BETA-BLOCKERS

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BETA-BLOCKER OPTIONS FOLLOWING FUNDING CHANGES TO **BETALOC CR**

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This document is based on a combination of evidence, information from the Medsafe data sheets and clinical experience. It has been reviewed by both General Practitioners and Cardiologists.

KEY MESSAGES

This information has been developed to help general practitioners maintain best practice prescribing in the context of changes to the funding of Betaloc CR.

BETALOC CR

The supplier has notified a price increase for all strengths of Betaloc CR. This price increase is planned for the 1st of October 2007.

This change will mean that:

1. All patients on Betaloc CR prior to 1 October 2007 will continue to have their prescriptions fully funded where the prescription is endorsed 'certified condition' or 'on metoprolol succinate prior to 1 October 2007'.

2. All post-myocardial infarction patients (even when first prescribed after 1 October 2007) will be able to obtain metoprolol succinate fully funded where the prescription is endorsed 'certified condition' or 'post-myocardial infarction'.

3. New patients requiring a beta-blocker (other than post-myocardial infarction patients) will need to be prescribed an alternative fully funded beta-blocker, or pay a part charge for Betaloc CR.

We recommend:

1. Clinicians endorse prescriptions for Betaloc CR with the phrase 'certified condition' for:
    - current patients (first prescribed before 1 October 2007); and,
    - new post myocardial infarction patients

2. For new patients requiring a beta-blocker (other than post myocardial patients) clinicians prescribe an alternative, fully funded beta-blocker as per the guidance in this document.

Dr Sam Entwistle
NZMC Reg No. A88984-3

Item Count:
Subsidy Card:

Mr Arnold Smith

Flat 1, 76 Alexander Street, Newmarket, Auckland

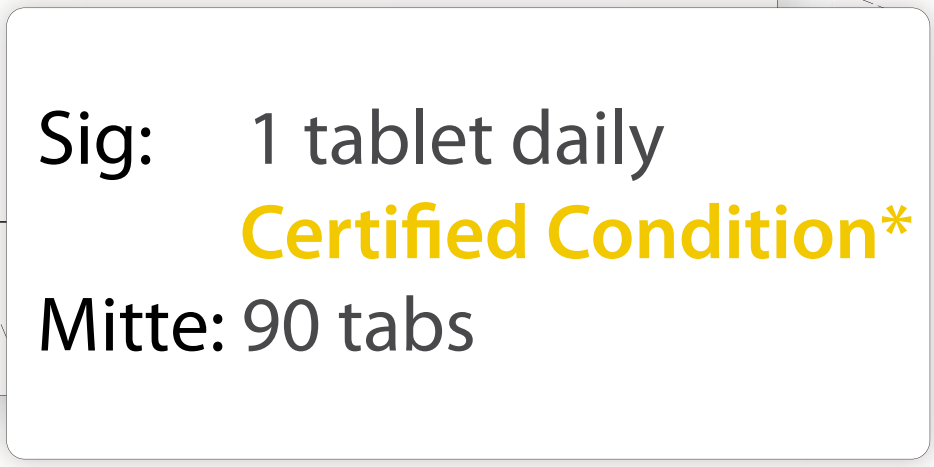
GMS: A3 DOB: 1 Feb 1934 NHI: BCR1234

Rx **Aug 2007**

Metoprolol Succinate 95 mg Controlled Release Tab

Sig: 1 tablet daily
Certified Condition
Mitte: 90 tabs

Dr Sam Entwistle_



* 'Certified Condition' can be computer generated

BETA-BLOCKERS

TABLE 1: FULLY FUNDED BETA-BLOCKERS AND APPROVED INDICATIONS IN NEW ZEALAND

Approved Indications*	Hypertension	Angina	Post MI	Arrhythmia	Heart failure (Adjunct)	Brand
acebutolol	✓	✓		✓		*ACB*
atenolol**	**	✓	**	✓		*Loten*
carvedilol	✓	✓	✓		✓	*Dilatrend*
celiprolol	✓	✓				*Celol*
metoprolol tartrate (oral)	✓	✓	***	✓	***	*Lopressor* *Slow Lopressor****
nadolol	✓	✓		✓		*Apo-nadolol*
timolol	✓	✓	✓	✓		*Apo-timol*
propranolol	✓	✓	✓	✓		*Cardinol* *Cardinol LA*
pindolol	✓	✓		✓		*Pindol*
labetalol	✓	✓				*Hybloc*

✓ Traditionally these drugs have not been used for these indications, however there is literature which suggests efficacy.

**Based on manufacturers datasheets*

***A recent meta analysis concluded that there is insufficient evidence for the use of atenolol in secondary prevention post MI, and it was associated with increased mortality compared to other antihypertensive treatments. (Lyndholm et al)*

****Lopressor is not approved for use in these indications in New Zealand, however international literature provides evidence for its use*

*****Slow-Lopressor 200 mg is a once daily divitab (fractionable sustained-release tablet) which can be split, therefore it can also provide a 100 mg once daily dose.*

BETA-BLOCKER CHOICE

BETA-BLOCKERS FOR CARDIOVASCULAR INDICATIONS

Beta-blockers are used for a number of cardiovascular indications including the treatment of hypertension, angina pectoris, cardiac arrhythmias, as secondary prevention post myocardial infarction and in heart failure.

