was 67.9% and 78.8% in the usual care and intervention groups, respectively (difference, 10.9 percentage points [95% CI, 5.0 to 16.7 percentage points]) during the intervention period, but these salutary effects dissipated in the 3-month postintervention follow-up period, in which taking adherence was 66.7% and 70.6%, respectively (difference, 3.9 percentage points [CI, -5.9 to 6.5 percentage points]) (Table 2). Taking adherence was statistically significantly greater in the intervention group than the usual care group for the following cardiovascular medications commonly used by patients with heart failure: ACE inhibitors (difference, 10.5 percentage points [CI, 2.8 to 18.2 percentage points]),  $\beta$ -blockers (difference, 14.7 percentage points [CI, 6.4 to 22.9 percentage points]), digoxin (difference, 13.9 percentage points [CI, 3.5 to 24.3 percentage points]), and loop diuretics (difference, 9.8 percentage points [CI, 1.2 to 18.4 percentage points]).

Overall scheduling adherence was 47.2% and 53.1% in the usual care and intervention groups, respectively (difference, 5.9 percentage points [CI, 0.4 to 11.5 percentage points]) during the 9-month intervention (Table 2). Sim-

ilar to that of taking adherence, this effect dissipated during the 3-month postintervention period (difference, 0.3 percentage point [CI, -5.9 to 6.5 percentage points]). Scheduling adherence effects were statistically significantly greater for ACE inhibitors (difference, 7.7 percentage points [CI, 0.3 to 15.2 percentage points]) and  $\beta$ -blockers (difference, 12.1 percentage points [CI, 5.1 to 19.2 percentage points]).

Refill adherence data indicated that patients in both groups were well supplied with medications by the pharmacy. Compared with the usual care group, the intervention group had statistically greater overall refill adherence (2-sample Wilcoxon test) (105.2% vs. 109.4%, respectively; difference, 4.2 percentage points [ $P = 0.007$ ]) and had increased refill adherence for  $\beta$ -blockers (122.2% vs. 108.4%; difference, 13.8 percentage points [ $P = 0.002$ ]), digoxin (86.4% vs. 76.4%; difference, 10.0 percentage points [ $P = 0.039$ ]), and loop diuretics (148.8% vs. 105.0%; difference, 43.8 percentage points [ $P = 0.027$ ]). However, refill adherence of ACE inhibitors was slightly but statistically significantly greater for the usual care group (98.3% vs. 96.9%; difference, -1.4 percentage points [ $P = 0.018$ ]). Finally, differences in self-reported adherence between groups were small. The modest increase in the intervention group (and overall) in the analysis of medians was not statistically significant (1.0 for the intervention group vs. 0.8 for the usual care group;  $P = 0.48$ , 2-sample Wilcoxon test).

### Heart Failure Exacerbations

As shown in Table 3, the intervention group had 19.4% fewer exacerbations on the combined end point of hospital admission or emergency department visit (incidence risk ratio, 0.82 [CI, 0.70 to 0.95]). Fewer hospital admissions occurred in the intervention group for the various reasons for admission (heart failure, all cardiovascular, and all-cause). Multivariable models controlling for patient functional class, counts of prescribed drugs, ejection fraction, and comorbid conditions showed that taking adherence was an independent, statistically significant predictor of the number of hospitalizations for heart failure, cardiovascular reasons, and all causes and of all emergency department visits for cardiovascular reasons. Scheduling adherence predicted emergency department visits for heart failure and all causes (data not shown).

Disease-specific quality of life improved from baseline to 6 months and 12 months by 0.28 and 0.39, respectively, for the intervention group compared with 0.21 and 0.24 for the usual care group, respectively ( $P = 0.52$  at 6 months;  $P = 0.21$  at 12 months). The overall improvement in patient satisfaction from baseline to 12 months was greater in the intervention group than the usual care group (1.0 vs. 0.7;  $P = 0.022$ ).

### Total Direct Costs

The overall actual mean fixed cost of developing the intervention and the variable costs of implementing it were

Table 1. Baseline Characteristics\*

| Characteristic                                     | Usual Care Group (n = 192) | Intervention Group (n = 122) |
|--|----------------------------|------------------------------|
| Mean age (SD), y                                   | 62.6 (8.8)                 | 61.4 (7.7)                   |
| Sex, n (%)   |                            |                              |
| Women  | 127 (66.1)                 | 83 (68.0)                    |
| Men  | 65 (33.9)                  | 39 (32.0)                    |
| Race, n (%)  |                            |                              |
| Black  | 100 (52.1)                 | 55 (45.1)                    |
| White  | 90 (46.9)                  | 66 (54.1)                    |
| Other  | 2 (1.0)                    | 1 (0.8)                      |
| Sufficient income, n (%)†                          | 123 (64)                   | 76 (62)                      |
| Mean education (SD), y                             | 11 (3)                     | 11 (2)                       |
| Married, n (%)                                     | 50 (26)                    | 34 (28)                      |
| Living alone, n (%)                                | 72 (38)                    | 45 (38)                      |
| Health literate, n (%)‡                            | 136 (71)                   | 88 (72)                      |
| Insurance type, n (%)                              |                            |                              |
| Medicare   |                            |                              |
| Yes  | 108 (56.3)                 | 66 (54.1)                    |
| No   | 84 (43.8)                  | 56 (45.9)                    |
| Medicaid   |                            |                              |
| Yes  | 70 (36.5)                  | 37 (30.3)                    |
| No   | 122 (63.5)                 | 85 (69.7)                    |
| NYHA class, n (%)                                  |                            |                              |
| I  | 38 (19.8)                  | 23 (18.9)                    |
| II   | 78 (40.6)                  | 51 (41.8)                    |
| III  | 67 (34.9)                  | 43 (35.3)                    |
| IV   | 9 (4.7)                    | 5 (4.1)                      |
| Mean ejection fraction (SD)                        | 0.50 (0.16)                | 0.49 (0.17)                  |
| Mean pro-BNP level (SD), ng/L                      | 1406 (3486)                | 1122 (1940)                  |
| Mean log-transformed pro-BNP level (SD), ng/L      | 6.0 (1.6)                  | 5.9 (1.6)                    |
| Mean body weight (SD), kg                          | 92.5 (24.4)                | 91.5 (25.8)                  |
| Mean body mass index (SD), kg/m <sup>2</sup>       | 34.1 (10.2)                | 34.1 (9.5)                   |
| Mean systolic blood pressure (SD), mm Hg           | 135.4 (25.2)               | 132.9 (23.6)                 |
| Mean diastolic blood pressure (SD), mm Hg          | 70.5 (15.6)                | 68.9 (14.1)                  |
| Mean hematocrit (SD), %                            | 37.6 (5.7)                 | 37.7 (5.2)                   |
| Mean serum creatinine level (SD)                   |                            |                              |
| μmol/L   | 106.1 (61.9)               | 106.1 (44.2)                 |
| mg/dL  | 1.2 (0.7)                  | 1.2 (0.5)                    |
| Hypertension, n (%)                                | 186 (96.9)                 | 114 (93.4)                   |
| Coronary artery disease, n (%)                     | 146 (76.0)                 | 77 (63.1)                    |
| Diabetes, n (%)                                    | 131 (68.2)                 | 74 (60.7)                    |
| Stroke, n (%)                                      | 29 (15.1)                  | 16 (13.1)                    |
| COPD, n (%)  | 67 (34.9)                  | 39 (32.0)                    |
| Atrial fibrillation, n (%)                         | 27 (14.0)                  | 14 (11.5)                    |
| Mean emergency department visits at 1 year (SD), n | 3.4 (6.0)                  | 3.0 (4.9)                    |
| Mean hospital admissions at 1 year (SD), n         | 1.3 (2.4)                  | 1.1 (2.1)                    |
| Long-term medications, n                           | 11 (4)                     | 10 (4)                       |
| Medication type, n (%)                             |                            |                              |
| ACE inhibitor                                      |                            |                              |
| Yes  | 137 (71.4)                 | 75 (61.5)                    |
| No   | 55 (28.6)                  | 47 (38.5)                    |
| ARB  |                            |                              |
| Yes  | 22 (11.5)                  | 16 (13.1)                    |
| No   | 170 (88.5)                 | 106 (86.9)                   |
| β-Blocker  |                            |                              |
| Yes  | 120 (62.5)                 | 71 (58.2)                    |
| No   | 72 (37.5)                  | 51 (41.8)                    |
| Digoxin  |                            |                              |
| Yes  | 52 (27.1)                  | 34 (27.9)                    |
| No   | 140 (72.9)                 | 88 (72.1)                    |
| Loop diuretic                                      |                            |                              |
| Yes  | 118 (61.5)                 | 69 (56.6)                    |
| No   | 74 (38.5)                  | 53 (43.4)                    |
| Thiazide diuretic                                  |                            |                              |
| Yes  | 29 (15.1)                  | 22 (18.0)                    |
| No   | 163 (84.9)                 | 100 (82.0)                   |
| Spironolactone                                     |                            |                              |
| Yes  | 31 (16.2)                  | 14 (11.5)                    |
| No   | 161 (83.8)                 | 108 (88.5)                   |

\* ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; BNP = brain natriuretic peptide; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association.

† Income satisfaction was assessed by asking whether the patient has an income that is comfortable, just enough to get by, or not even enough to get by.

‡ Health literacy was measured by using the Short Test of Functional Health Literacy in Adults (54).

Table 2. Adherence to Cardiovascular Medications\*

| Adherence                   | Intervention Period |                         | Postintervention Period |                         |
|-----------------------------|---------------------|-------------------------|-------------------------|-------------------------|
|                             | Patients, n         | Doses Taken (95% CI), % | Patients, n             | Doses Taken (95% CI), % |
| <b>Taking adherence</b>     |                     |                         |                         |                         |
| Overall†                    |                     |                         |                         |                         |
| Intervention                | 122                 | 78.8 (74.9 to 82.7)     | 122                     | 70.6 (64.9 to 76.2)     |
| Usual care                  | 192                 | 67.9 (63.8 to 72.1)     | 192                     | 66.7 (62.3 to 70.9)     |
| Difference‡                 |                     | 10.9 (5.0 to 16.7)      |                         | 3.9 (-2.8 to 10.7)      |
| ACE inhibitor               |                     |                         |                         |                         |
| Intervention                | 77                  | 82.9 (78.1 to 87.7)     | 65                      | 74.7 (67.1 to 82.3)     |
| Usual care                  | 127                 | 72.4 (67.2 to 77.7)     | 104                     | 72.1 (65.9 to 78.2)     |
| Difference‡                 |                     | 10.5 (2.8 to 18.2)      |                         | 2.6 (-7.2 to 12.4)      |
| ARB                         |                     |                         |                         |                         |
| Intervention                | 15                  | 77.1 (59.2 to 95.0)     | 15                      | 80.0 (63.6 to 96.3)     |
| Usual care                  | 24                  | 71.0 (58.7 to 83.3)     | 21                      | 55.1 (37.2 to 72.9)     |
| Difference‡                 |                     | 6.1 (-14.2 to 26.4)     |                         | 24.9 (0.5 to 49.3)      |
| β-Blocker                   |                     |                         |                         |                         |
| Intervention                | 70                  | 78.7 (73.1 to 84.4)     | 64                      | 65.2 (56.8 to 73.6)     |
| Usual care                  | 122                 | 64.1 (58.7 to 64.1)     | 104                     | 63.4 (57.2 to 69.5)     |
| Difference‡                 |                     | 14.7 (6.4 to 22.9)      |                         | 1.8 (-8.3 to 11.9)      |
| Digoxin                     |                     |                         |                         |                         |
| Intervention                | 35                  | 89.1 (83.3 to 94.9)     | 31                      | 84.2 (76.1 to 92.3)     |
| Usual care                  | 50                  | 75.2 (67.4 to 83.0)     | 43                      | 72.9 (64.1 to 81.8)     |
| Difference‡                 |                     | 13.9 (3.5 to 24.3)      |                         | 11.3 (-1.0 to 23.6)     |
| Loop diuretic               |                     |                         |                         |                         |
| Intervention                | 70                  | 71.5 (65.6 to 77.3)     | 61                      | 61.5 (53.3 to 69.7)     |
| Usual care                  | 116                 | 61.7 (56.0 to 67.4)     | 94                      | 60.4 (53.6 to 67.2)     |
| Difference‡                 |                     | 9.8 (1.2 to 18.4)       |                         | 1.1 (-9.5 to 11.7)      |
| Spironolactone              |                     |                         |                         |                         |
| Intervention                | 16                  | 84.4 (72.3 to 96.4)     | 13                      | 78.3 (61.6 to 95.0)     |
| Usual care                  | 28                  | 69.7 (58.1 to 81.3)     | 22                      | 73.4 (61.0 to 85.8)     |
| Difference‡                 |                     | 14.6 (-2.8 to 14.6)     |                         | 4.9 (-14.9 to 24.7)     |
| <b>Scheduling adherence</b> |                     |                         |                         |                         |
| Overall†                    |                     |                         |                         |                         |
| Intervention                | 122                 | 53.1 (49.1 to 57.1)     | 122                     | 48.9 (43.7 to 54.1)     |
| Usual care                  | 192                 | 47.2 (43.4 to 50.9)     | 192                     | 48.6 (44.7 to 52.6)     |
| Difference‡                 |                     | 5.9 (0.4 to 11.5)       |                         | 0.3 (-5.9 to 6.5)       |
| ACE inhibitor               |                     |                         |                         |                         |
| Intervention                | 77                  | 60.7 (55.5 to 65.9)     | 65                      | 54.9 (48.0 to 61.8)     |
| Usual care                  | 127                 | 53.0 (48.1 to 57.8)     | 104                     | 54.1 (48.3 to 60.0)     |
| Difference‡                 |                     | 7.7 (0.3 to 15.2)       |                         | 0.8 (-8.4 to 9.9)       |
| ARB                         |                     |                         |                         |                         |
| Intervention                | 15                  | 55.9 (38.8 to 73.0)     | 15                      | 63.1 (45.6 to 80.5)     |
| Usual care                  | 24                  | 51.0 (40.1 to 61.8)     | 21                      | 39.2 (26.4 to 51.9)     |
| Difference‡                 |                     | 4.9 (-13.6 to 23.5)     |                         | 23.9 (3.7 to 44.2)      |
| β-Blocker                   |                     |                         |                         |                         |
| Intervention                | 70                  | 49.2 (43.5 to 55.0)     | 64                      | 39.9 (33.3 to 46.5)     |
| Usual care                  | 122                 | 37.1 (32.9 to 41.3)     | 104                     | 40.8 (35.7 to 40.8)     |
| Difference‡                 |                     | 12.1 (5.1 to 19.2)      |                         | -0.1 (-9.2 to 7.4)      |
| Digoxin                     |                     |                         |                         |                         |
| Intervention                | 35                  | 66.8 (59.4 to 74.1)     | 31                      | 61.0 (52.5 to 69.6)     |
| Usual care                  | 50                  | 57.7 (50.2 to 65.2)     | 43                      | 55.5 (46.7 to 64.2)     |
| Difference‡                 |                     | 9.1 (-1.7 to 19.8)      |                         | 5.6 (-6.8 to 18.0)      |
| Loop diuretic               |                     |                         |                         |                         |
| Intervention                | 70                  | 41.7 (35.8 to 47.5)     | 61                      | 38.1 (31.6 to 44.5)     |
| Usual care                  | 116                 | 38.3 (33.2 to 43.4)     | 94                      | 37.9 (32.3 to 43.6)     |
| Difference‡                 |                     | 3.4 (-4.5 to 11.3)      |                         | 0.2 (-8.5 to 8.8)       |
| Spironolactone              |                     |                         |                         |                         |
| Intervention                | 16                  | 57.8 (44.0 to 71.7)     | 13                      | 54.2 (39.4 to 69.0)     |
| Usual care                  | 28                  | 51.0 (41.3 to 60.7)     | 22                      | 56.3 (43.7 to 68.9)     |
| Difference‡                 |                     | 6.8 (-9.3 to 22.9)      |                         | -2.1 (-21.3 to 17.2)    |

\* The intervention lasted 9 months and was followed by a 3-month nonintervention period. ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker.

