

27 July 2010

Consultation on a proposal relating to Ezetimibe, Ezetimibe with Simvastatin, Mianserin Hydrochloride and Oestriol

PHARMAC is seeking feedback on a proposal which would result in greater funded access to the cholesterol lowering pharmaceutical ezetimibe and also greater funded access to the antidepressant mianserin.

This proposal arises as a result of a provisional agreement with the supplier of these medicines, Merck Sharpe and Dohme, and in response to consideration of comments received to an earlier consultation regarding ezetimibe (detailed later).

Proposal summary

The following changes would be effective from 1 October 2010.

Ezetimibe (Ezetrol)

- Funded access to ezetimibe would be widened (under Special Authority) to include patients whose LDL-cholesterol treatment goals are not achieved with the use of statins.
- Clinicians able to apply for Special Authorities would include General Practitioners.
- Price reductions and confidential rebates would apply.

Ezetimibe with Simvastatin (Vytorin)

- Funded access to ezetimibe with simvastatin would be widened (under Special Authority) to include patients whose LDL-cholesterol treatment goals are not achieved with the use of the maximally tolerated dose of atorvastatin.
- Clinicians able to apply for Special Authorities would include General Practitioners.
- Price reductions and confidential rebates would apply.

Mianserin hydrochloride (Tolvon)

- Funded access to mianserin hydrochloride would be widened (under Special Authority) to include patients who have not responded to other antidepressants.
- Price reductions and subsidy and delisting protection would apply.

Oestriol (Ovestin)

- Price reductions and subsidy and delisting protection would apply.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by Wednesday 11 August 2010 to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Details of the proposals

Ezetimibe (Ezetrol)

Access to Ezetrol would be widened so that it would be funded for patients who have a 5-year CVD risk of at least 15% with a LDL cholesterol level of 2.0 mmol/litre or greater and who:

- have rhabdomyolysis following treatment with one statin; or,
- are intolerant to both simvastatin and atorvastatin; or,
- have not reduced their LDL cholesterol level to 2.0 mmol/litre with the use of the maximal tolerated dose of atorvastatin.

Ezetrol would be able to be used in combination with atorvastatin for patients who do not reduce their LDL cholesterol level to 2.0 mmol/litre and Special Authority applications (both initials and renewals) would be able to be applied for by relevant practitioners (this includes General Practitioners).

The Special Authority criteria that would apply to Ezetrol would be as follows:

Initial application from a relevant practitioner. Approvals valid for 2 years for applications meeting the following criteria:

Both:

1 Patient has a calculated absolute risk of cardiovascular disease of at least 15% over 5 years; and

2 Patient's LDL cholesterol is 2.0 mmol/litre or greater: and

3 Either:

3.1 The patient has rhabdomyolysis (defined as muscle aches and creatine kinase more than 10 x normal) when treated with one statin; or,

3.2 The patient is intolerant to both simvastatin and atorvastatin; or,

3.3 The patient has not reduced their LDL cholesterol to less than 2.0 mmol/litre with the use of the maximal tolerated dose of atorvastatin.

Note

A patient who has failed to reduce their LDL cholesterol to ≤ 2.0 mmol/litre with the use of a less potent statin should use a more potent statin prior to consideration being given to the use of non-statin therapies.

Other treatment options including fibrates, resins and nicotinic acid should be considered after failure of statin therapy.

Renewal - from any relevant practitioner. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.

The prices and subsidies (ex-manufacturer, excluding GST) for Ezetrol would be reduced in Section B of the Pharmaceutical Schedule as follows:

Chemical	Presentation	Brand	Pack size	Current price and subsidy	Proposed price and subsidy Feb 2011	Proposed price and subsidy July 2013
Ezetimibe	Tab 10 mg	Ezetrol	30	\$57.60	\$45.90	\$34.43

Ezetimibe would be subject to confidential rebates.

