

19 June 2009

Proposal to Reference Price Betaloc CR to AFT-Metoprolol CR

Summary

- Metoprolol succinate is a medicine used to treat high blood pressure, and heart failure. It is currently supplied by AstraZeneca Ltd under the brand name Betaloc CR.
- A new brand of metoprolol succinate, supplied by AFT Pharmaceuticals Ltd and called AFT-Metoprolol CR, has been fully funded since 1 June 2009.
- We propose to reduce the subsidy that is paid for Betaloc CR so that it is the same as the subsidy paid for AFT-Metoprolol CR (reference pricing). This would create savings of around \$14 million per year.
- Medsafe has established the quality of AFT-Metoprolol CR by comparison of it to Betaloc CR.
- If the proposal is approved, its effect on people taking Betaloc CR would depend upon how AstraZeneca Ltd responds to the pricing competition. If AstraZeneca Ltd reduced the price of Betaloc CR so that the price is the same as the proposed subsidy, then there would be no effect on patients (both AFT-Metoprolol CR and Betaloc CR would be fully funded). However, if AstraZeneca Ltd did not reduce the price, then an additional charge would be required for Betaloc CR and patients would have to decide whether to pay this additional charge or change to the fully funded AFT-Metoprolol CR.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback please submit it in writing by 5 pm on Friday 10th of July 2009 to:

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PHARMAC	
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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.

Details of the Proposal

In order to increase the available funding for new medicines we need to consider proposals that reduce the cost of existing medicines.

It is proposed that from 1 September, the subsidy for Betaloc CR is reduced to the relevant per-tablet subsidy for AFT-Metoprolol CR, through the application of reference pricing, as shown in the table below.

Strength	Brand	Pack Size	Current list price	Current subsidy ¹	Proposed subsidy
23.75 mg	Betaloc CR	30	\$6.20	\$5.20	\$2.73
	AFT-Metoprolol CR	30	\$2.73	\$2.73	\$2.73
47.5 mg	Betaloc CR	30	\$7.80	\$6.50	\$3.41
	AFT-Metoprolol CR	30	\$3.41	\$3.41	\$3.41
95 mg	Betaloc CR	30	\$13.20	\$11.20	\$5.88
	AFT-Metoprolol CR	30	\$5.88	\$5.88	\$5.88
190 mg	Betaloc CR	30	\$21.00	\$20.25	\$10.63
	AFT-Metoprolol CR	30	\$10.63	\$10.63	\$10.63

¹ A higher subsidy for Betaloc CR (which equates to the list price) is available under endorsement criteria. Currently most patients are receiving fully subsidised Betaloc CR.

In addition, the endorsement that currently applies to Betaloc CR would be removed resulting in no patients taking Betaloc CR being fully funded.

For patients, the effect of this proposal would depend upon how AstraZeneca Ltd responds.

If AstraZeneca Ltd reduced the price of Betaloc CR to meet the proposed subsidy then both AFT-Metoprolol CR and Betaloc CR would be fully funded. If AstraZeneca Ltd did not, then the subsidy provided for Betaloc CR would be lower than its price and it would therefore not be fully funded for any patients. If Betaloc CR is not fully funded then:

- Patients wishing to obtain fully funded metoprolol succinate would need to change brands to AFT-Metoprolol CR.
- Patients taking Betaloc CR, who wish to continue taking that brand rather than change to AFT-Metoprolol CR, would need to pay a part-charge. The magnitude of the part-charge would vary dependent on the strength of metoprolol succinate required and depending upon the pharmacy supplying it. It is likely that any part-charge would be between \$19.36 and \$57.86 (GST inclusive) for three months supply.

Background

In 2007, following consultation, PHARMAC entered into a contract with AFT Pharmaceuticals Ltd (AFT) for the funding of its brand of metoprolol succinate tablets, AFT-Metoprolol CR (subject to regulatory approval by Medsafe).

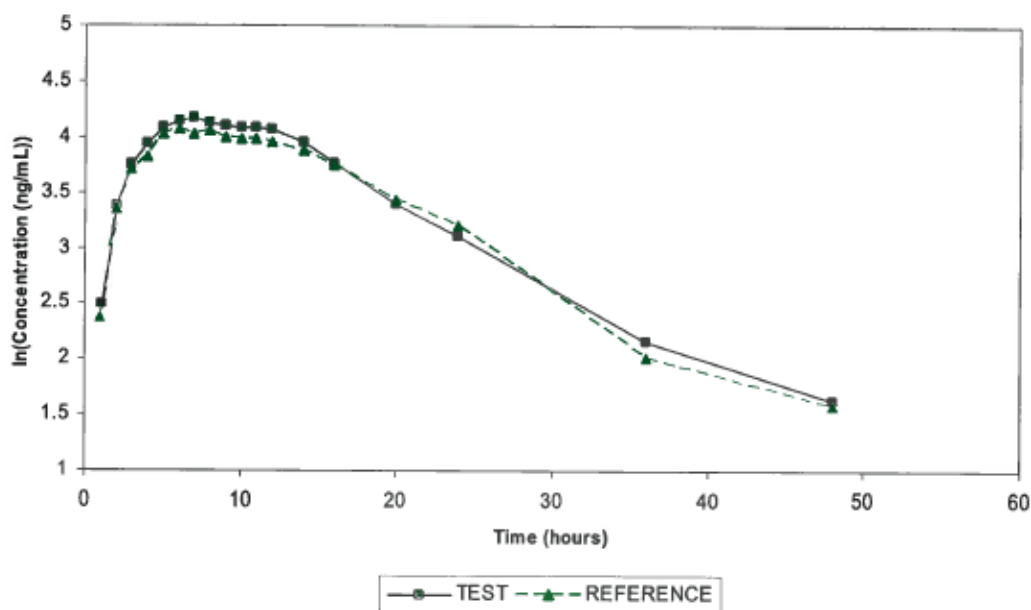
Medsafe subsequently approved AFT's product, and AFT-Metoprolol CR has been fully funded since 1 June 2009 (without an endorsement requirement).