† Based on multiple imputation.

‡ Differences are reported in percentage points.

Table 3. Emergency Department Visits and Hospitalizations\*

| Variable              | Emergency Department Visits     |                               | Hospital Admissions             |                               | Combined Outcome                |                               |
|-----------------------|---------------------------------|-------------------------------|---------------------------------|-------------------------------|---------------------------------|-------------------------------|
|                       | Intervention Group<br>(n = 122) | Usual Care Group<br>(n = 192) | Intervention Group<br>(n = 122) | Usual Care Group<br>(n = 192) | Intervention Group<br>(n = 122) | Usual Care Group<br>(n = 192) |
| <b>All causes</b>     |                                 |                               |                                 |                               |                                 |                               |
| Mean (SD), n          | 2.16 (3.31)                     | 2.68 (4.87)                   | 0.78 (1.66)                     | 0.97 (1.78)                   | 2.94 (4.69)                     | 3.65 (6.26)                   |
| Median (IQR), n       | 1 (0-3)                         | 1 (0-3)                       | 0 (0-1)                         | 0 (0-1)                       | 1 (0-3)                         | 1.5 (0-4)                     |
| IRR (95% CI)†         | 0.82 (0.70-0.95)                |                               | 0.81 (0.64-1.04)                |                               | 0.82 (0.72-0.93)                |                               |
| <b>Cardiovascular</b> |                                 |                               |                                 |                               |                                 |                               |
| Mean (SD), n          | 0.57 (1.39)                     | 0.65 (1.63)                   | 0.31 (0.86)                     | 0.37 (0.91)                   | 0.61 (1.72)                     | 0.67 (1.95)                   |
| IRR (95% CI)‡         | 0.94 (0.51-1.73)                |                               | 0.86 (0.45-1.63)                |                               | 0.96 (0.48-1.91)                |                               |
| <b>Heart failure</b>  |                                 |                               |                                 |                               |                                 |                               |
| Mean (SD), n          | 0.30 (1.03)                     | 0.30 (1.27)                   | 0.11 (0.46)                     | 0.15 (0.58)                   | 0.40 (1.47)                     | 0.44 (1.79)                   |
| IRR (95% CI)‡         | 1.09 (0.42-2.87)                |                               | 0.77 (0.28-2.10)                |                               | 1.00 (0.36-2.77)                |                               |

\* IQR = interquartile range; IRR = incidence rate ratio.

† Using log-linear regression based on Poisson distribution.

‡ Using log-linear regression based on negative binomial distribution.

\$205 per patient\* (Appendix Table 3, available at [www.annals.org](http://www.annals.org)). Outpatient health care was \$886 lower for patients in the intervention group (CI, -\$2289 to \$660) and was lower across all cost categories except drugs. Moreover, the cost of inpatient health care was \$2277 less in the intervention group (CI, -\$6329 to \$1225). The mean difference in the overall cost of health care was \$3165 lower in the intervention group (CI, -\$7800 to \$1138). Considering the costs of development and implementation, the intervention saved \$2960 per patient (CI, -\$7603 to \$1338). However, no cost comparisons between groups were statistically significant because of the large variability in costs.

#### Adverse Drug Events and Medication Errors

Adverse drug events and medication errors did not statistically differ between groups. In the usual care group, 91 of 192 patients (47.4%) had an adverse event or medication error compared with 42 of 112 patients (37.5%) in the intervention group (chi-square = 2.81;  $P = 0.094$ ). The between-group rates of these events were not statistically significant ( $P = 0.108$ ).

#### DISCUSSION

The pharmacist intervention improved adherence to cardiovascular medications, including the proportion of medications taken, the reliability of scheduling these medications, and the amounts of medications refilled. However, the effects of the intervention on taking and scheduling adherence observed during the 9-month active intervention period dissipated in the 3-month postintervention period. Patients in the intervention group had fewer exacerbations requiring emergency room visits and hospital care and reported greater satisfaction with pharmacist services than did patients receiving usual care. Costs of care were lower and improvements in disease-specific quality of life were greater in the intervention group but

were not statistically significant. With respect to costs, as more patients receive the intervention, the intervention development costs become negligible and the overall cost savings per patient approaches \$3000. Indeed, the return on investment in our study is \$14 for every dollar spent on the intervention, which contrasts greatly from the return on investment of \$6.5 for every dollar spent in a recent meta-analysis of more intensive postdischarge interventions in older adults with heart failure (40).

We searched MEDLINE, available adherence bibliographies, and references from English-language publications of trials of similar pharmacist interventions for adults with heart failure up to December 2006. We found that previous randomized, controlled trials of pharmacist involvement in heart failure medication management programs have been encouraging. Gattis and colleagues (41) assessed how all-cause mortality and hospital admissions were affected by adding a clinical pharmacist to a multidisciplinary heart failure management team at a cardiology referral clinic. Similar to our intervention, the pharmacist in Gattis and colleagues' study conducted an initial evaluation of medication use and patient education, provided recommendations to patients' physicians, and performed follow-up monitoring by telephone for 6 months. A special effort was made to ensure that patients received the dosage of ACE inhibitor that is supported by heart failure guidelines. Compared with the usual care group, the intervention group had more patients receiving recommended ACE inhibitor dosages and fewer cardiovascular events. Although the authors used a questionnaire to determine self-reported adherence, they did not report these data. Health-related quality of life, patient satisfaction, and the costs of health care were not measured in the study. Tsuyuki and colleagues (42) also targeted ACE inhibitors in their 10-center trial of a pharmacist or nurse postdischarge intervention involving patient education, diaries, and adherence

support. They found a reduction in cardiovascular emergency department use between the intervention and usual care groups, but differences in refill adherence were not statistically significant. Bouvy and colleagues (43) studied a pharmacist intervention on treatment gaps in diuretic adherence, as measured by using electronic monitors. The intervention group had fewer missed diuretic days than the usual care group, but the groups did not statistically differ in other outcomes. Goodyer and colleagues (44) studied elderly patients receiving a 3-month intensive in-home medication counseling program. Adherence (measured by pill count) improved by 32% in the intervention group and remained unchanged in the control group. Exercise performance improved from baseline in the intervention group but worsened in the control group. Two additional small trials of pharmacist interventions for patients with heart failure (45, 46) were encouraging but had flaws in their design, execution, or both. These generally favorable results of pharmacist interventions are consistent with those of several other recent reports of multidisciplinary interventions, most of which promoted treatment adherence.

Multidisciplinary heart failure management programs that reduced hospital readmissions were more likely to include an inpatient component of care, patient education, self-care support, improvements to the medical regimen, and processes to identify and manage clinical exacerbation (47). These programs differed in intervention intensity, the personnel delivering the intervention, the type of intervention (telephone or personal contact), and complexity (48). Generally, multidisciplinary programs were more intense and comprehensive than our pharmacist intervention. Advanced practice nurses who specialize in disease management and work closely with a physician have been at the core of several of these programs (49, 50). Medication components of these programs often include verbal instruction and written support, but their descriptions are often vague in intensity, timing, method of delivery, and targeted health literacy level.

Although some programs involved a pharmacist (51–53), we are unaware of any that were managed from a pharmacy by a pharmacist who dispensed medications and provided other helpful functions. Because pharmacotherapy is central to the management of heart failure, almost all management programs promoted appropriate use of medications and adherence. However, only some programs measured adherence (49, 50). The pharmacist in our study dispensed medications to patients in the intervention group with tailored medication instructions that emphasized the importance of adherence to physicians' prescriptions. The pharmacist contacted physicians and nurses as needed, but most core functions were derived from the pharmacist's work with the patients. Overall, however, our intervention by a trained dispensing pharmacist seems to be much less comprehensive and less intense than previous interventions led by nurses or pharmacists. Nonetheless, the improvements in treatment adherence and modest re-

ductions in health care use and costs that resulted from our intervention could be a worthwhile complement to existing multidisciplinary programs that lack such a pharmacist component (54).

Our study has several limitations. First, patients were recruited from a health center that serves a predominantly indigent population. Second, to ascertain adherence, we required patients to use electronic monitor containers and excluded patients who used special pill box adherence aids. Third, the intervention was delivered by a single pharmacist and precludes study of other factors, such as pharmacist attitudes or behaviors, that may have promoted delivery of the intervention. These factors may limit the generalizability of our findings. Finally, because the intervention had several components, such as verbal counseling and written materials, that were aimed at persons with low health literacy, we could not attribute intervention effects to any single component.

In conclusion, we found that our pharmacy-based intervention for outpatients with heart failure improved adherence to cardiovascular medications and decreased health care use. Because the salutary effects on adherence quickly dissipated when the intervention ended, continued intervention is probably necessary. If these study results are confirmed in other health care settings, policymakers might consider emphasizing the importance of pharmacists in promoting medication adherence for the reduction in health care use and associated costs of chronic diseases, such as heart failure.

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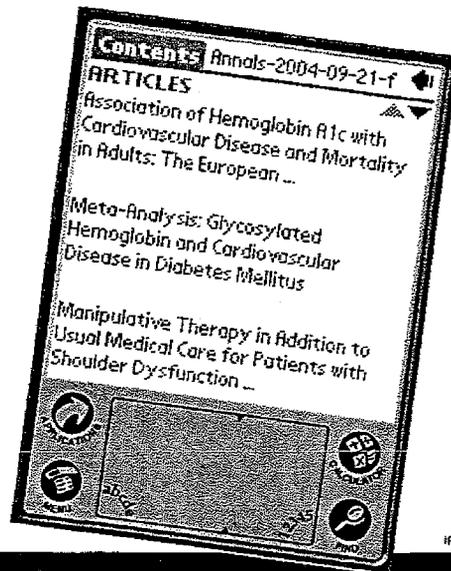
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# A Randomized Trial of Direct-to-Patient Communication to Enhance Adherence to $\beta$ -Blocker Therapy Following Myocardial Infarction

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**Background:** Although  $\beta$ -blockers are routinely prescribed at hospital discharge after myocardial infarction (MI), patients' adherence has been shown to decline substantially over time. We sought to test the hypothesis that a simple, direct-to-patient intervention can improve adherence to  $\beta$ -blocker therapy following MI.

**Methods:** We conducted a cluster randomized controlled trial in 4 geographically dispersed health maintenance organizations testing the hypothesis that a simple direct-to-patient intervention could improve adherence. The study was carried out from June 2004 to March 2005. The primary analyses were based on 836 post-MI patients who were dispensed a  $\beta$ -blocker prescription after discharge. The intervention consisted of 2 mailings 2 months apart describing the importance of  $\beta$ -blocker use. The main outcomes were proportion of days covered with  $\beta$ -blocker therapy and percentage of patients with at least 80% of days covered in the 9 months after the first mailing. Analyses were adjusted for age, sex, total

medications dispensed, days between MI and intervention, and intervention site.

**Results:** Over the entire follow-up period, patients in the treatment arm had a mean absolute increase of 4.3% of days covered per month compared with patients in the control arm (a 5.7% relative change from baseline), representing 1.3 extra days ( $P = .04$ ). Treatment patients were 17% more likely (relative risk, 1.17; 95% confidence interval, 1.02-1.29) to have 80% of days covered. For every 16 patients receiving the intervention, 1 additional patient would become adherent (80% or more days covered per month).

**Conclusion:** A low-cost, easily replicable effort to increase adherence can have a demonstrable impact on  $\beta$ -blocker adherence following MI.

**Trial Registration:** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT00211172

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**M**ORE THAN 13 MILLION adult Americans have coronary heart disease (CHD); more than 7 million have had myocardial infarction (MI).<sup>1</sup> The joint American Heart Association and American College of Cardiology guidelines address the treatment of patients with MI and recommend that post-MI patients receive antiplatelet and  $\beta$ -blocker therapy and that many patients should also receive lipid-lowering agents and angiotensin-converting enzyme inhibitors (ACEIs).<sup>2,3</sup>

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Adherence to these guidelines leads to better survival outcomes.<sup>4</sup> While use of these agents immediately following MI is important, persistent use is essential to improve survival,<sup>2,4,5</sup> but various investiga-

tors have found disappointingly low rates of use.<sup>6-11</sup>

Investigators estimate that if all MI survivors in 2000 in the United States persisted with  $\beta$ -blocker use for 20 years, 45 000 life-years would be gained<sup>12</sup> and that MI patients discontinuing  $\beta$ -blocker use are almost twice as likely to die in the next year.<sup>5</sup>

## See Invited Commentary at end of article

Efforts to improve initiation of  $\beta$ -blocker prescribing following MI within hospital settings often target physicians,<sup>11</sup> but patient-oriented strategies are likely needed to encourage prolonged use in the community. Maintaining adherence after MI requires that patients understand the therapeutic benefits, recognize the need for long-term use, and are motivated to adhere<sup>13</sup> to the regimen despite inconvenience, cost, potentially conflicting messages from family or friends,

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and potential adverse effects. Studies to enhance medication adherence have often been multimodal,<sup>14</sup> making it impossible to disentangle the effects of a single intervention. The findings of previous studies in patients with MI and cardiac events suggest that mailed reminders may be able to increase medication refills<sup>15</sup> and uptake,<sup>16</sup> but the studies were not designed to detect moderate effects and have been criticized on other grounds.<sup>17,18</sup>

We sought to improve on the existing literature by using a rigorous randomized control design powered to detect a 10% difference and by informing the intervention material content using qualitative methods. Unlike interventions providing general education, our intervention provided a specific message about long-term adherence to  $\beta$ -blocker therapy. We directed the intervention to patients with acute MI, with simultaneous reinforcement in communication with their physicians. We used an easily replicable, low-cost approach embracing physician behavior change principles of brevity, repetition, and reinforcement.<sup>19</sup>

## METHODS

We carried out a cluster randomized trial in 4 geographically diverse sites, including Boston, Massachusetts, Minneapolis, Minnesota, Atlanta, Georgia, and Portland, Oregon, testing the hypothesis that mailed communications to patients and primary care providers would be more effective than usual care at promoting adherence to  $\beta$ -blocker therapy following MI.

