

17 December 2008

Changes to the available preparations of Diltiazem Hydrochloride

We would like to announce the following changes (effective 1 June 2009) to the preparations of diltiazem hydrochloride that will be available:

Preparations that will be delisted	Preparations that will remain available
Dilzem SR 90 mg and 120 mg (twice daily) sustained release capsules	Dilzem 30 mg and 60 mg immediate release tablets
Dilzem LA 180 mg and 240 mg long-acting (once daily) tablets	Cardizem CD 120 mg, 180 mg and 240 mg long-acting (once daily) capsules

Extensive consultation and clinical advice regarding which presentations should be available was considered in the decision. After considering all these views, and other relevant factors, it was decided that in the long-term the rationalisation of the funded products was appropriate. We note that no specific group that will be affected by the decision was unified in its feedback. For example some cardiologists, general practitioners and pharmacists supported the whole proposal, while other cardiologists, general practitioners and pharmacists opposed either parts of the proposal or the whole proposal.

Details of the Decision

This notification is the result of a decision taken by the PHARMAC Board regarding which diltiazem preparations will be available and its approval of agreements with Douglas Pharmaceuticals Limited and Sanofi-Aventis New Zealand Limited. The decision and these agreements mean that the following will occur:

- From 1 June 2009, the following diltiazem preparations will be delisted from the Pharmaceutical Schedule (until then they will remain fully funded):

Brandname	Strength	Form	Presentation	Dosing frequency
Dilzem SR	90 mg	Capsule	Sustained release	Twice daily
Dilzem SR	120 mg	Capsule	Sustained release	Twice daily
Dilzem LA	180 mg	Tablet	Long-acting	Once daily
Dilzem LA	240 mg	Tablet	Long-acting	Once daily

- The following, currently listed, diltiazem preparations will remain listed on the Pharmaceutical Schedule until at least 31 December 2011:

Brandname	Strength	Form	Presentation	Dosing frequency
Dilzem	30 mg	Tablet	Immediate release	3 - 4 times daily
Dilzem	60 mg	Tablet	Immediate release	3 - 4 times daily
Cardizem CD	120 mg	Capsule	Long-acting	Once daily
Cardizem CD	180 mg	Capsule	Long-acting	Once daily
Cardizem CD	240 mg	Capsule	Long-acting	Once daily

The prices and subsidies (ex-manufacturer, exclusive of GST) of the diltiazem preparations that will remain listed in Section B and in Part II of Section H of the Pharmaceutical Schedule, will alter as follows:

Brandname	Strength and Form	Pack Size	Current price and Subsidy	Price and Subsidy from 1 December 2008	Price and Subsidy from 1 June 2009
Dilzem	30 mg tab	100	\$4.50	\$4.60	\$4.60
Dilzem	60 mg tab	100	\$8.50	\$8.50	\$8.50
Cardizem CD	120 mg cap	30	\$5.10	\$4.72	\$4.34
Cardizem CD	180 mg cap	30	\$7.65	\$7.08	\$6.50
Cardizem CD	240 mg cap	30	\$10.20	\$9.44	\$8.67

Both the Dilzem and Cardizem CD brands of diltiazem will have Community and Hospital Sole Supply Status from 1 June 2009 until 31 December 2011.

The Clinical Implications of the Decision

The decision by the PHARMAC Board will mean that the only diltiazem hydrochloride preparations available in the community and hospital settings will be Dilzem immediate release tablets and Cardizem CD once daily long-acting capsules.

The delisting of Dilzem SR (sustained release) and Dilzem LA (long-acting) will require current patients to be switched to another presentation. We suggest the following:

Currently taking	Suggested new presentation
Dilzem SR 90 mg capsule (twice daily)	Cardizem CD 180 mg capsule (once daily)
Dilzem SR 120 mg capsule (twice daily)	Cardizem CD 240 mg capsule (once daily)
Dilzem LA 180 mg tablet (once daily)	Cardizem CD 180 mg capsule (once daily)
Dilzem LA 240 mg tablet (once daily)	Cardizem CD 240 mg capsule (once daily)

Titration to a higher or lower dose may be necessary and should be initiated as clinically warranted.

For patients taking Dilzem SR 90 mg or 120 mg once daily (even if it is not the recommended dosing regimen due to blood levels not being maintained above the minimum therapeutic level for 24 hours), we suggest the following:

Currently taking	Suggested new presentation
Dilzem SR 90 mg capsule (once daily)	Cardizem CD 120 mg capsule (once daily)
Dilzem SR 120 mg capsule (once daily)	Cardizem CD 120 mg capsule (once daily)

These patients may be more likely to experience a change in effect therefore they should be monitored following the change.

New patients can be initiated on a long-acting capsule (Cardizem CD 120 mg, 180 mg, or 240 mg), or if there are concerns regarding tolerability then there treatment can be initiated with an immediate release tablet (Dilzem 30 mg or 60 mg) and then switched to a long-acting capsule once tolerability is established.

We will send advice to assist clinicians and pharmacists when switching patients. A copy of the "Diltiazem Clinical Advice" is available on the PHARMAC website.