Ezetimibe with simvastatin (Vytorin)

Access to Vytorin would be widened so that it would be funded for patients who have a 5-year CVD risk of at least 15% with a LDL cholesterol level of 2.0 mmol/litre or greater and who have not reduced their LDL cholesterol level to less than 2.0 mmol/litre with the use of the maximally tolerated dose of atorvastatin.

Special Authority applications (initials and renewals) would be able to be written by relevant practitioners (this includes General Practitioners).

The Special Authority criteria that would apply to Vytorin would be as follows:

Initial application from a relevant practitioner. Approvals valid for two years for applications meeting the following criteria:

Both:

- 1 Patient has a calculated absolute risk of cardiovascular disease of at least 15% over 5 years; and
- 2 Patient's LDL cholesterol is 2.0 mmol/litre or greater: and,
- 3 The patient has not reduced their LDL cholesterol to less than 2.0 mmol/litre with the use of the maximal tolerated dose of atorvastatin

Note

A patient who has failed to reduce their LDL cholesterol to ≤ 2.0 mmol/litre with the use of a less potent statin should use a more potent statin prior to consideration being given to the use of non-statin therapies.

Other treatment options including fibrates, resins and nicotinic acid should be considered after failure of statin therapy.

If a patient's LDL cholesterol cannot be calculated because the triglyceride level is too high then a repeat test should be performed and if the LDL cholesterol again cannot be calculated then it can be considered that the LDL cholesterol is greater than 2.0 mmol/litre.

Renewal - from any relevant practitioner. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.

The prices and subsidies (ex-manufacturer, excluding GST) for Vytorin would be reduced in Section B of the Pharmaceutical Schedule as follows:

Chemical	Presentation	Brand	Pack size	Current price and subsidy	Proposed price and subsidy Feb 2011	Proposed price and subsidy July 2013
Ezetimibe with simvastatin	Tab 10 mg ezetimibe with 10 mg simvastatin	Vytorin	30	\$69.00	\$48.90	\$36.68
Ezetimibe with simvastatin	Tab 10 mg ezetimibe with 20 mg simvastatin	Vytorin	30	\$75.00	\$51.60	\$38.70
Ezetimibe with simvastatin	Tab 10 mg ezetimibe with 40 mg simvastatin	Vytorin	30	\$103.50	\$55.20	\$41.40
Ezetimibe with simvastatin	Tab 10 mg ezetimibe with 80 mg simvastatin	Vytorin	30	\$123.00	\$60.60	\$45.45

Vytorin would be subject to confidential rebates.

Mianserin hydrochloride (Tolvon)

The current Special Authority that applies to mianserin hydrochloride would be widened to include patients who have not responded to other antidepressants as follows (additions in bold):

Initial application from any relevant practitioner. Approvals valid for 2 years for applications meeting the following criteria:

Either:

- 1 Both:
 - 1.1 Depression; and
 - 1.2 Either:
 - 1.2.1 Co-existent bladder neck obstruction; or
 - 1.2.2 Cardiovascular disease; or
- 2 **Both:**
 - 2.1 The patient has a severe major depressive episode; and**
 - 2.2 Either:**
 - 2.2.1 The patient must have had a trial of two different antidepressants and was unable to tolerate the treatments or failed to respond to an adequate dose over an adequate period of time (usually at least four weeks); or**
 - 2.2.2 Both:**
 - 2.2.2.1 The patient is currently a hospital in-patient as a result of an acute depressive episode; and**
 - 2.2.2.2 The patient must have had a trial of one other antidepressant and either could not tolerate it or failed to respond to an adequate dose over an adequate period of time.**

Renewal from any relevant practitioner. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.

From 1 October 2010 the price and subsidy (ex-manufacturer, excluding GST) for mianserin hydrochloride (Tolvon) 30 mg tablets would reduce in Section B of the Pharmaceutical Schedule from \$29.25 to \$24.86 per pack of 30 tablets.

Tolvon would have subsidy and delisting protection until 1 October 2012.