### INTERVENTION DESIGN

Using accepted qualitative methods,<sup>20</sup> we developed the format and content of materials with focus groups (including cognitive pretesting). Focus group participants were MI patients who had been dispensed a  $\beta$ -blocker prescription and whose MI had occurred in the 365 days prior to the focus group meeting. Participants revealed that major barriers to  $\beta$ -blocker adherence included concerns of adverse effects, forgetting to refill prescriptions, and interruptions in routine. Suggestions for informational content for the mailings included the following: (1) reasons the drugs are important in MI treatment, (2) risks of not taking them, and (3) information on adverse effects. Patients wanted the letters to be personalized and written in lay language. They also thought that they would be most likely to open and read a letter if it came from their clinician; resource constraints prohibited this goal, but the letter did come from a health plan physician-administrator.

The intervention consisted of 2 mailed communications. A personalized letter was mailed first, followed approximately 2 months later by a similar letter and an accompanying brochure. Both mailings also included a wallet card that suggested questions for the patient to ask their clinician, space to list their medications, and space to record additional queries. The communications contained nearly identical information, stressing the importance of lifetime use of  $\beta$ -blockers following MI and that adverse effects can be managed and the importance of remembering to refill their prescription. They also included a brief mention of other therapies (statins, ACEIs, and aspirin).

Primary care clinicians of patients randomized to the intervention arm received sample materials and a letter alerting them that their patients with MI would be receiving materials developed with input from patients and clinicians in primary care and cardiology. The letters asked the primary care clinicians to support the initiative and reminded them of guidelines on lifetime use of  $\beta$ -blockers following MI.

Because we wanted to study the intervention's effects compared with usual care, neither patients nor clinicians randomized to the control group were contacted but were followed using the same data systems as the intervention group.

### ELIGIBILITY CRITERIA

We included people with a discharge diagnosis of MI (*International Classification of Diseases, Ninth Revision* codes 410.xx) between December 1, 2003 (start of enrollment), and June 18, 2004 (end of enrollment), who were at least 18 years old and had a  $\beta$ -blocker prescription dispensed (first  $\beta$ -blocker prescription was the index) before June 18, 2004. The intervention mailing took place at the end of July 2004; thus, a patient may have had their MI from 1 to 7.5 months before to the date of the mailing. Between the date of the qualifying MI and the mailed intervention, patients were required to have health plan and prescription eligibility and to have survived. For efficiency and to replicate methods commonly used by health plans, we mailed materials to each site's patients on the same calendar date.

### RANDOMIZATION, FOLLOW-UP, AND DATA SOURCES

At 3 sites, physician practices were listed from highest to lowest according to the number of eligible patients and then randomly assigned by computer to intervention or usual care in sequential pairs (blocks of 2). This approach to randomization was undertaken to avoid contamination of the usual care group and to ensure that the 2 arms were of comparable sizes. One site (40% of the population) failed to randomize by practice and instead performed simple randomization by patient; this conservative error could only decrease the effect size of the intervention through increased contamination. Group assignment was concealed until allocation; outcome assessment was blinded, and randomization by protocol was done by analysts at each site. Patients were followed for 9 months after the date of the first intervention. The institutional review board at each participating site approved the study.

Electronically stored data at each site were used, including membership files, inpatient and ambulatory visits, and pharmacy data.

### OUTCOMES

The primary outcome measure was  $\beta$ -blocker adherence (degree of prescription filling in an interval) derived from pharmacy prescription records by constructing a proportion-of-days-covered (PDC)<sup>21</sup>-per-month (defined as 30 days) measure, using the quantity dispensed and days supplied from each prescription. Previous analyses found good agreement between the recorded day's supply and audit of directions for use.<sup>22</sup> For consistency with other literature, we analyzed medication adherence as a continuous measure, as well as a monthly PDC of 80% or greater.

All patients were part of the primary outcome measure. Since not all patients necessarily had a current prescription at the time of the intervention, we undertook 2 secondary analyses to assess whether the intervention was associated with changes in discontinuation of  $\beta$ -blocker therapy or time to restarting  $\beta$ -blocker therapy. Discontinuation was defined as a complete lack of prescription filling during a given interval. Because of uncertainty regarding the definition of  $\beta$ -blocker discontinuation, we examined gaps of at least 1, 2, 3, and 4 months. We also examined time to restarting  $\beta$ -blocker therapy for patients without a current prescription at the time of the intervention. Since the wallet card materials also advised the patient to discuss the use of statins and ACEIs with their physician, we examined changes

in use of these agents as secondary end points. Data on over-the-counter aspirin use were not available.

We estimated the replication cost<sup>23</sup> of the intervention, including nonlabor costs of postage and printing, as well as labor costs of preparing the materials (eg, graphics and mailing) from prices paid and effort expended during the study.

### SAMPLE SIZE

We aimed to enroll 1000 patients to achieve 80% power using a 5% significance level (after taking account of clustering) to detect a 10% difference in adherence. A total of 907 patients met inclusion criteria, and after excluding patients who died or lost health plan eligibility before the intervention and during the follow-up period, the study population comprised 836 patients (intervention arm, n=426; and control arm, n=410).

### ANALYSIS

We examined the effectiveness of randomization by comparing demographic characteristics and preintervention PDC per month (ie, PDC from the date of the first  $\beta$ -blocker prescription following MI discharge until the intervention date) of intervention and control arm patients.

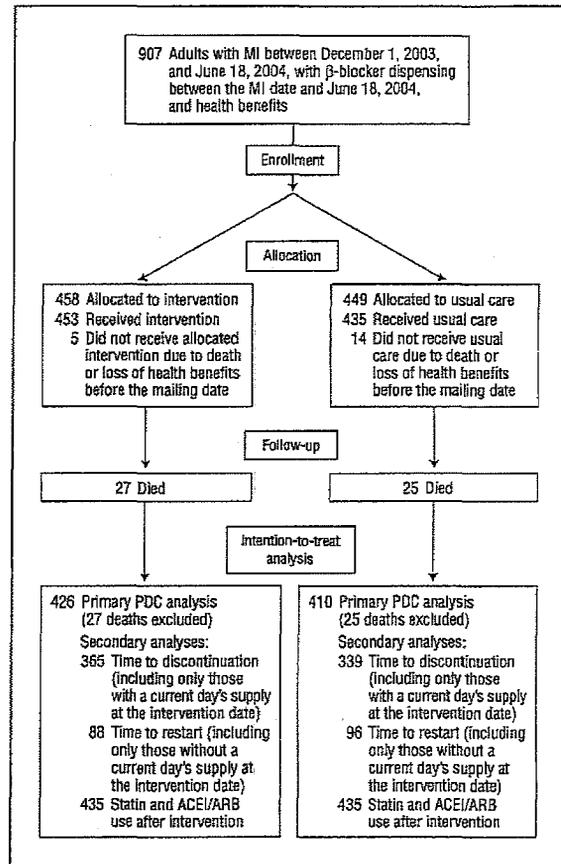
All analyses controlled for patient age, sex, annualized number of medications in the year before the intervention date (as comorbidity adjustment),<sup>24</sup> time between index  $\beta$ -blocker prescription and intervention date, and intervention site. Interactions between study arm and covariates were also investigated. We controlled for prior statin or ACEI and/or ARB use in secondary analyses on their postintervention use. Because the most common antiplatelet drug, aspirin, is over the counter, we were not able to control for prior antiplatelet drugs. All analyses were carried out using SAS version 8.2 (SAS Institute Inc, Cary, North Carolina) and HLM 6.0 (SSI, Lincolnwood, Illinois) statistical software.

#### Primary Analyses

Growth curve analysis<sup>25</sup> (also called multilevel modeling), a technique to estimate change in a patient's outcome over time, was used to evaluate the effect of the intervention on PDC. Time in months formed the first level of the model, with PDC as the dependent variable. For ease of interpretation, time was grand centered, setting the midpoint of the follow-up time to zero. In the second level, we modeled both the intercept and the time slope as a function of the covariates and study arm. Practice formed the third level of the model as individuals were nested within practices. Because one site did not perform randomization by practice, we tested site-by-arm interaction to determine whether the intervention's effect varied by level of randomization performed. Growth curve analysis was also used to estimate the likelihood of patients having at least an 80% PDC during the postintervention period using logistic regression; we also calculated the number of patients needed to treat. Because a PDC of 80% occurred more than 10% of the time in our sample, we corrected the resulting odds ratio so it could be interpreted as a relative risk (RR).<sup>26</sup>

#### Secondary Analyses

The secondary end points were (1) discontinuation of  $\beta$ -blocker therapy among patients with a current  $\beta$ -blocker prescription at the start of the intervention and (2) restarting  $\beta$ -blocker therapy among patients without a current  $\beta$ -blocker prescription at the start of the intervention. For these analyses we used Cox proportional hazards to model time to discon-



**Figure 1.** Patient flow diagram. ACEI indicates angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; MI, myocardial infarction; and PDC, proportion of days covered.

tinuation and time to restart, accounting for clusters, with treatment assignment as the main effect and variables to control for differences in medication supply and time between end of the last preintervention  $\beta$ -blocker prescription and the date of the intervention. Finally, we examined differences in statin or ACEI and/or ARB use between intervention and control patients using negative binomial regression, with correction for overdispersion and clustering.

## RESULTS

As **Figure 1** shows, a total of 907 patients in 142 total practices (13, 15, 19, and 95, by site) met all inclusion criteria and were enrolled in the study; 458 patients were randomized to the intervention arm and 449 to the control arm. Before the intervention date, 19 patients died or lost health plan eligibility (intervention arm, n=5; and control arm, n=14), another 52 patients (6%) died during the 9-month follow-up period (intervention arm, n=27; and control arm, n=25). Therefore, the primary analyses were based on 836 patients (intervention arm, n=426; and control arm, n=410). At the time of the first mailing, patients in the intervention group were a mean 138 days after MI (range, 34-225 days), and those in the control group were 134 days after MI (range, 38-226 days). Patients in the intervention arm and those in the control arm were similar in terms of

demographic and clinical characteristics (**Table 1**), and PDC per month in the 6-month period from MI discharge to the initial mailing was also similar between the 2 study arms (**Table 2**). In the intervention arm, PDC declined to 75% at the time of the initial direct-to-patient mailing, and PDC declined to 74% in the control arm. Baseline monthly PDC over time exhibited a similar pattern of drop-off for both groups, totaling about 13% per month in the first 2 months after the index  $\beta$ -blocker prescription, then slowing to less than 3%.

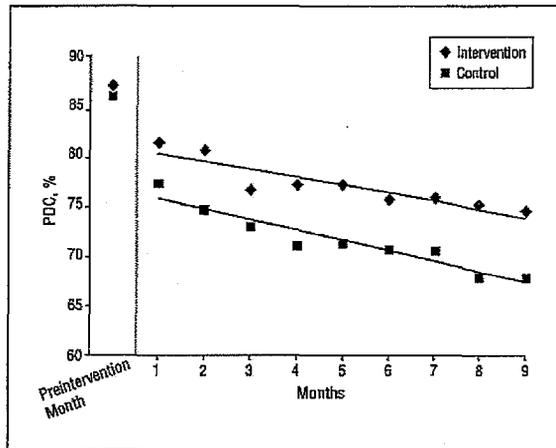
Our analysis showed that over the entire follow-up period, patients in the treatment arm had a mean absolute increase of 4.3% of days covered per month compared

with patients in the control arm (a 5.7% relative change from baseline), representing approximately 1.3 extra days of  $\beta$ -blocker coverage per month ( $P=.04$ ) (**Figure 2**). The intervention group experienced a smaller immediate drop in monthly PDC, and the subsequent rate of decline in PDC was not different between the 2 arms ( $P=.68$ ), indicating that the effect was immediate and sustained over time. We did not find a site-by-arm interaction, indicating that the treatment effect was consistent across sites. The intraclass correlation for practice was 0.016. To avoid estimating PDC after death, only patients who did not die during follow-up were included in the analysis ( $n=836$ ). An analysis including all patients yielded nearly identical results. Proportion of days covered in the month before the intervention did not differ appreciably (control arm, 86%; and intervention arm, 87%). None of the interactions of arm with the covariates were significant.

Across all months of follow-up, a mean of 64.8% of intervention patients had a PDC of 80% or greater compared with 58.5% of control group patients, suggesting a number needed to treat of 16. Patients in the intervention arm were 17% more likely (RR, 1.17; 95% CI, 1.02-

| Characteristic  | Intervention (n = 453) | Control (n = 435) |
|---|------------------------|-------------------|
| Male sex, %   | 68.7                   | 66.0              |
| Age, mean (SD), y   | 64.69 (14.19)          | 65.04 (13.38)     |
| Medicare, %   | 46.4                   | 47.1              |
| Medicaid, %   | 1.6                    | 1.6               |
| First $\beta$ -blocker after MI, %  |                        |                   |
| Acebutolol (n = 2)  | 0                      | 0.5               |
| Atenolol (n = 370)  | 41.5                   | 41.8              |
| Bisoprolol (n = 6)  | 0.7                    | 0.7               |
| Carvedilol (n = 44)   | 5.3                    | 4.6               |
| Labetalol (n = 3)   | 0.4                    | 0.2               |
| Metoprolol (n = 455)  | 51.0                   | 51.5              |
| Nadolol (n = 1)   | 0                      | 0.2               |
| Propranolol hydrochloride (n = 6)   | 0.9                    | 0.5               |
| Days from MI to index $\beta$ -blocker prescription, mean (SD)  | 12.04 (21.52)          | 11.79 (22.52)     |
| Days from MI to intervention, mean (SD)   | 134.13 (49.96)         | 138.29 (50.39)    |
| No. of angiotensin-converting enzyme inhibitor prescriptions 1 year before to the intervention, mean (SD) | 3.38 (3.16)            | 3.56 (3.40)       |
| No. of angiotensin receptor blocker prescriptions 1 year before to the intervention, mean (SD)            | 0.64 (2.12)            | 0.63 (2.05)       |
| No. of statin prescriptions 1 year before to the intervention, mean (SD)                                  | 4.35 (3.06)            | 4.35 (3.17)       |
| Total No. of unique medications 1 year before to the intervention, mean (SD)                              | 9.52 (7.74)            | 8.83 (7.48)       |

Abbreviation: MI, myocardial infarction.