The selection of a specific beta-blocker for an individual patient depends on several factors including;

- Clinical evidence of effectiveness and approved datasheet indication.
- Individual patient tolerability. For example, more lipid soluble beta-blockers (e.g. propranolol) may cause more CNS effects than more water soluble drugs such as atenolol.
- Cardioselectivity. Non-cardioselective agents are more likely to cause respiratory symptoms such as bronchospasm in susceptible people.
- Organ function. Beta-blockers vary in the relative extent of hepatic metabolism versus renal excretion. Atenolol, nadolol and sotalol, for example, are renally excreted and require careful dose adjustment if they have to be used in people with renal impairment.
- Intrinsic sympathomimetic activity - ISA. Pindolol and celiprolol have ISA and cause less bradycardia and so are less suitable in angina. On the other hand, drugs with ISA may be less likely to cause fatigue or coldness of extremities.
- Specific indications. For example, sotalol has specific antiarrhythmic effects and its use should be limited to these indications.

BETA-BLOCKERS AND DIABETES

Beta-blockers are not contraindicated in people with diabetes but they can reduce glucose tolerance and interfere with the metabolic and autonomic responses to hypoglycaemia. Cardioselective beta-blockers such as metoprolol or atenolol are preferable and beta-blockers should be avoided in people with frequent episodes of hypoglycaemia.

WITHDRAWAL OF BETA-BLOCKERS

Abrupt withdrawal of beta-blockers has sometimes resulted in angina, myocardial infarction, ventricular arrhythmias, and death. Patients on long-term treatment with a beta-blocker should have their medication discontinued gradually over a period of 1 to 2 weeks.

BETA-BLOCKERS FOR HYPERTENSION

Beta-blockers are no longer considered first line therapy in hypertension when there is no co-morbidity (e.g. angina) for which a beta-blocker is indicated. We recently discussed the changing role of beta-blockers in the management of hypertension (Best Practice Journal; Issue 6) and the key points are summarised below.

- While beta-blockers in general, are looking less desirable as first-line blood pressure lowering medicines in uncomplicated hypertension, atenolol is potentially the least effective.
- Beta-blockers are appropriate first-line blood pressure lowering medications when there is a concurrent medical condition for which beta-blockers have been proven effective, such as angina, previous myocardial infarction, heart failure or atrial fibrillation.
- In general, the dose of beta-blockers does not have to be high. Start with the lowest dosage of beta-blocker and increase if required.
- An enhanced antihypertensive effect is seen when other antihypertensives are given with beta-blockers e.g. thiazide diuretics
- Beta-blockers are effective for reducing blood pressure but other antihypertensives are usually more effective for reducing the incidence of stroke, myocardial infarction, and cardiovascular mortality, especially in the elderly. Other antihypertensives are therefore preferred for routine initial treatment of uncomplicated hypertension.

TABLE 2. TYPICAL DOSES FOR BETA-BLOCKERS USED FOR HYPERTENSION

Beta-blocker	Usual doses in hypertension	Brand
atenolol*	25–100 mg daily	Loten
celiprolol	200 mg daily increased gradually at 2 to 4 week intervals to 400–600 mg daily	Celol
carvedilol**	Initially 12.5 mg once daily, increased after 2 days to usual dose of 25 mg once daily; if necessary may be increased at intervals of at least 2 weeks to max. 50 mg daily in 1–2 divided doses; ELDERLY initial dose of 12.5 mg daily may provide satisfactory control.	Dilatrend
metoprolol succinate	Initially 47.5 mg once daily, increased if necessary to 95–190 mg daily	Betaloc CR
metoprolol tartrate (ordinary release)	100–200 mg daily in 1–2 divided doses	Lopressor
metoprolol tartrate (controlled release)	100–200 mg daily	Slow Lopressor***
nadolol	40 mg daily, increased gradually to a usual maintenance dose of 80–120 mg daily (higher doses rarely necessary)	Apo-nadolol
timolol	Initially, 10 mg (single or divided daily dose), increased according to response to a maximum of 60 mg daily; doses above 20 mg should be administered on a divided dose schedule	Apo-timolol
propranolol	Initially 80 mg twice daily, increased at weekly intervals as required; maintenance 160–320 mg daily. In practice doses greater than 160 mg are rarely required.	Cardinol Cardinol LA

** Note recent data suggests atenolol may be less effective than other antihypertensive drugs in preventing cardiovascular events.*

*** Traditionally carvedilol has not been used for this indication, however there is literature which suggests efficacy.*

****Slow-Lopressor 200 mg is a once daily divitab (fractionable sustained-release tablet) which can be split, therefore can also provide a 100 mg once daily dose*

BETA-BLOCKERS IN HEART FAILURE

- Some beta-blockers (carvedilol, metoprolol) are beneficial in the treatment of heart failure by blocking sympathetic activity.
- Beta-blockers are recommended in combination with ACE inhibitors and diuretics as part of standard therapy in patients with clinically stable, mild to severe chronic heart failure.
- They are used as an adjunct to conventional treatments (ACE inhibitor, loop diuretic and digoxin). Treatment should be initiated by those experienced in the management of heart failure.