Background Information to the Decision

The DHBNZ Safety and Quality of Medicines Group have indicated that they have concerns regarding the occurrence of prescribing and dispensing errors as a result of confusion between the currently listed presentations of diltiazem hydrochloride.

In order to gain a greater understanding of these concerns and to determine possible options we issued a request for information which sought advice on the preferred diltiazem preparations. A number of responses were received, many of which acknowledged that the current number of brands and formulations available are confusing and have resulted in a number of errors in their administration and prescribing. Overall, the responses supported a reduction in the available presentations, although they did differ regarding what presentations should remain available.

All of the responses were reviewed by the Cardiovascular Sub-Committee of PTAC (the Pharmacology and Therapeutic Advice Committee). The Sub-Committee recommended that the twice daily preparations should be removed from the Pharmaceutical Schedule and that only one brand of the long-acting preparations should be available.

On 28 February 2008, we issued a letter indicating that there may be a number of changes to the listings of diltiazem in the Pharmaceutical Schedule as a result of concerns regarding their prescribing and dispensing (the concerns were not related to the quality of the pharmaceuticals). The letter also indicated that the changes may include the delisting of Dilzem SR 90 mg and 120 mg (twice daily) preparations, and the delisting of either the long-acting tablets or the long-acting capsules (but not both).

Following the letter we issued a request for proposals for the supply of immediate-release and long-acting preparations. We also received some additional feedback regarding which preparations were required. This additional information was also considered by the Cardiovascular Sub-Committee of PTAC.

Finally on 10 October 2008 we consulted on a proposal. This decision is the result of this process.

Feedback Received regarding the Proposal

The changes to the available diltiazem preparations were the subject of a consultation letter dated 10 October 2008. We appreciated all the feedback that was received as a result of this consultation and acknowledge the time that people took to respond.

The feedback that we received acknowledged that the current diltiazem preparations are confusing, that mistakes occur, and that the range of preparations should be simplified. However, there was variation as to how any simplification should be done.

Support for the proposal focused on it simplifying the use and dispensing of diltiazem and therefore:

- reducing confusion for those who do not understand the different release characteristics of the available preparations;
- reducing the chances of dosing, prescribing and dispensing errors occurring; and,
- increasing patient's safety.

There was little feedback regarding the affect of the proposal on the immediate release and long-acting preparations (it was generally supportive). However, concern was expressed at the proposed delisting of the 90 mg and the 120 mg sustained release (twice daily) Dilzem SR preparations.

A number of issues were raised regarding these preparations. The following table illustrates the main issues and also PHARMAC's response to these concerns:

Issue	PHARMAC's response
<p>There are differences in bio-availability between the two sustained-release preparations and prescribers will need to be aware of this.</p> <p>Switching patients to preparations of equivalent dose may result in changes in serum levels and hence efficacy and side-effects.</p>	<p>The clinical information that will be provided to assist in switching patients includes comments indicating that monitoring and titration may be necessary as clinically warranted.</p>
<p>The twice daily preparations (90 mg or 120 mg) are used as a once daily preparation when:</p> <ul style="list-style-type: none"> • clinicians require blood pressure control during the day but also want to avoid hypotension at night (nocturnal bradycardia). • treatment is being initiated and the lowest possible dose is sought. 	<p>The Cardiovascular Subcommittee of PTAC considers that the Cardizem CD 120 mg capsule (once daily) would be an appropriate substitute for both of these patients groups as it would provide a similar clinical effect.</p> <p>We also note that Dilzem SR is not indicated for once daily dosage (except when initiating treatment for hypertension) because blood levels are not maintained above the minimum therapeutic level for 24 hours, and therefore confusion with once daily products would result in patients being under-dosed.</p>
<p>Switching patients to the immediate release preparations from the twice daily preparations will result in compliance problems.</p>	<p>The Cardiovascular Subcommittee of PTAC recommended Cardizem capsules (once daily) as the most appropriate substitute for these patients in the first instance. Other available alternatives include other calcium channel blockers such as verapamil or dihydropyridine calcium channel blockers.</p>
<p>Some lung and heart transplant patients have been stabilised on the SR preparations and some of these are receiving a once daily dose (diltiazem is used as its enzyme inhibiting properties mean calcineurin inhibitor levels are achieved at lower doses).</p>	<p>Other diltiazem preparations could be used although monitoring will be required to determine if the immunosuppressant dosing would require adjusting. Feedback from a transplant physician indicates that slight changes should not be an issue as long as the inhibitory effect remains predictable.</p>
<p>The implications of switching patients from the SR 90 mg and 120 mg tablets (twice per day) preparations outweigh the savings/safety implications.</p>	<p>We appreciate that changing patient's medication is a concern of a number of responders. However, the desire to maintain patients on their current medication had to be weighed up against the undesirability of the current situation. We note that there were a number of responses supporting the proposal and we consider that while the changes will result in some short-term inconvenience, this is not insurmountable and the proposal would be a long-term improvement.</p>

More information

If you have any queries about these changes please contact the PHARMAC helpline on 0800 66 00 50 (9 am to 5 pm weekdays).