**Figure 2.** Growth curve plot of proportion of days covered (PDC) by randomized group in the postintervention period. Estimated trend line from growth curve modeling, controlling for PDC in the month before the intervention, age, sex, baseline medication supply, total number of medications, and time since first  $\beta$ -blocker prescription.

| Months After Index $\beta$ -Blocker Prescription | Intervention |             |            |      |       | Control   |     |             |            |      | Total |           |     |             |            |      |       |           |
|--|--------------|-------------|------------|------|-------|-----------|-----|-------------|------------|------|-------|-----------|-----|-------------|------------|------|-------|-----------|
|  | No.          | Mean PDC, % | % With PDC |      |       |           | No. | Mean PDC, % | % With PDC |      |       |           | No. | Mean PDC, % | % With PDC |      |       |           |
|  |              |             | 0          | 1-20 | 21-79 | $\geq 80$ |     |             | 0          | 1-20 | 21-79 | $\geq 80$ |     |             | 0          | 1-20 | 21-79 | $\geq 80$ |
| 1  | 453          | 99.1        | 0          | 0.2  | 0.9   | 98.9      | 435 | 98.6        | 0          | 0    | 2.8   | 97.2      | 888 | 98.9        | 0          | 0.1  | 1.8   | 98.1      |
| 2  | 377          | 85.6        | 8.0        | 1.3  | 9.8   | 80.9      | 368 | 84.4        | 9.5        | 2.5  | 6.5   | 81.5      | 745 | 85.0        | 8.7        | 1.9  | 8.2   | 81.2      |
| 3  | 304          | 82.5        | 10.2       | 1.3  | 11.8  | 76.6      | 301 | 81.4        | 11.3       | 2.7  | 8.3   | 77.7      | 605 | 81.9        | 10.7       | 2.0  | 10.1  | 77.2      |
| 4  | 227          | 79.6        | 12.8       | 4.0  | 7.1   | 76.2      | 222 | 77.7        | 12.6       | 3.6  | 12.2  | 71.6      | 449 | 78.7        | 12.7       | 3.8  | 9.6   | 73.9      |
| 5  | 139          | 76.5        | 15.1       | 2.9  | 10.1  | 71.9      | 156 | 75.5        | 16.0       | 1.9  | 12.8  | 69.2      | 295 | 76.0        | 15.6       | 2.4  | 11.5  | 70.5      |
| 6  | 73           | 74.9        | 16.4       | 5.5  | 45.5  | 72.6      | 82  | 73.8        | 19.5       | 1.2  | 11.0  | 68.3      | 155 | 74.3        | 18.1       | 3.2  | 8.4   | 70.3      |

\*Not all patients had a full month of observation after their MI to calculate a meaningful monthly PDC. Because patients may have had their MI up to 7.5 months before the date of the intervention mailing, fewer patients were observed with each passing month. The index  $\beta$ -blocker prescription is the first  $\beta$ -blocker prescription between the date of MI and the intervention date.

**Table 3. Cox Regression of Discontinuation by Study Arm Among Those With Current Day's Supply at Time of Intervention**

| Discontinuation, Months of Gap in Filling Prescription | No. (%) With Gap |          | Crude Hazard Ratio <sup>a</sup> (95% Confidence Interval) | Adjusted Hazard Ratio (95% Confidence Interval) |
|--|------------------|----------|---|---|
|  | Intervention     | Control  |   |   |
| 1  | 104 (23)         | 110 (25) | 0.85 (0.65-1.12)  | 0.89 (0.67-1.19)                                |
| 2  | 63 (14)          | 67 (15)  | 0.86 (0.61-1.22)  | 0.95 (0.67-1.33)                                |
| 3  | 43 (9)           | 51 (12)  | 0.77 (0.51-1.16)  | 0.87 (0.60-1.26)                                |
| 4  | 30 (7)           | 37 (9)   | 0.74 (0.46-1.20)  | 0.85 (0.54-1.35)                                |

<sup>a</sup>Because the crude hazard ratio comes from a Cox regression model (and thus accounts for time), the crude hazard ratio cannot be derived directly from the Table.

**Table 4. Per-Person Use of ACEIs, ARBs, and Statins Following the Intervention**

|                   | Mean No. of Prescriptions |                   | Rate Ratio (95% Confidence Interval) |
|-------------------|---------------------------|-------------------|--------------------------------------|
|                   | Intervention (n = 453)    | Control (n = 435) |                                      |
| ACEIs and/or ARBs | 4.27                      | 3.72              | 1.18 (1.04-1.33)                     |
| Statins           | 4.85                      | 4.68              | 1.03 (0.96-1.12)                     |

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers.

1.29) to have a PDC of 80% or greater over the entire postintervention period (data not shown); the rate of decline was not different between the 2 arms ( $P = .40$ ).

For the subset of 704 patients (79%) with a current day's supply at the time of the intervention, no difference was seen in the hazard ratio for discontinuation of  $\beta$ -blocker therapy between intervention and control groups (Table 3; ie, the 95% CIs contained 1.0). Similarly, time to restart (data not shown) for the 184 patients (21%) without a current day's supply at the time of the intervention was not statistically different (hazard ratio, 1.41; 95% CI, 0.97-2.04).

We found that postintervention prescriptions dispensed for ACEIs and ARBs increased by 17% (Table 4) for the intervention group relative to the control group (RR, 1.18; 95% CI, 1.04-1.33), but there was no difference in prescriptions dispensed for statins (RR, 1.03; 95% CI, 0.96-1.12).

The replication cost of the intervention was estimated to be \$5 to \$10 per patient, with larger health plans at the lower end of the range; this excludes cost offsets (eg, decreased cardiac events) from enhanced adherence.

#### COMMENT

Using a simple, low-cost, direct-to-patient mass mailing, we found that 17% more post-MI patients had a PDC of at least 80% (RR, 1.17; 95% CI, 1.02-1.29) with  $\beta$ -blocker therapy. The number of intervention packets mailed for 1 additional adherent patient was 16. Our findings are important because many health care providers, particularly integrated delivery systems, routinely use mass mailed interventions as a way to promote healthy behaviors. We studied the intervention's effect in a real-world

setting with very few inclusion requirements, maximizing the finding's applicability. Perhaps most importantly, we assessed all eligible post-MI patients at the participating sites; limited participation was an important limitation to other adherence studies.<sup>14</sup> Rarely are such interventions tested in a randomized fashion, as we did. Our findings are largely consistent with existing literature in other diseases showing modest, positive effects for mailed interventions (but often multimodal) on medication adherence.<sup>27</sup>

Studies of methods to improve the use of  $\beta$ -blockers following MI in the US health care system have focused mainly on providers.<sup>28,29</sup> Mailed prompts to patients and providers have shown only marginal success in other health care settings<sup>16</sup>; to our knowledge, our randomized trial is the first to assess the impact of a customized, direct-to-patient intervention designed to increase adherence to  $\beta$ -blocker therapy following MI in the US health care setting.

Our finding that 17% more patients are adherent is encouraging. Poor adherence has been linked to worsening outcomes, including death, in the context of post-MI use of  $\beta$ -blockers,<sup>5,30</sup> so it seems likely that enhancing patient adherence to  $\beta$ -blocker therapy following MI leads to improved outcomes. For example, Choudhry and colleagues<sup>31</sup> estimate that if only 2.5% more patients adhere to therapy, providing secondary MI prevention medications (including  $\beta$ -blockers) for free (much more expensive than our intervention) would be cost saving to a health plan through decreased cardiac events.

Similar to other studies,<sup>6</sup> we found the drop-off in adherence to be most dramatic in the initial 2 months after the index  $\beta$ -blocker prescription (about 13%). This suggests that patients in the initial post-MI period deserve particular attention, but like previous studies, the decline in adherence we observed continues at a fairly steady rate (about 3% per month).

We studied the intervention's effect in prepaid integrated care delivery, potentially limiting the generalizability to other insurance types. We did not find evidence of statistical interaction, but our study may have been underpowered to detect modest interactions. We used a proxy for adherence, namely prescriptions dispensed, that reflects the health care system's capability to deliver medication to the patient; actual drug-taking behavior may differ. In addition, we have little empirical evidence to use for determining the minimal level of medication adherence necessary in the context of post-MI  $\beta$ -blocker use. We used a PDC of 80%, similar to other

research in this clinical area,<sup>6,21</sup> and also report the mean adherence level observed. Our estimates of adherence did not take account of the following 2 competing explanations for adherence: (1) changes to a patient's regimen after dispensing, making our estimates susceptible to both overestimation and underestimation of adherence, and (2) we did not correct for hospital stays, during which time a patient's outpatient medication supply would likely not be used. Because we were most interested in the comparative effect of the intervention, our randomized design minimizes both of these concerns. As others<sup>14</sup> have noted, assessment of the impact on outcomes is missing in most adherence studies; our study is similarly limited. In addition, future work should consider both the potential cost-effectiveness of such an adherence intervention and the opportunity costs of focusing on 1 therapy (eg, diminishing adherence to other therapies).

Increasing adherence to evidence-based therapies for patients with MI is a priority for improving quality of care. We found that a low-cost, easily replicable intervention can have an impact on patient's adherence to  $\beta$ -blocker therapy following MI.

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## INVITED COMMENTARY

The decline in mortality from cardiovascular disease in the United States over the past 30 years has been due in large part to the steady adoption of new preventive and therapeutic strategies. Over the past 10 to 15 years, there has been increasing recognition that broad adoption of established strategies may have value equivalent to that of the adoption of new strategies. As a result of this recognition, there have been large-scale efforts to improve rates of prescription of proven medications, and these efforts are achieving success.<sup>1</sup> On the heels of this success, quality-of-care efforts are evolving further and are beginning to focus on ensuring that patients actually take these proven medications once they have been prescribed.

The study by Smith and colleagues of an intervention to improve  $\beta$ -blocker adherence in this issue of the *Archives* is thus a welcome addition to the literature. The authors sent information about  $\beta$ -blockers to patients who had had a myocardial infarction and assessed the effect of the mailing on subsequent adherence. Strengths of the study include the use of focus groups to tailor the content of the mailing, a sample size large enough to detect a small benefit, and reliance on a simple, easily reproduced intervention. The principal finding of the study was that the proportion of days covered, a standard measure of adherence based on pharmacy records,<sup>2</sup> was modestly but significantly greater by approximately 5% in the intervention group. One concern with interventions targeted at a single medication is that they may improve performance related to that medication but lower performance related to other medications. In the study by Smith and colleagues, use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers improved and statin use remained stable, suggesting that the intervention was not a "zero sum game," although it will be important in the future to assess for negative effects on adherence to medications for important comorbid conditions such as diabetes. The authors were also unable to assess

aspirin use, but since aspirin prescription is universally high in contemporary practice, this is unlikely to be an important covariate. Moving the intervention closer to hospital discharge may have enhanced its benefits, since the fall-off in adherence is steepest approximately 1 month after discharge.

Readers should not be discouraged by the relatively modest reported improvement. Adherence is a complex behavior affected by a number of factors, some intrinsic to patients such as their understanding of the medication and their belief in their abilities to improve their health and some extrinsic to patients such as medication cost and regimen complexity.<sup>3</sup> An intervention designed to affect only 1 of these factors would be expected to have a small effect. As pointed out by the authors, even a small improvement in adherence with  $\beta$ -blockers following myocardial infarction is likely to have a large effect at a population level. Other health maintenance organizations seeking to improve cardiovascular outcomes should consider adopting the strategy that Smith and colleagues have reported on, and adaptation of the strategy for other settings should be investigated.

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AMENDED IN SENATE APRIL 10, 2008  
AMENDED IN SENATE MARCH 27, 2008

**SENATE BILL**

**No. 1270**

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**Introduced by Senator Cedillo**

February 19, 2008

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~~An act to amend Sections 4034 and 4163 of, and to repeal Sections 4163.1 and 4163.5 of, the Business and Professions Code, relating to pharmacy.~~ *An act to add and repeal Section 4014 of the Business and Professions Code, relating to pharmacy.*

LEGISLATIVE COUNSEL'S DIGEST

SB 1270, as amended, Cedillo. Pharmacy: ~~dangerous drug and device pedigrees.~~ *Electronic Pedigree Task Force.*

Existing law, the Pharmacy Law, provides for the licensure and regulation of the practice of pharmacy and the sale of dangerous drugs or dangerous devices by the California State Board of Pharmacy, in the Department of Consumer Affairs. On and after January 1, 2009, existing law requires a pedigree, as defined, to accompany each distribution of a dangerous drug, and prohibits a wholesaler or pharmacy from selling, trading, transferring, or acquiring a dangerous drug without a pedigree. Existing law authorizes the board to extend the compliance date for these pedigree requirements to January 1, 2011, in specified circumstances. ~~Existing law provides exceptions from the pedigree requirements for certain transactions. A knowing violation of the Pharmacy Law is a crime.~~

~~This bill would delete the pedigree provisions and would instead require the certification or pedigree of distributors or persons who distribute dangerous drugs manufactured on or after January 1, 2009, outside of the normal chain of distribution, as defined. The bill would authorize the board to require verification of specific transactions. The~~

~~bill would prohibit a wholesaler from selling, trading, transferring, or acquiring a dangerous drug without complying with this requirement, and would, commencing January 1, 2011, prohibit a pharmacy from acquiring, selling, trading, or transferring a dangerous drug without complying with this requirement. The bill would exempt specified transactions from these requirements.~~

~~Because this bill would impose new requirements under the Pharmacy Law, the knowing violation of which would be a crime, it would impose a state-mandated local program.~~

~~The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.~~

~~This bill would provide that no reimbursement is required by this act for a specified reason.~~

*This bill would require the board to establish the Electronic Pedigree Task Force, with a specified membership, and would require the staff of the board to support the needs of the task force. The bill would impose specified duties on the task force, including the duty to submit an annual report regarding task force findings to the board and specified legislative committees. The bill would make the provisions regarding the task force inoperative on the later of July 1, 2012, or the date upon which requirements for a pedigree become effective, and would repeal them as of January 1 of the next year.*

Vote: majority. Appropriation: no. Fiscal committee: yes.  
State-mandated local program: *yes-no.*

*The people of the State of California do enact as follows:*

- 1 *SECTION 1. Section 4014 is added to the Business and*
- 2 *Professions Code, to read:*
- 3 *4014. (a) The board shall establish the Electronic Pedigree*
- 4 *Task Force. The task force shall be comprised of the following*
- 5 *members, who shall serve voluntarily and without compensation:*
- 6 *(1) One member from the California Retailers Association.*
- 7 *(2) One member from the Health Systems Pharmacists*
- 8 *Association.*
- 9 *(3) One member from the California Pharmacists Association.*
- 10 *(4) One member of the California Primary Care Association.*
- 11 *(5) One member from the California Hospital Association.*

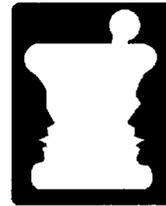
- 1 (6) One member from the California State Association of  
2 Counties.
- 3 (7) One member from an animal veterinary association.
- 4 (8) Two members from the Pharmaceutical Research and  
5 Manufacturers of America.
- 6 (9) Two members from the California Healthcare Institute, Inc.
- 7 (10) Two members from the Generic Pharmaceutical  
8 Association.
- 9 (11) One member from the Healthcare Distribution Management  
10 Association.
- 11 (12) One member from AltaMed Health Services Corporation.
- 12 (13) One member from the National Coalition of Pharmacies.
- 13 (14) One member from the National Association of Chain Drug  
14 Stores.
- 15 (15) One member from the pedigree technology manufacturers.
- 16 (b) The task force shall hold quarterly public meetings at various  
17 locations within the state. A majority of members shall be present  
18 in order to conduct a meeting of the task force.
- 19 (c) The task force shall elect a chairperson and a vice  
20 chairperson.
- 21 (d) The task force shall have the following duties:
  - 22 (1) To provide the board with updates regarding the status of  
23 task force member organizations with regard to implementing the  
24 statutory electronic pedigree requirements.
  - 25 (2) To notify the board of implementation challenges regarding  
26 electronic pedigree law.
  - 27 (3) To submit an annual report to the board and to the Senate  
28 Committee on Business, Professions and Economic Development  
29 and the Assembly Committee on Business and Professions  
30 regarding task force findings.
- 31 (e) The staff of the board shall support the needs of the task  
32 force.
- 33 (f) This section shall become inoperative on either July 1, 2012,  
34 or the date upon which the requirements for a pedigree set forth  
35 in Sections 4034 and 4163 become effective, as determined by the  
36 board, whichever is later, and, as of January 1 of the next year  
37 shall be repealed.