Bioequivalence of AFT-Metoprolol CR and Betaloc CR

Medsafe is responsible for establishing the quality of AFT-Metoprolol CR and this has been done during the registration process by comparison to Betaloc CR. As part of the registration process Medsafe evaluators assessed AFT-Metoprolol CR for safety, bioequivalence and quality according to international standards.

Bioequivalence was investigated under fasting, fed and steady state conditions. We have provided the results of the comparative single dose bioequivalence study in the fed state by way of an example below:

Figure 1. Drug plasma profiles of Metoprolol AFT CR (test) and Betaloc CR (reference)



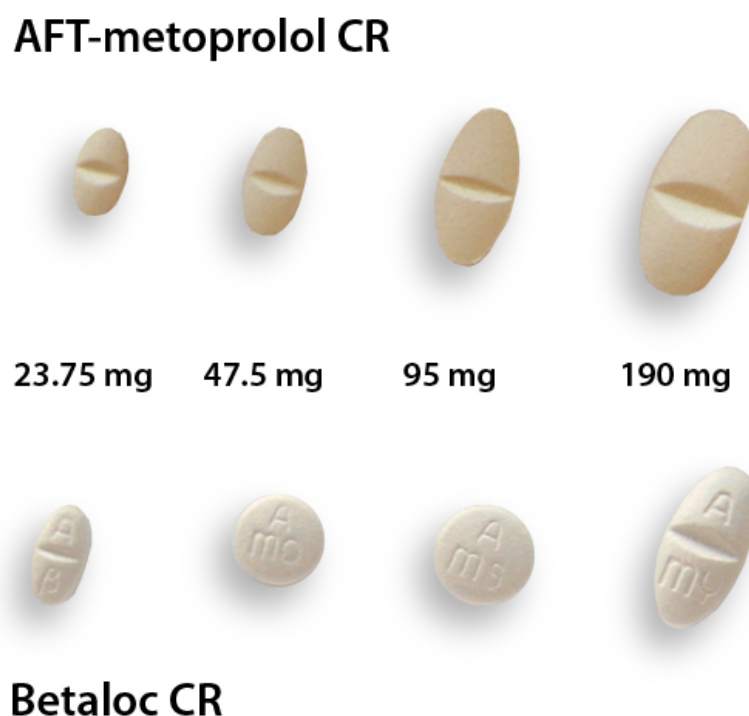
We note that the 90% confidence intervals for the relevant parameters (C_{max} , and AUC_T) were also within the internationally accepted ranges of 80% to 125%.

For more information on Medsafe's approval of multi-source (generic) medicines see <http://www.medsafe.govt.nz/Consumers/regulate.asp#Mult>.

Differences between Metoprolol-AFT CR and Betaloc CR

While the amount of the active ingredient is identical in each brand, there are some differences in the physical characteristics of the two brands resulting in the brands having different sizes and shapes, as illustrated below:

Figure 2. Physical appearance of each strength of AFT-Metoprolol CR (top row) and Betaloc CR (bottom row) tablets



PHARMAC has taken advice from its Tender Medical Advisory Committee – a group of practising clinicians and pharmacists – regarding the suitability of AFT-Metoprolol CR. The Committee noted the differences in physical characteristics between AFT-Metoprolol CR and Betaloc CR and considered that either brand was acceptable.

Metoprolol succinate manufacturing in the United States

We are aware that there has been some manufacturing issues with metoprolol succinate in the United States. These include:

- a voluntary recall of approximately 40 medicines, including metoprolol succinate, as a precautionary measure – because the medicines may not have been manufactured under conditions that complied with current Good Manufacturing Practice.
- a warning letter from the FDA to a different manufacturer relating to deviations from current Good Manufacturing Practice.

We can confirm that AFT-Metoprolol CR and Betaloc CR are not manufactured by either of the above manufacturers.

Fiscal effect of the proposal

The cost of AFT-Metoprolol CR is approximately 55% lower than the price of Betaloc CR (there is a variation between strengths).

This proposal would reduce expenditure on metoprolol succinate from about \$26 million to \$11 million per annum; providing savings in excess of \$14 million per year. Such savings would be used for the funding of other medicines.