Oestriol (Ovestin)

From 1 October 2010 the prices and subsidies (ex-manufacturer, excluding GST) for oestriol (Ovestin) would be reduced in Section B of the Pharmaceutical Schedule as follows:

Brand	Presentation	Pack size	Current Subsidy	Proposed Subsidy
Ovestin	Oestriol 2 mg tab	30	7.00	7.00
Ovestin	Pessaries 500mcg	15	7.25	6.53
Ovestin	Oestriol Crm 1 mg per g with applicator	15 g	7.00	6.30

Oestriol would have subsidy and delisting protection until 1 October 2012.

Background to the proposals

Ezetimibe (Ezetrol) / Ezetimibe with Simvastatin (Vytorin)

On 26 April 2010, PHARMAC issued a consultation document which included proposed changes to the funding of atorvastatin, ezetimibe (Ezetrol) and the ezetimibe and simvastatin (Vytorin) combination product.

www.pharmac.govt.nz/2010/04/26/2010-04_Consultation_letter_-_atorvastatin_and_statin_algorithm.pdf

Some consultation responses requested consideration of widening access to ezetimibe so that it could be used in patients who fail to reach their LDL cholesterol targets on statins.

This proposal is the result of consideration of these issues and further discussions with the supplier Merck Sharp & Dohme (New Zealand) Limited (MSD).

Currently ezetimibe individual tablets (Ezetrol) and ezetimibe simvastatin combination tablets (Vytorin) are funded via Special Authority for:

- Patients with a calculated absolute risk of cardiovascular disease > 20% over 5 years, who cannot tolerate a statin dose ≥ 40 mg day, and who have an LDL cholesterol ≥ 2.0 mmol/litre (if they have a CABG) or ≥ 2.5 mmol/litre (if they do not have a CABG).
- Patients with homozygous familial or heterozygous familial hypercholesterolemia, who are on maximal dose statin therapy and who have an LDL cholesterol ≥ 5 mmol/litre.

However, ezetimibe is not currently funded if it is used in combination with atorvastatin, and both initial and renewal applications require a Specialist application.

The access criteria for ezetimibe and ezetimibe with simvastatin were considered by the Cardiovascular Subcommittee of PTAC in August 2008. The Subcommittee:

- considered that maximal use of statins should be utilised in preference to other lipid modifying agents.
- noted that other treatment options, in addition to ezetimibe, should also be considered after failure of statin therapy.
- recommended that ezetimibe be made available, for use in combination with atorvastatin, for patients who have failed to reach their LDL-treatment target on simvastatin and then on atorvastatin with a medium priority
- recommended that intolerance of both simvastatin and atorvastatin should be required before a patient can access ezetimibe and that this change occurs with a high priority.
- considered that PHARMAC should wait until the results of further ezetimibe trials become available, such as IMPROVE-IT, before any consideration is given to enabling ezetimibe to be used before the currently available statins.
- considered that in light of the results of the ENHANCE study that atorvastatin plus ezetimibe is preferable to Vytorin; however, it also acknowledged that Vytorin may offer a compliance advantage and therefore considered that it should remain available
- considered that if a patient has rhabdomyolysis (defined as muscle aches and creatine kinase more than 10 x normal) upon treatment with simvastatin then they should be able to access ezetimibe without trialling atorvastatin

Mianserin hydrochloride (Tolvon)

Mianserin hydrochloride is currently funded for patients with depression and co-existent bladder neck obstruction or cardiovascular disease. The Mental Health Subcommittee of PTAC has advised that there are few funded antidepressant options for patients who do not meet the current mianserin restrictions and who require treatment with a non-serotonergic antidepressant, particularly if they cannot tolerate nortriptyline. The Subcommittee recommended that the Special Authority criteria for initial applications be amended, as proposed in this consultation letter, with a high priority.

The full minute of the Subcommittee's discussion can be found on PHARMAC's website at [www.pharmac.govt.nz/2010/01/29/?q=mental health](http://www.pharmac.govt.nz/2010/01/29/?q=mental+health).

Oestriol (Ovestin)

Currently oestriol is funded without restriction.