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**All matter omitted in this version of the bill  
appears in the bill as amended in Senate,  
March 27, 2008 (JR11)**

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**CALIFORNIA STATE BOARD OF PHARMACY  
BILL ANALYSIS**



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**BILL NUMBER: SB 1270**

**VERSION: As Amended April 10, 2008**

**AUTHOR: Cedillo**

**SPONSOR: Pharmaceutical industry**

**RECOMMENDED POSITION:**

**SUBJECT: Pharmacy: dangerous drug and devices pedigree**

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**EXISTING LAW:**

1. On or after January 1, 2009 requires an electronic pedigree to accompany each distribution of a dangerous drug.
2. Prohibits a wholesaler or pharmacy from selling, trading, transferring, or acquiring a dangerous drug without a pedigree.
3. Authorizes the board to extend the compliance date for these pedigree requirements to January 1, 2011.
4. Provides exceptions from the pedigree requirements for certain transactions.

**THIS BILL WOULD:**

1. Would create an Electronic Pedigree Taskforce, consisting of specified representatives from the pharmaceutical industry drug supply chain, to provide the board with updates regarding industry readiness of the implementation on the pedigree requirement and the challenges thereof.
2. It also requires the task force to provide an annual report to the board and the Senate and Assembly policies committees with jurisdiction over the issue.

**HISTORY:**

**Dates Actions**

03/27/08 Mar. 27 From committee with author's amendments. Read second time.  
Amended. Re-referred to Com. on B., P. & E.D.

03/13/08 Mar. 13 Set for hearing April 7.

02/28/08 Feb. 28 To Com. on B., P. & E.D.

02/20/08 Feb. 20 From print. May be acted upon on or after March 21.

02/19/08 Feb. 19 Introduced. Read first time. To Com. on RLS. for assignment. To print.



AMENDED IN SENATE APRIL 3, 2008

**SENATE BILL**

**No. 1504**

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**Introduced by Senator Ridley-Thomas**

February 21, 2008

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An act to amend Sections 4052.5 and 4073 of the Business and Professions Code, relating to pharmacies.

LEGISLATIVE COUNSEL'S DIGEST

SB 1504, as amended, Ridley-Thomas. Antiepileptic drug products: substitution.

Existing law, the Pharmacy Law, provides for the licensure and regulation of pharmacists by the California State Board of Pharmacy, and makes a knowing violation of the act a crime. Existing law authorizes a pharmacist filling a prescription order for a drug product prescribed by its trade or brand name to substitute a generic drug product, subject to specified requirements. Existing law authorizes a pharmacist filling a prescription order for a drug product to substitute a drug product with a different form of medication having the same active chemical ingredients of equivalent strength and duration of therapy as the prescribed drug product, subject to specified requirements.

This bill would prohibit a pharmacist filling a prescription order for an antiepileptic drug or formulation of an antiepileptic drug, prescribed by its trade, brand, or generic name for the treatment or prevention of epileptic seizures, from substituting a drug product pursuant to those provisions without prior notification of the prescriber and the signed consent of the patient or the patient's parent, legal guardian, or spouse.

Because this bill would impose a new prohibition under the Pharmacy Law, the violation of which would be a crime, it would impose a state-mandated local program.

The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

Vote: majority. Appropriation: no. Fiscal committee: yes.  
State-mandated local program: yes.

*The people of the State of California do enact as follows:*

1 SECTION 1. Section 4052.5 of the Business and Professions  
2 Code is amended to read:

3 4052.5. (a) In addition to the authority allowed under Section  
4 4073, but subject to the express prohibition set forth in subdivision  
5 (f) of Section 4073, a pharmacist filling a prescription order for a  
6 drug product may select a different form of medication with the  
7 same active chemical ingredients of equivalent strength and  
8 duration of therapy as the prescribed drug product when the change  
9 will improve the ability of the patient to comply with the prescribed  
10 drug therapy.

11 (b) In no case shall a selection be made pursuant to this section  
12 if the prescriber personally indicates, either orally or in his or her  
13 own handwriting, "Do not substitute" or words of similar meaning.  
14 Nothing in this subdivision shall prohibit a prescriber from  
15 checking a box on a prescription marked "Do not substitute" if the  
16 prescriber personally initials the box or checkmark.

17 (c) Selection pursuant to this section is within the discretion of  
18 the pharmacist, except as provided in subdivision (b). The  
19 pharmacist who selects the drug product to be dispensed pursuant  
20 to this section shall assume the same responsibility for selecting  
21 the dispensed drug product as would be incurred in filling a  
22 prescription for a drug product using the prescribed form of  
23 medication. There shall be no liability on the prescriber for an act  
24 or omission by a pharmacist in selecting, preparing, or dispensing  
25 a drug product pursuant to this section.

26 (d) This section shall apply to all prescriptions, including those  
27 presented by or on behalf of persons receiving assistance from the  
28 federal government or pursuant to the California Medical  
29 Assistance Program set forth in Chapter 7 (commencing with

1 Section 14000) of Part 3 of Division 9 of the Welfare and  
2 Institutions Code.

3 (e) When a substitution is made pursuant to this section, the use  
4 of the different form of medication shall be communicated to the  
5 patient, and the name of the dispensed drug product shall be  
6 indicated on the prescription label, unless the prescriber orders  
7 otherwise.

8 (f) This section shall not permit substitution between long-acting  
9 and short-acting forms of a medication with the same chemical  
10 ingredients or between one drug product and two or more drug  
11 products with the same chemical ingredients.

12 SEC. 2. Section 4073 of the Business and Professions Code is  
13 amended to read:

14 4073. (a) A pharmacist filling a prescription order for a drug  
15 product prescribed by its trade or brand name may select another  
16 drug product with the same active chemical ingredients of the same  
17 strength, quantity, and dosage form, and of the same generic drug  
18 name as determined by the United States Adopted Names (USAN)  
19 and accepted by the federal Food and Drug Administration (FDA),  
20 of those drug products having the same active chemical ingredients.

21 (b) In no case shall a selection be made pursuant to this section  
22 if the prescriber personally indicates, either orally or in his or her  
23 own handwriting, "Do not substitute," or words of similar meaning.  
24 Nothing in this subdivision shall prohibit a prescriber from  
25 checking a box on a prescription marked "Do not substitute";  
26 provided that the prescriber personally initials the box or  
27 checkmark. To indicate that a selection shall not be made pursuant  
28 to this section for an electronic data transmission prescription as  
29 defined in subdivision (c) of Section 4040, a prescriber may  
30 indicate "Do not substitute," or words of similar meaning, in the  
31 prescription as transmitted by electronic data, or may check a box  
32 marked on the prescription "Do not substitute." In either instance,  
33 it shall not be required that the prohibition on substitution be  
34 manually initialed by the prescriber.

35 (c) Selection pursuant to this section is within the discretion of  
36 the pharmacist, except as provided in subdivisions (b) and (f). The  
37 person who selects the drug product to be dispensed pursuant to  
38 this section shall assume the same responsibility for selecting the  
39 dispensed drug product as would be incurred in filling a  
40 prescription for a drug product prescribed by generic name. There

1 shall be no liability on the prescriber for an act or omission by a  
2 pharmacist in selecting, preparing, or dispensing a drug product  
3 pursuant to this section. In no case shall the pharmacist select a  
4 drug product pursuant to this section unless the drug product  
5 selected costs the patient less than the prescribed drug product.  
6 Cost, as used in this subdivision, is defined to include any  
7 professional fee that may be charged by the pharmacist.

8 (d) This section shall apply to all prescriptions, including those  
9 presented by or on behalf of persons receiving assistance from the  
10 federal government or pursuant to the California Medical  
11 Assistance Program set forth in Chapter 7 (commencing with  
12 Section 14000) of Part 3 of Division 9 of the Welfare and  
13 Institutions Code.

14 (e) When a substitution is made pursuant to this section, the use  
15 of the cost-saving drug product dispensed shall be communicated  
16 to the patient and the name of the dispensed drug product shall be  
17 indicated on the prescription label, except where the prescriber  
18 orders otherwise.

19 (f) In no case shall a pharmacist filling a prescription order for  
20 an antiepileptic drug, or formulation of an antiepileptic drug  
21 prescribed by its trade, brand, or generic name for the treatment  
22 or prevention of epileptic seizures, substitute a drug product  
23 pursuant to this section or subdivision (a) of Section 4052.5 without  
24 prior notification of the prescriber and the signed consent to the  
25 substitution from the patient or the patient's parent, legal guardian,  
26 or spouse.

27 For purposes of this subdivision, the following definitions apply:

28 (1) "Antiepileptic drug" means any drug approved by the United  
29 States Food and Drug Administration (FDA) for the treatment of  
30 epilepsy or the treatment or prevention of epileptic seizures.

31 (2) "Epilepsy" means a neurological condition characterized by  
32 recurrent seizures.

33 (3) "Seizure" means an acute clinical change secondary to a  
34 brief disturbance in the electrical activity of the brain.

35 (4) ~~"Substitute"~~ "Select," "selection," "substitute," or  
36 "substitution" means the substitution for an antiepileptic drug  
37 originally prescribed ~~of a~~ *with any other* version of the same  
38 antiepileptic drug, including a generic version for the prescribed  
39 generic version, a generic version by one manufacturer for a generic  
40 version by a different manufacturer, or a different formulation of

1 ~~the prescribed antiepileptic drug.~~ *antiepileptic drug, including, but*  
2 *not limited to, any of the following:*

3 (A) *A generic version for the prescribed trade or brand name*  
4 *drug.*

5 (B) *A trade or brand name drug for the prescribed generic*  
6 *version.*

7 (C) *A generic drug produced by one manufacturer for a generic*  
8 *drug produced by a different manufacturer.*

9 (D) *Any dosage form of that prescribed antiepileptic drug that*  
10 *differs from the dosage form originally prescribed by the*  
11 *prescriber.*

12 SEC. 3. No reimbursement is required by this act pursuant to  
13 Section 6 of Article XIII B of the California Constitution because  
14 the only costs that may be incurred by a local agency or school  
15 district will be incurred because this act creates a new crime or  
16 infraction, eliminates a crime or infraction, or changes the penalty  
17 for a crime or infraction, within the meaning of Section 17556 of  
18 the Government Code, or changes the definition of a crime within  
19 the meaning of Section 6 of Article XIII B of the California  
20 Constitution.

AMENDED IN SENATE APRIL 9, 2008

**SENATE BILL**

**No. 1594**

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**Introduced by Senator Steinberg**

February 22, 2008

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An act to add Article 5 (commencing with Section 125286.1) to Chapter 2 of Part 5 of Division 106 of the Health and Safety Code, relating to bleeding disorders.

LEGISLATIVE COUNSEL'S DIGEST

SB 1594, as amended, Steinberg. Bleeding disorders: blood clotting products.

Existing law, the Holden-Moscone-Garamendi Genetically Handicapped Person's Program, requires the Director of Health Care Services to establish and administer a program for the medical care of persons with genetically handicapping conditions, including hemophilia.

This bill would impose specified requirements on providers of blood clotting products for home use used for the treatment and prevention of symptoms associated with bleeding disorders, including all forms of hemophilia. This bill would ~~also~~ authorize the State Department of Health Care Services to adopt regulations necessary to implement these provisions.

*This bill would require the California State Board of Pharmacy to administer and enforce the above provisions.*

Vote: majority. Appropriation: no. Fiscal committee: yes.  
State-mandated local program: no.

*The people of the State of California do enact as follows:*

1 SECTION 1. Article 5 (commencing with Section 125286.1)  
2 is added to Chapter 2 of Part 5 of Division 106 of the Health and  
3 Safety Code, to read:

4  
5 Article 5. Standards of Service for Providers of Blood Clotting  
6 Products for Home Use Act

7  
8 125286.1. This article shall be known and may be cited as the  
9 Standards of Service for Providers of Blood Clotting Products for  
10 Home Use Act.

11 125286.2. The Legislature hereby finds and declares all of the  
12 following:

13 (a) Hemophilia is a rare, hereditary, bleeding disorder affecting  
14 at least 4,000 persons in California and is a chronic, lifelong, and  
15 incurable, but treatable, disease.

16 (b) Until the 1970's, people with severe hemophilia suffered  
17 from uncontrollable internal bleeding, crippling orthopedic  
18 deformities, and a shortened lifespan. More recently, the production  
19 of highly purified blood clotting factors have provided people with  
20 hemophilia and other bleeding disorders with the opportunity to  
21 lead normal lives, free of pain and crippling arthritis.

22 (c) The preferred method of treatment of hemophilia today is  
23 intravenous injection, or infusion, of prescription blood clotting  
24 products several times per week, along with case management and  
25 specialized medical care at a federally designated regional  
26 hemophilia treatment center.

27 (d) Pharmacies and other entities specializing in the delivery of  
28 blood clotting products and related equipment, supplies, and  
29 services for home use form a growing enterprise in California.  
30 ~~Some~~ All of these entities are licensed by the state or are located  
31 at federally designated regional hemophilia treatment centers, or  
32 both, ~~but many of these entities are neither licensed nor located at~~  
33 ~~hemophilia treatment centers.~~

34 (e) Timely access to federally designated regional hemophilia  
35 centers and appropriate products and services in the home,  
36 including infusion of blood clotting products and related  
37 equipment, and supplies and services for persons with hemophilia  
38 and other bleeding disorders, reduces mortality and bleeding-related

1 hospitalizations, and is extremely cost effective, according to the  
2 federal Centers for Disease Control and Prevention and the Medical  
3 and Scientific Advisory Council of the National Hemophilia  
4 Foundation.