TABLE 3. TYPICAL DOSES FOR BETA-BLOCKERS USED FOR HEART FAILURE

Beta-blocker	Usual doses in heart Failure	Brand
carvedilol *drug of choice*	Adjunct in heart failure, initially 3.125 mg twice daily (with food), dose increased at intervals of at least 2 weeks to 6.25 mg twice daily, then to 12.5 mg twice daily, then to 25 mg twice daily In some patients (who's weight is over 85 kg) up to 50 mg twice daily may be required. We would suggest a cardiology opinion in these patients.	Dilatrend
metoprolol succinate	Adjunct in chronic heart failure, initially 23.75 mg once daily for 2 weeks (moderate to severe failure, NYHA Class III-IV, half a 23.75 mg tablet once daily for 1 week then 23.75 mg once daily for 1-week); increase by doubling dose every 2 weeks to 190 mg once daily, if tolerated	Betaloc CR
metoprolol tartrate	Lopressor is not approved for use in heart failure in New Zealand; however international literature provides evidence for the use of metoprolol tartrate	Lopressor Slow Lopressor

BETA-BLOCKERS FOR SECONDARY PREVENTION POST MYOCARDIAL INFARCTION

- Atenolol and metoprolol may reduce early mortality after intravenous and subsequent oral administration in the acute phase.
- There is evidence that carvedilol, metoprolol, propranolol, and timolol have protective value when started in the early convalescent phase post MI.
- The role of other beta-blockers in the prevention of secondary events post MI has not been established.

TABLE 4. TYPICAL ORAL DOSES OF FULLY FUNDED BETA-BLOCKERS USED POST MI

Beta-blocker	Usual oral doses post MI	Brand
atenolol*	50-100 mg daily	Loten
carvedilol	Post-myocardial infarction, at 3–21 days post-infarct, initially 6.25 mg, then if tolerated, 6.25 mg twice daily, increased after intervals of 3–10 days to 12.5 mg twice daily, then to maximum 25 mg twice daily if tolerated. Traditionally carvedilol has not been used for this indication, however there is literature which suggests efficacy.	Dilatrend
propranolol	Prophylaxis after myocardial infarction, beginning 5–21 days after infarction, 40 mg 4 times daily for 2–3 days, then 80 mg twice daily or modified-release capsules, 160 mg daily	Cardinol Cardinol LA
timolol	10 mg twice daily	Apo-timolol
metoprolol succinate	Commence on 23.75 mg or 47.5 mg and titrate dose to between 47.5 and 95 mg daily, depending on heart rate	Betaloc CR
metoprolol tartrate	Lopressor is not approved for use post MI in New Zealand; however international literature provides evidence for the use of metoprolol tartrate	Lopressor Slow Lopressor

**Note recent concerns about the use of atenolol in post MI patients*

BETA-BLOCKERS FOR ANGINA

There are several beta-blockers approved for the treatment of angina in New Zealand (Table 1). Choice is governed by factors such as availability, prescriber familiarity, and the drug's specific characteristics and tolerance. Drugs with a long duration of action such as metoprolol tartrate controlled release (Slow-Lopressor) or atenolol may be preferred to improve patient compliance.

TABLE 5. TYPICAL DOSES OF BETA-BLOCKERS USED FOR THE PROPHYLAXIS OF ANGINA

Beta-blocker	Usual doses for angina	Brand
atenolol	50–100 mg daily as a single or divided dose	Loten
carvedilol	Initially, 12.5 mg twice daily for two days, then 25 mg twice daily Maximum 50 mg twice daily. Traditionally carvedilol has not been used for this indication, however there is literature which suggests efficacy.	Dilatrend
metoprolol succinate	47.5–190 mg once daily in the morning	Betaloc CR
metoprolol tartrate (ordinary release)	100–200 mg daily in two divided doses; may increase to 400 mg daily	Lopressor
metoprolol tartrate (controlled release)	100–200 mg daily May repeat in evening if necessary	Slow Lopressor

BETA-BLOCKERS FOR ARRHYTHMIAS AND RATE CONTROL.

Drug selection and dose is governed by the type of arrhythmia and indication. Drugs approved for treatment of arrhythmias are listed in Table 1. Please refer to individual drug's product data sheet/prescribing information for more details.

(N.B. Sotalol has class III antiarrhythmic activity and has specific indications for the acute treatment and prevention of supraventricular ventricular arrhythmia. It is not approved for other indications such as hypertension or angina).

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