5 (f) Eligible persons with hemophilia or other bleeding disorders  
6 may receive treatment through the Genetically Handicapped  
7 Persons Program, the California Children's Services Program, and  
8 Medi-Cal. Access to quality blood clotting products for home use  
9 and related equipment, supplies, and services for people with  
10 hemophilia or other bleeding disorders promotes cost containment  
11 in each of these publicly funded programs as well as in the health  
12 insurance and health care industries more generally.

13 (g) For the benefit of persons with hemophilia or other bleeding  
14 disorders, as well as for cost containment in health care, the  
15 purposes of this article are to do the following:

16 (1) Establish standards of service for entities that deliver blood  
17 clotting products and related equipment, supplies, and services for  
18 home use.

19 (2) Promote access to a full range of essential, cost-effective,  
20 lifesaving, blood clotting products and related equipment, supplies,  
21 and high-quality services for home use for persons with hemophilia  
22 and other bleeding disorders.

23 125286.3. Unless context otherwise requires, the following  
24 definitions shall apply for purposes of this article:

25 (a) "340B Program" means an outpatient pharmacy licensed to  
26 dispense blood clotting products in California and that is  
27 conditionally or fully designated as a covered entity under the  
28 Veterans Health Care Act of 1992 (Public Law 102-585), which  
29 enacted Section 340B of the Public Health Service Act (41 U.S.C.  
30 Sec. 201 et seq.).

31 (b) "Assay" means the amount of a particular constituent of a  
32 mixture or of the biological or pharmacological potency of a drug.

33 (c) "Ancillary infusion equipment and supplies" means the  
34 equipment and supplies required to infuse a blood clotting product  
35 into a human vein, including, but not limited to, syringes, needles,  
36 cyro cuffs, sterile gauze, field pads, gloves, alcohol swabs, numbing  
37 creams, tourniquets, medical tape, sharps or equivalent biohazard  
38 waste containers, and cold compression packs.

39 (d) "Bleeding disorder" means a medical condition characterized  
40 by a severe deficiency or absence of one or more essential blood

1 clotting proteins in the human blood, often called “factors,”  
2 including all forms of hemophilia and other bleeding disorders  
3 that result in uncontrollable bleeding or abnormal blood clotting.

4 (e) “Blood clotting product” means an intravenously  
5 administered medicine manufactured from human plasma or  
6 recombinant biotechnology techniques, approved for distribution  
7 by the federal Food and Drug Administration, that is used for the  
8 treatment and prevention of symptoms associated with bleeding  
9 disorders. Blood clotting products include, but are not limited to,  
10 Factor VII, Factor VIIa, Factor VIII, and Factor IX products, von  
11 Willebrand Factor products, bypass products for patients with  
12 inhibitors, and activated prothrombin complex concentrates.

13 (f) “Consumer” means a person needing a blood clotting product  
14 for home use.

15 (g) “Emergency” means a situation in which a prudent layperson  
16 could reasonably believe that the consumer’s condition requires  
17 immediate medical attention.

18 (h) “Hemophilia” means a human bleeding disorder caused by  
19 a hereditary deficiency of the Factors I, VII, VIII, IX, XI, or XII  
20 blood clotting protein in human blood.

21 (i) “Hemophilia treatment center” means a facility for the  
22 treatment of bleeding disorders, including, but not limited to,  
23 hemophilia, that receives funding from the federal government  
24 sources, including, but not limited to, the federal Centers for  
25 Disease Control and Prevention and the federal Health Resources  
26 and Services Administration (HRSA) of the United States  
27 Department of Health and Human Services.

28 (j) “Home nursing services” means specialized nursing care  
29 provided in the home setting to assist a patient in the reconstitution  
30 and administration of blood clotting products.

31 (k) “Home use” means infusion or other use of a blood clotting  
32 product in a place other than a state-recognized hemophilia  
33 treatment center. Places where home use occurs include, without  
34 limitation, a home, hospital, emergency room, clinic, or other  
35 physician office.

36 (l) “Provider of blood clotting products for home use” means a  
37 seller and provider of blood clotting products, ancillary infusion  
38 equipment, home nursing services, and patient assistance for the  
39 management of bleeding disorders for home use. These providers  
40 include, without limitation, ~~340~~ 340B programs, other pharmacies,

1 and, when treatment is not provided onsite, hemophilia treatment  
2 centers.

3 125286.4. Each provider of blood clotting products for home  
4 use shall meet all of the following requirements:

5 (a) Have sufficient knowledge and understanding of bleeding  
6 disorders and the medical and psychosocial management thereof,  
7 including, but not limited to, home therapy.

8 (b) Have sufficient experience providing services to persons  
9 with bleeding disorders.

10 (c) Ensure that its customer service staff meets the requirements  
11 of subdivisions (a) and (b).

12 (d) Have a pharmacist available at all times, 24 hours a day,  
13 seven days a week, every day of the year, either onsite or on call,  
14 to fill prescriptions for blood clotting products.

15 (e) Supply blood clotting products and home nursing services,  
16 as prescribed by the consumer's treating physician, and not make  
17 any substitutions of blood clotting products or assay amounts  
18 without the prior written approval of the treating physician.

19 (f) Ask the prescribing physician which specific blood clotting  
20 product is intended whenever a prescription does not indicate the  
21 specific product and then use the product named in the physician's  
22 response.

23 (g) Supply all brands of blood clotting products approved by  
24 the federal Food and Drug Administration in multiple assay ranges  
25 (low, medium, and high, as applicable) and vial sizes, including  
26 products manufactured from human plasma and those manufactured  
27 with recombinant biotechnology techniques.

28 (h) Supply all needed ancillary infusion equipment and supplies  
29 with each prescription.

30 (i) Maintain adequate stocks of blood clotting products and  
31 ancillary infusion equipment and supplies.

32 (j) Store and ship, or otherwise deliver, all blood clotting  
33 products in conformity with all *state and* federally mandated  
34 standards.

35 (k) When home nursing services are prescribed by the treating  
36 physician, provide these services either directly or through a  
37 reliable third party and coordinate pharmacy services with the third  
38 party when one is used to provide home nursing services.

- 1 (l) Upon receiving a nonemergency prescription, ship the  
2 prescribed blood clotting products and ancillary infusion equipment  
3 and supplies to the consumer within:
- 4 (1) Forty-eight hours or less for established consumers.  
5 (2) Three business days or less for new consumers.
- 6 (m) Upon receiving a prescription for an emergency situation,  
7 deliver prescribed blood products, ancillary infusion equipment  
8 and supplies, medications, and home nursing services to the  
9 consumer within three hours after receipt of the prescription.
- 10 (n) Maintain 24-hour oncall service seven days a week for every  
11 day of the year, adequately screen phone calls for emergencies,  
12 and respond to all phone calls within one hour or less.
- 13 (o) Provide consumers who have ordered their products with a  
14 designated contact phone number for reporting problems with a  
15 delivery and respond to these calls immediately.
- 16 (p) Provide patients with notification of recalls and withdrawals  
17 of blood clotting products and ancillary infusion equipment within  
18 24 hours and participate in the National Patient Notification System  
19 for blood clotting product recalls.
- 20 (q) Provide language translation services, both over the phone  
21 and in person, as needed by the consumer.
- 22 (r) Have a detailed plan for meeting the requirements of this  
23 article in the event of a natural or manmade disaster or other  
24 disruption of normal business operations.
- 25 (s) Provide for proper collection, removal, and disposal of  
26 hazardous waste pursuant to state and federal law, including, but  
27 not limited to, sharps containers for the removal and disposal of  
28 medical waste.
- 29 (t) Clearly inform the consumer of his or her copay, deductible,  
30 and coinsurance payment responsibilities each time he or she orders  
31 a blood clotting product.
- 32 (u) Provide consumers with a copy of all billing invoices.
- 33 (v) Provide appropriate and necessary recordkeeping and  
34 documentation as required by state and federal law, including, but  
35 not limited to:
- 36 (1) Documenting the pedigree of all concentrates of blood  
37 clotting products so that the path of a bottle of any product can be  
38 traced from the time it left the manufacturer to the time it is  
39 delivered to the consumer.

1 (2) Having prescriptions available for treating physicians and  
2 consumers.

3 (w) Comply with the privacy and confidentiality requirements  
4 of the Health Insurance Portability and Accountability Act of 1996  
5 (HIPAA).

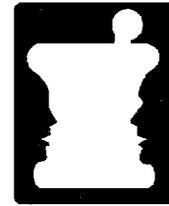
6 ~~125286.5. — A pharmacy licensed pursuant to Article 7~~  
7 ~~(commencing with Section 4110) of Chapter 9 of Division 2 of~~  
8 ~~the Business and Professions Code, shall be deemed to meet the~~  
9 ~~requirements of Section 125286.4.~~

10 ~~125286.6.~~

11 125286.5. The State Department of Health Care Services may  
12 adopt regulations necessary to implement this article in accordance  
13 with the rulemaking provisions of the Administrative Procedure  
14 Act (Chapter 3.5 (commencing with Section 11340) of Part 1 of  
15 Division 3 of Title 2 of the Government Code).

16 125286.6. *The California State Board of Pharmacy shall*  
17 *administer and enforce the provisions of this article.*

**CALIFORNIA STATE BOARD OF PHARMACY  
BILL ANALYSIS**



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**BILL NUMBER: SB 1594**

**VERSION: As Amended April 9, 2008**

**AUTHOR: Steinberg**

**SPONSOR: Hemophilia Council of California**

**RECOMMENDED POSITION:**

**SUBJECT: Bleeding disorders: blood clotting products**

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**EXISTING LAW:**

Requires the Director of Health Care Services to establish and administer a program for the medical care of persons with genetically handicapping conditions, including hemophilia.

**THIS BILL WOULD:**

1. Define a "provider of blood clotting products for home use" as a seller and provider of blood clotting products, ancillary infusion equipment, home nursing services, and patient assistance, for the management of bleeding disorders for home use.
2. Specify that federally designated entities, pharmacies and hemophilia treatment centers would meet the definition of a provider of blood clotting products for home use.
3. Would require that each such provider have a pharmacist available, at all times, to fill prescriptions for blood clotting products; providing prescribed home nursing services either directly or through a reliable third party, and coordinating pharmacy services with a third party;
4. Would require the pharmacy to:
  - supply blood clotting products and home nursing services as prescribed, unless permitted by the prescriber to substitute or adjust a product and seeking clarification from the prescriber which specific blood clotting product is intended when a prescription does not indicate the specific product;
  - supply all brands of blood clotting products approved by the FDA, as well as all necessary infusion equipment and supplies with each prescription;
  - maintain an adequate supply of such products and ship the product, infusion equipment and supplies to consumers within a specified timeframes;
  - provide language translation services, as needed by the consumer, maintain and 24-hour on-call service to screen phone calls for

- emergencies, and provide a designated contact phone number for consumers to report problems with product delivery.
- participate in national notification systems for product recalls, notify patients of the recall within 24-hours and establish plans to meet the requirements of the bill in the event of a disaster;
  - inform consumers about copay, deductible and coinsurance payment responsibilities each time a product is ordered and provide consumers with a copy of all billing invoices
  - meet various state and federal laws relating to the storage and shipping of products and the proper collection, removal and disposal of hazardous waste, recordkeeping and documentation and patient privacy.
5. Would require the Department of Healthcare Services to adopt regulations to implement these requirements.
  6. Would require the Board of Pharmacy to administer and enforce the provisions of the article.

**AUTHOR'S INTENT:**

According to the author, intravenous injection or infusion of prescribed blood clotting products, coupled with case management and specialized medical care, is the preferred method of treatment of hemophilia. The author states that the number of providers delivering blood clotting products and related equipment, supplies, and services for home use is rising. The author states that, while these providers are either pharmacies licensed by the state, or providers located in federally designated HTC's, there are currently no formal standards of service in California for providers of blood clotting products for home use. The author states that this bill will enact those standards for the benefit of persons with hemophilia and other bleeding disorders, and will maintain the current cost effective model of hemophilia care for future generations.

**COMMENTS:**

Supporters of this bill state that this proposal will protect patients from substandard service and improve the lives of those with hemophilia and other bleeding disorders.

According to the sponsor, this proposal is a result of specialty pharmacies working together to define the necessary regulation of blood clotting products.

**SUPPORT/OPPOSITION:**

Support

Hemophilia Council of California (sponsor)  
Accredo Health Group, Inc.  
American Federation of State, County, and Municipal Employees  
Critical Care Systems, Inc.

Herndon Pharmacy  
Plasma Protein Therapeutics Association  
Walgreens Home Care  
Two individuals

Opposition

None

**HISTORY:**

| <b>Dates</b> | <b>Actions</b>  |
|--------------|---|
| 04/09/08     | Apr. 9 Read second time. Amended. Re-referred to Com. on APPR.  |
| 04/08/08     | Apr. 8 From committee: Do pass as amended, but first amend, and re-refer to Com. on APPR. (Ayes 11. Noes 0. Page 3286.) |
| 03/13/08     | Mar. 13 Set for hearing April 2.  |
| 03/06/08     | Mar. 6 To Com. on HEALTH.   |
| 02/25/08     | Feb. 25 Read first time.  |
| 02/24/08     | Feb. 24 From print. May be acted upon on or after March 25.   |
| 02/22/08     | Feb. 22 Introduced. To Com. on RLS. for assignment. To print.   |

# Attachment 4

## *SB 1702 (Machado) Medi-Cal: Fraud*

- Bill
- Bill Analysis

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**Introduced by Senator Machado**

February 22, 2008

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An act to add Section 14131.2 to the Welfare and Institutions Code, relating to Medi-Cal.

LEGISLATIVE COUNSEL'S DIGEST

SB 1702, as introduced, Machado. Medi-Cal.

Existing law provides for the Medi-Cal program, which is administered by the State Department of Health Care Services and under which qualified low-income persons receive health care benefits. A beneficiary may elect to receive Medi-Cal benefits by choosing providers who are reimbursed on a fee-for-service basis or by enrolling in a prepaid managed health care plan, pilot program, or fee-for-service case management provider program that has agreed to make Medi-Cal services readily available to enrolled Medi-Cal beneficiaries.

This bill would require the department to perform a review and, if necessary, a field audit of a Medi-Cal provider, with certain exceptions, for purposes of detecting fraudulent activity and protecting program resources for any calendar month when the number of out-of-county Medi-Cal recipients served by a provider exceeds a threshold percentage, established as prescribed, of the total amount of beneficiaries served by that provider. This bill would make its implementation contingent upon an appropriation in the annual Budget Act or other statute.

Vote: majority. Appropriation: no. Fiscal committee: yes.  
State-mandated local program: no.

*The people of the State of California do enact as follows:*

1 SECTION 1. Section 14131.2 is added to the Welfare and  
2 Institutions Code, to read:

3 14131.2. (a) (1) For any calendar month when the number of  
4 out-of-county Medi-Cal recipients served by a provider exceeds  
5 a threshold percentage of the total amount of beneficiaries served  
6 by that provider, the department shall perform a review and, if  
7 necessary, a field audit of the provider for purposes of detecting  
8 fraudulent activity and protecting program resources.

9 (2) The department, in conjunction with the Bureau of Medi-Cal  
10 Fraud in the office of the Attorney General, may use ZIP Codes  
11 in lieu of county subdivisions if the department determines the use  
12 of ZIP Codes to be more effective and practical in implementing  
13 this section.

14 (b) For purposes of this section, “out-of-county Medi-Cal  
15 recipient” means a Medi-Cal recipient who resides in a county  
16 other than the county in which the benefits are provided.

17 (c) (1) The threshold percentage shall be established, and  
18 adjusted when appropriate, by the department in conjunction with  
19 the Bureau of Medi-Cal Fraud in the office of the Attorney General.

20 (2) The department, in conjunction with the Bureau of Medi-Cal  
21 Fraud in the office of the Attorney General, may establish a  
22 statewide threshold percentage or individual threshold percentages  
23 for distinct areas of the Medi-Cal program, including, but not  
24 limited to, the following:

25 (A) Provider types.

26 (B) Services.

27 (C) Aid code categories.

28 (D) Geographic areas.

29 (d) Subdivision (a) does not apply to the following providers:

30 (1) A primary care, rural, or hospital out-patient clinic licensed  
31 by the department pursuant to Chapter 1 (commencing with Section  
32 1200) of Division 2 of the Health and Safety Code and certified  
33 by the department to participate in the Medi-Cal program.

34 (2) A clinic meeting the requirements to qualify as exempt from  
35 clinic licensure pursuant to subdivision (b) or (h) of Section 1206  
36 of the Health and Safety Code, including an intermittent clinic that  
37 is operated by a licensed primary care clinic on separate premises  
38 or an affiliated mobile health care unit licensed or approved under

1 Chapter 9 (commencing with Section 1765.101) of Division 2 of  
2 the Health and Safety Code, if the exempt from licensure clinic is  
3 operated by a licensed primary care clinic and, with respect to an  
4 intermittent clinic or mobile health care unit, if the licensed primary  
5 care clinic directly or indirectly provides all staffing, protocols,  
6 equipment, supplies, and billing services for the intermittent clinic  
7 or mobile health care unit.

8 (3) A health facility licensed by the department pursuant to  
9 Chapter 2 (commencing with Section 1250) of Division 2 of the  
10 Health and Safety Code and certified by the department to  
11 participate in the Medi-Cal program.

12 (4) A health facility, school, or college under the general  
13 supervision of a California Children's Services program panel  
14 physician and surgeon, including a family physician or podiatrist  
15 who is board certified with expertise in the care of children and  
16 who meets the qualifications of Sections 123880 and 123885 of  
17 the Health and Safety Code.

18 (5) A children's hospital, as defined in Section 10727.

19 (6) A hospital or a primary care clinic specified in subdivision  
20 (a) of Section 1204 of the Health and Safety Code that is directly  
21 maintained and operated by a political subdivision or district of  
22 the state or by any city.

23 (7) A provider who has provided services, directly or indirectly,  
24 to less than, or caused a claim to be submitted for less than, 10  
25 Medi-Cal beneficiaries in a calendar month.

26 (8) A provider who provides emergency services, directly or  
27 indirectly, for a general acute care hospital licensed by the  
28 department, pursuant to Section 1255 of the Health and Safety  
29 Code and is approved in accordance with subdivision (c) of Section  
30 1277 of the Health and Safety Code to offer special services,  
31 including an emergency center, to the hospital and its outpatient  
32 departments.

33 (9) A provider who provides neonatal delivery services.

34 (e) Services to the following aid categories shall not be included  
35 in a determination of whether a provider has exceeded a threshold  
36 percentage under subdivision (a):

37 (1) Foster care beneficiaries.

38 (2) Any other provider type or aid code, upon a determination  
39 by the department, in conjunction with the Bureau of Medi-Cal  
40 Fraud in the office of the Attorney General, that the exclusion of

1 the provider type or aid code is sufficiently justified under this  
2 section.

3 (f) The requirements of this section shall not diminish any  
4 existing authority provided by law or regulation to the department  
5 to detect, prevent, audit, or investigate fraudulent activity.

6 (g) Implementation of the changes required by this section shall  
7 be contingent upon an appropriation for this purpose in the annual  
8 Budget Act or other statute.

**CALIFORNIA STATE BOARD OF PHARMACY  
BILL ANALYSIS**



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**BILL NUMBER: SB 1702**

**VERSION: As Introduced February 22, 2008**

**AUTHOR: Machado**

**SPONSOR: Author**

**BOARD POSITION:**

**SUBJECT: Medi-Cal**

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**EXISTING LAW:**

1. Establishes Medi-Cal which is administered by the Department of Health Care Services (DHCS) to provide health benefits to qualifying Californians.
2. Provides the mechanisms for delivering Medi-Cal services, managed care, and fee for service.
3. Creates the Bureau of Medi-Cal fraud in the Office of the Attorney General and authorizes the office to conduct a statewide program for investigating and prosecuting for violations of applicable laws and requires DHCS to work with the Bureau of Medi-Cal fraud to identify those areas of the fee-for-service program that are at greatest risk for fraud or abuse.
4. Provides a number of penalties for Medi-Cal provider fraud.

**THIS BILL WOULD:**

1. Require DHCS to perform a review and, if necessary, conduct a field audit to detect fraudulent activity during any calendar month in which the number of out-of-county Medi-Cal recipients served by the provider exceeds a threshold percentage of the total amount of beneficiaries served by that provider.
2. Require DHCS to work with the Bureau of Medi-Cal Fraud to establish the threshold percentage and would allow DHCS to use zip codes in lieu of county subdivisions if it determines the use to be more effective and practical in implementing this bill.
3. Would exempt certain providers as specified.
4. Would define "out-of-county Medi-Cal recipient" as a Medi-Cal recipient who resides in a county other than the county in which the benefits are provided.

**AUTHOR'S INTENT**

According to the author, the purpose of this bill is to discourage Medi-Cal fraud involving "capping," which is a fraudulent scheme where Medi-Cal beneficiaries

are enticed to see providers who bill for unnecessary services or services that are not provided. According to the author, DHCS has estimated that Medi-Cal makes approximately \$500 million in payment errors in a calendar year, and of that, \$250 million represents payments that are fraudulent.

## **COMMENTS**

At the request of CRA, this bill is being forwarded to the board for review.

## **PRIOR HISTORY/RELATED BILLS**

SB 1850, Machado, which was identical to SB 1702, was vetoed by Governor Schwarzenegger over concerns that only an out-of county-claims test was required in the bill. The veto message noted that, while this test may be viable, fraud detection methodologies need to be dynamic to keep up with rapidly changing fraud trends. The Governor objected to mandating, in statute, a specific type of analysis on a widespread and routine basis. The Governor also noted that the impact on the general fund should be balanced against the programs that already exist in DHCS to combat fraud and abuse in the Medi-Cal program.

SB 1358 (Escutia and Brulte) Chapter 185, Statutes of 2004, authorized any agent, investigator, or auditor of the Bureau of Medi-Cal Fraud to inspect, at any time, the business location of any Medi-Cal provider for the purpose of investigating Medi-Cal fraud or patient abuse violations.

SB 1359 (Brulte) Chapter 394, Statutes of 2004, required the State Department of Health Care Services, in conjunction with the State Department of Justice, to identify those areas of the fee-for-service Medi-Cal program that are at greatest risk of fraud or abuse.

SB 1360 (Brulte) Chapter 395, Statutes of 2004, authorized the State Department of Justice to pay rewards for information leading to the recovery of funds paid as a result of Medi-Cal fraud.

SB 1361 (Brulte) of 2004 would have created a new two-year felony enhancement and a fine of up to \$10,000 for any person who falsifies, conceals, or covers up a material fact in the investigation of Medi-Cal fraud in the administration of the program. Held in Assembly Public Safety Committee.

SB 857 (Speier) Chapter 601, Statutes of 2003, established new Medi-Cal application requirements for new providers, existing providers at new locations, and providers applying for continued enrollment.

AB 1098 (Romero) Chapter 322, Statutes of 2000, expanded the definition of the crime of fraud, increased penalties for fraud, and prohibited enrollment of providers who have been convicted of fraud in any government program.

AB 1107 (Cedillo) Chapter 146, Statutes of 1999, allows DHCS to withhold payments and to temporarily suspend providers suspected of committing fraud, and tightens the provider enrollment process.

**SUPPORT/OPPOSITION**

Support

None on file

Opposition

None on file

**HISTORY:**

| <b>Dates</b> | <b>Actions</b>   |
|--------------|--|
| 04/16/08     | Apr. 16 From committee: Do pass as amended, but first amend, and re-refer to Com. on APPR. (Ayes 11. Noes 0. Page 3370.) |
| 03/13/08     | Mar. 13 To Com. on HEALTH. Set for hearing April 9.  |
| 02/25/08     | Feb. 25 Read first time.   |
| 02/24/08     | Feb. 24 From print. May be acted upon on or after March 25.  |
| 02/22/08     | Feb. 22 Introduced. To Com. on RLS. for assignment. To print.  |
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# Attachment 5

*Third Quarterly Report on Committee  
Goals for 2007/08*

# LEGISLATION AND REGULATION COMMITTEE

**Goal 3:** Advocate legislation and promulgate regulations that advance the vision and mission of the Board of Pharmacy.

**Outcome:** Improve the health and safety of Californians.

|               |   |
|---------------|---|
| Objective 3.1 | Annually identify and respond with legislative changes to keep pharmacy laws current and consistent with the board's mission.   |
| Measure:      | 100 percent successful enactment of promoted legislative changes.   |
| Tasks:        | <ol style="list-style-type: none"> <li>1. Secure extension of board's sunset date.           <p><i>Sept. 30, 2006: Governor signs SB 1476 which delays the board's sunset date two years (until 2010), and requires the board's sunset report in 2008.</i></p> <p><i>June 2007: SB 963 (Ridley-Thomas) is amended to alter the sunset review process.</i></p> </li> <li>2. Sponsor legislation to update pharmacy law.           <p><i>Sept. 30, 2006: Governor signs SB 1475 containing provisions that:</i></p> <ol style="list-style-type: none"> <li>(a) Allow a check-off box on electronic prescriptions that if marked by a prescriber, would prevent generic substitution at a pharmacist's discretion (B&amp;P 4073).</li> <li>(b) Clarify requirements for reporting to the board when a licensee is impaired to the extent it affects the licensee's safe practice or who has stolen or diverted drugs (B&amp;P 4104).</li> <li>(c) Establish the authority to issue a temporary sterile injectable compounding license following a change in ownership (B&amp;P 4127.8).</li> <li>(d) Exempt government-owned wholesalers from having to post a \$100,000 bond (B&amp;P 4162).</li> <li>(e) Exempt drug manufacturers who hold a biologics license application from the FDA from having to post a \$100,000 bond otherwise required for nonresident wholesalers (B&amp;P 4162.5).</li> <li>(f) Make technical changes in the licensure requirements for clinics (B&amp;P 4180 - 4182, 4190 - 4192).</li> </ol> <p><i>June 2007: Senate Business and Professions Committee omnibus bill (SB 1048) is amended to include board provisions that:</i></p> <ol style="list-style-type: none"> <li>(a) Revise section to include schedule IV controlled substances to the CURES reporting requirements for hospitals. (B&amp;P 4068)</li> <li>(b) Allow board inspectors to embargo a prescription drug when the inspector has probable cause that it is misbranded. (B&amp;P 4084)</li> <li>(c) Change the term "exemptee" to "designated representative." (B&amp;P) 4101</li> <li>(d) Revise section to specify temporary license fee of \$550. Current law does not specify the temporary fee. (B&amp;P 4160 (f) &amp; 4161 (k))</li> <li>(e) Extend bonding requirements for wholesalers from 2011 to 2015 to match the extension given to implement the e-pedigree requirements, restoring provisions in SB 1476 chaptered out by SB 1475. (B&amp;P 4162 &amp; 4162.5)</li> <li>(f) Change in the name of the exam to more accurately reflect the requirements described in B&amp;P 4200.2. The new name will be the "California Practice Standards and Jurisprudence Examination for Pharmacists" (CPJE). (B &amp; P 4200, 4200.1 &amp; 4200.2)</li> <li>(g) Revise requirements for intern licenses to allow the board the discretion to extend the duration of an intern license. (B&amp;P 4208)</li> </ol> </li> </ol> |

(h) Allow the board to cite and fine licensees for violations of Health and Safety Code sections 150200-150206 which authorize a county to establish by local ordinance, a repository and distribution program for specified unused medications from skilled nursing homes to medically indigent patients served by government-owned pharmacies. (B&P 4314 & 4315)

Oct. 2007: Governor signs SB 1048 (Chapter 588, Statutes of 2007) containing board omnibus provisions.

Oct. 2007: Legislation and Regulation Committee considers omnibus provisions for introduction in 2008. Four types of changes are discussed.

(1) Omnibus changes specific to the PIC and DRC requirements

- Section 4022.5 – Designated Representative; Designated Representative-in-Charge
- Section 4036.5 – Pharmacist-in-Charge
- Section 4101 – Pharmacist-in-Charge; Designation Representative-in-Charge; Termination of Status; Duty to Notify the Board.
- Section 4113 – Pharmacist-in-Charge; Approval; Responsibilities; Notifications
- Section 4160 – Wholesaler Licenses
- Section 4196 – Veterinary Food-Animal Drug Retailer Licenses; Persons Allowed in Areas Where Drugs are Stored, Possessed, or Repacked
- Section 4305 – Pharmacist-in-Charge; Notice to Board; Disciplinary Action
- Section 4329 – Nonpharmacists; Prohibited Acts
- Section 4330 – Proprietors; Prohibited Acts

(2) Omnibus changes to allow for the use of mobile pharmacies

- Section 4062 Furnishing Dangerous Drugs During an Emergency.
- Section 4110 License Required, Temporary Permit Upon Transfer of Ownership.

(3) General omnibus changes

- Section 4059.5 Who May order Dangerous Drugs or Devices, Exceptions.
- Section 4081 - Records of Dangerous Drugs and Devices Kept Open for Inspection; Maintenance of Records, Current Inventory
- Section 4126.5 – Furnishing Dangerous Drugs by Pharmacy.
- Section 4231 – Requirements for Renewal of Pharmacist License: Clock Hours; Exemption for New Licensee.
- Section 4362 – Entry Into Pharmacists Recovery Program.  
H&SC 11165 – Controlled Substance Utilization Review and Evaluation System: Establishment; Operation; Funding; Reporting to Legislature.

(4) Omnibus changes based on recodification of Business and Professions Code section 4052

- Section 733 – Dispensing Prescription Drugs and Devices
- Section 4027 – Skilled Nursing Facility – Intermediate Care Facility – Other Health Care Facilities
- Section 4040 – Prescription; Content Requirements
- Section 4051 – Conduct Limited to Pharmacist; Conduct Authorized by Pharmacist
- Section 4060 – Controlled Substance – Prescription Required, Exceptions
- Section 4076 – Prescription Container – Requirements for Labeling
- Section 4111 – Restrictions on Prescriber Ownership
- Section 4174 – Dispensing by Pharmacist Upon Order of Nurse Practitioner
- H&SC 11150 – Persons Authorized to Write or Issue a Prescription

*Jan. 2008: Staff provides language to Senate Business and Professions Committee for inclusion in omnibus bill.*

*Board approved language for omnibus bill.*

3. Advocate the board's role and its positions regarding pharmacists' care and dispensing of dangerous drugs and devices (AB 2408).

*Sept. 30, 2006: Governor signs AB 2408. Amendments taken in August remove provisions that would have described the professional services provided by pharmacists, and authorized pharmacists outside California to provide pharmacists' care services to patients in California if licensed here or working within the framework of a nonresident pharmacy. Remaining provisions restructure pharmacist protocol provisions and several other changes.*

4. Secure statutory standards for pharmacies that compound medications (AB 595).

*Aug. 2006: Amendments made to remove opposition of DHS regarding pharmacy contracting with another pharmacy for compounded drugs triggers opposition from pharmacy organizations. Board drops AB 595, but will advance regulations developed for compounding pharmacies in the future.*

5. Secure implementation of e-pedigrees on prescription drugs dispensed in California (SB 1476).

*Sept. 30, 2006: Governor signs SB 1476 which contains board amendments to delay implementation of the e-pedigree requirements until 2009, or upon board action, until 2011. Amendments also require interoperability, serialization, returned drug products to retain the initiating pedigree, require notice to the board of suspected or actual counterfeiting, and continuation of the pedigree through repackaging operations.*

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|  | <p>6. Advocate the board's position on pending legislation affecting pharmacy practice and/or the board's jurisdiction.</p> <p><i>AB 110 (Laird) Drug Paraphernalia: Clean Needle and Syringe Exchange Projects.</i></p> <p><i>AB 249 (Eng) Healing Arts: Settlement Agreements.</i></p> <p><i>AB 543 (Plescia) Ambulatory Surgical Centers: Licensure.</i></p> <p><i>AB 1025 (Bass) Professions and Vocations: Denial of Licensure.</i></p> <p><i>SB 472 (Corbett) Prescription Drugs: Labeling Requirements.</i></p> <p><i>SB 615 (Oropeza) Pharmacy Technicians: Scholarship Fund.</i></p> <p><i>SB 606 (Scott) Pharmaceutical Information: Clinical Data Trial.</i></p> <p><i>SB 963 (Ridely-Thomas) Regulatory Boards: Operations.</i></p> <p><i>SB 966 (Simitian) Pharmaceutical Drug Disposal.</i></p> <p><b>Oct. 2007:</b> <b>Governor signs the following:</b></p> <p><i>AB 110 (Chapter 707, Statutes of 2007) Drug Paraphernalia: Clean Needle and Syringe Exchange Projects.</i></p> <p><i>SB 472 (Chapter 470, Statutes of 2007) Prescription Drugs: Labeling Requirements.</i></p> <p><i>SB 966 (Chapter 542, Statutes of 2007) Pharmaceutical Drug Disposal.</i></p> <p><b>Oct. 2007:</b> <b>Governor vetoes the following:</b></p> <p><i>AB 249 (Eng) Healing Arts: Settlement Agreements.</i></p> <p><i>AB 543 (Plescia) Ambulatory Surgical Centers: Licensure.</i></p> <p><i>AB 1025 (Bass) Professions and Vocations: Denial of Licensure.</i></p> <p><i>SB 615 (Oropeza) Pharmacy Technicians: Scholarship Fund.</i></p> <p><b>Jan. 2008:</b></p> <ol style="list-style-type: none"> <li><i>1. AB 501 (Swanson) Pharmaceutical Devices</i></li> <li><i>2. AB 865 (Davis) State Agencies: Live Customer Service Agents</i></li> <li><i>3. AB 1436 (Hernandez) Nurse Practitioner Scope of Practice</i></li> <li><i>4. AB 1587 (de la Torre) and SB 843 (Calderon) Medical Information Marketing</i></li> <li><i>5. SB 963 (Ridley Thomas) Regulatory Boards: Sunset Review</i></li> <li><i>6. AB 1 X (Nunez) Health Care Reform</i></li> </ol> <p>7. Expand the conditions under which a pharmacist may administer an immunization independent of physician protocol.</p> <p><b>March 2007:</b> <i>Licensing Committee considers and approves concept. More work is required.</i></p> <p><b>June 2007:</b> <i>Licensing Committee considers draft language and requests additional refinements to proposal for consideration at September 2007 committee meeting.</i></p> <p><b>Sept. 2007:</b> <i>Licensing Committee forwards to full board legislative proposal.</i></p> <p><b>Oct. 2007:</b> <i>Board approved draft legislation</i></p> <p><b>Nov. 2007:</b> <i>Staff meeting with stakeholders to elicit support for the proposal.</i></p> <p><b>Dec. 2007:</b> <i>Staff develop fact sheets and work with experts in immunizations.</i></p> <p><b>Jan. 2008:</b> <i>Seeking coalition to support initiative. Will pursue proposal in 2009.</i></p> |
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|  | <p>8. Advocate the board's role as an advocate for consumers by redesigning prescription label for all medicines dispensed to California patients.</p> <p><i>Oct. 2007: Governor signs SB 472 (Chapter 470, Statutes of 2007) Prescription Drugs: Labeling Requirements.</i></p> <p><i>Oct. 2007: Subcommittee of the board is created to facilitate changes to regulation. Members include: Dr. Schell, Chair; Dr. Ravnar; Dr. Conroy; Dr. Swart; and President Powers.</i></p> <p><i>Jan. 2008: Shirley Wheat added to the subcommittee.</i></p> <p><i>Apr. 2008: First public forum held in Fremont.</i></p> |
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| Objective 3.2 | Annually identify and respond with regulatory changes to keep pharmacy regulations current and consistent with the board's mission.  |
| Measure:      | Percentage successful enactment of promoted regulatory changes.  |
| Tasks:        | <ol style="list-style-type: none"> <li>1. Authorize technicians to check technicians in inpatient pharmacies with clinical pharmacist programs (sections 1793.7-1793.8). <ul style="list-style-type: none"> <li>Aug. 2006: Rulemaking file compiled and undergoing review by the Department of Consumer Affairs.</li> <li>Nov. 2006: Rulemaking file submitted to the Office of Administrative Law.</li> <li>Jan. 2007: Office of Administrative Law approves rulemaking. Regulation takes effect.</li> </ul> </li> <li>2. Authorize the use of prescription drop boxes and automated delivery machines for outpatient pharmacies (sections 1713 and 1717(e)). <ul style="list-style-type: none"> <li>Aug. 2006: Rulemaking file compiled and undergoing review by the Department of Consumer Affairs.</li> <li>Jan. 2007: Regulation takes effect following approval by the Office of Administrative Law.</li> </ul> </li> <li>3. Make technical changes in pharmacy regulations to keep the code updated. <ul style="list-style-type: none"> <li>Dec. 2006: Board notices regulation for 45 days of public comment. <ul style="list-style-type: none"> <li>Section 1775.4 contested citations</li> <li>Section 1706.2 criteria for abandonment of files</li> </ul> </li> <li>Jan. 2007: Board adopts regulations. <ul style="list-style-type: none"> <li>Section 1775.4 contested citations</li> <li>Section 1706.2 criteria for abandonment of files</li> </ul> </li> <li>Feb. 2007: Rulemaking file compiled and undergoing review by the Department of Consumer Affairs. <ul style="list-style-type: none"> <li>Section 1775.4 contested citations</li> <li>Section 1706.2 criteria for abandonment of files</li> </ul> </li> <li>April 2007: Section 1775.4 contested citations. DCA determines no regulation is needed to accomplish the requirement to allow 1 rescheduling of an office conference. This regulation is withdrawn.</li> <li>June 2007: Changes to 1706.2 take effect following approval by the Office of Administrative Law.</li> </ul> </li> <li>4. Repeal the requirement to post a notice regarding electronic files (section 1717.2). <ul style="list-style-type: none"> <li>July 2006: Regulation released for 45 days of public comment. Action to be taken at the October Board Meeting.</li> <li>Oct. 2006: Board approves regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration review.</li> <li>March 2007: Office of Administrative Law approves rulemaking. Regulation takes effect.</li> </ul> </li> <li>5. Revise and update Disciplinary Guidelines revision and update (section 1760). <ul style="list-style-type: none"> <li>Aug. 2006: Final changes to Disciplinary Guidelines being compiled by staff.</li> <li>Dec. 2006: Disciplinary Guidelines is being reformatted into strikeout and underscore version for eventual release for public comment.</li> <li>June 2007: Enforcement Committee reviews Disciplinary Guidelines and requests additional time to review before being submitted to the board.</li> <li>Sept. 2007: Enforcement Committee approves Disciplinary Guidelines and recommends board approval.</li> <li>Oct. 2007: Board approves Disciplinary Guidelines for 45-day comment period.</li> <li>Feb. 2008: Regulation released for 45 days of public comment.</li> </ul> </li> </ol> |

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|  | <p>6. Self-assessment of a wholesaler by the designated representative (section 1784).<br/> <i>July 2006: Regulation released for 45 days of public comment. Action to be taken at the October Board Meeting.</i></p> <p><i>Oct. 2006: Board approves regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration review.</i></p> <p><i>April 2007: Office of Administrative Law approves rulemaking. Regulation takes effect.</i></p> <p><i>May 2007: Wholesalers are notified of this requirement.</i></p> <p>7. Exempt the address of records of interns from display on the board's Web site (section 1727.1).<br/> <i>Sept. 2006: Office of Administrative Law approves rulemaking. Regulation takes effect October 2006.</i></p> <p>8. Modification of building standards for pharmacies – rulemaking by the California Building Standards Commission.<br/> <i>July 2006: Board notified that a new procedure now exists for adopting building standards. Staff will pursue these procedures in 2007.</i></p> <p><i>June 2007: Board staff submit rulemaking file to the California Building Standards Commission.</i></p> <p>9. Update Notice to Consumers Poster in conformance with AB 2583 (Chapter 487, Statutes 2006)(Section 1707.2).<br/> <i>Feb. 2007: Board notices regulation for 45 days comment period.</i></p> <p><i>April 2007: Board considers comments submitted during public comment period and modifies text regulation to reflect comments.</i></p> <p><i>May 2007: New section 1707.2 released for 45 days of public comment.</i></p> <p><i>July 2007: Board adopts regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration Review.</i></p> <p><i>Sept. 2007: File submitted to the Office of Administrative Law for review.</i></p> <p><i>Oct. 2007: Office of Administrative Law approves rulemaking.</i></p> <p><i>Nov. 2007: Regulation changes takes effect.</i></p> <p><i>Nov. 2007: Staff solicits design submissions from graphic designers.</i></p> <p><i>Jan. 2008: Communication and Public Education Committee make recommendations on design submissions.</i></p> |
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10. Secure changes without regulatory effect (Section 100 changes) to pharmacy regulations to keep them accurate and current.
- June 2007:* Submitted the following Section 100 changes:  
 Section 1707 – Waiver Requirements for Off-Site Storage of Records.  
 Section 1709.1 – Replace the term “Exemptee-in-Charge” with “Designated Representative-in-Charge”.  
 Section 1715 – Self-Assessment of a Pharmacy by the Pharmacist-in-Charge to Update for Changes in Pharmacy Law.  
 Section 1719 – Pharmacy Practice.  
 Sections 1780.1 and 1781 – Replace the term “Exemptee” with “Designated Representative”.  
 Section 1786 – Return of Exemptee Certificate.  
 Section 1787 – Authorization to Distribute Dialysis Drugs and Devices.  
 Section 1790 – Assembling and Packaging.  
 1793.8 – Update regulation reference to recodified Business and Professions Code section 4052.
- Aug. 2007:* Staff withdraw Section 100 Changes.  
*Nov. 2007:* Staff resubmit Section 100 Changes  
*Dec. 2007:* Office of Administrative Law approves Section 100 Changes.
11. Increase fees to keep the board's contingency fund solvent and maintain operations.
- March 2007:* Organization Development Committee reviews proposals and recommends approval.  
*April 2007:* Board approves the proposal.  
*May 2007:* Board releases language for the 45-day public comment period.  
*July 2007:* Board adopts proposed changes for a 15-day comment period and if no negative comments are received board adopts regulations.  
*Aug. 2007:* File submitted to the Department of Consumer Affairs to initiate Administration Review.  
*Oct. 2007:* File submitted to the Office of Administrative Law for review.  
*Nov. 2007:* Office of Administrative Law approves rulemaking.  
*Nov. 2007:* Staff complete necessary programming changes and begin advising licensees of the change.  
*Jan. 1, 2008:* New fees take effect.
12. Secure regulatory standards for pharmacies that compound.
- Dec. 2006:* Licensing Committee evaluates proposed compounding regulations developed in 2004. Some modifications may be needed.  
*March 2007:* Licensing Committee convenes discussion of amendments to compounding regulations. More work is required.  
*May 2007:* Licensing Committee holds detailed discussion on compounding regulations.  
*Sept. 2007:* Licensing Committee forwards regulation proposal to the board for review.  
*Nov. 2007:* Board releases language for the 45-day comment period.  
*Jan. 2008:* Board held regulation hearing and considers written comments and oral testimony.

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| Objective 3.3 | Review 5 areas of pharmacy law for relevancy, currency and value for consumer protection by June 30, 2011.  |
| Measure:      | Number of areas of pharmacy law reviewed.   |
| Tasks:        | <p>1. Initiate review of the pharmacist-in-charge requirement.</p> <p><i>Aug. 2007: Staff and counsel review pharmacist-in-charge and designated representative-in-charge statutes and regulations for reporting requirements and make recommendations to amend various statutes and regulations.</i></p> <p><i>Oct. 2007: Legislation and Regulation Committee reviews draft language to be incorporated into omnibus bill.</i></p> <p><i>Jan. 2008: Board approves omnibus language recommended by Legislation and Regulation Committee.</i></p> <ul style="list-style-type: none"> <li>• Section 4022.5 – Designated Representative; Designated Representative-in-Charge</li> <li>• Section 4036.5 – Pharmacist-in-Charge</li> <li>• Section 4101 – Pharmacist-in-Charge; Designation Representative-in-Charge; Termination of Status; Duty to Notify the Board.</li> <li>• Section 4113 – Pharmacist-in-Charge; Approval; Responsibilities; Notifications</li> <li>• Section 4160 – Wholesaler Licenses</li> <li>• Section 4196 – Veterinary Food-Animal Drug Retailer Licenses; Persons Allowed in Areas Where Drugs are Stored, Possessed, or Repacked</li> <li>• Section 4305 – Pharmacist-in-Charge; Notice to Board; Disciplinary Action</li> <li>• Section 4329 – Nonpharmacists; Prohibited Acts</li> <li>• Section 4330 – Proprietors; Prohibited Acts</li> </ul> |