

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

BETACARD

(Atenolol 100mg Tablet)

COMPOSITION

BETACARD-100

Each film coated tablet contains:

Atenolol I.P.....100 mg

Colours: Lake of Carmoisine, Lake of Brilliant Blue & Titanium Dioxide I.P.

INDICATIONS

Betacard is indicated for the treatment of hypertension.

DOSAGES AND ADMINISTRATION

Dosage must be individualized. Dosages should be determined by individual titration, dosages may be increased gradually until optimum blood pressure achieved.

Atenolol is usually given at a dosage of 25 to 100 mg per day.

Some renally impaired or elderly patients being treated for hypertension may require a lower starting dose of atenolol depending on the creatinine clearance (mL/min/1.73m²). If creatinine clearance is 15-35 and <15, the recommended dose is 50 mg and 25 mg given as one tablet a day. The full effect of this dose will usually be seen within one to two weeks.

If an optimal response is not achieved, the dosage should be increased to 100 mg given as one tablet a day. Increasing the dosage beyond 100 mg a day is unlikely to produce any further benefit. Atenolol may be used alone or concomitantly with other antihypertensive agents including thiazide type diuretics, hydralazine, prazosin, and alpha-methyldopa.

CONTRAINDICATIONS

Betacard, as with other beta-blockers, should not be used in patients with any of the following:

- hypersensitivity to the active substance, or to any of the excipients
- cardiogenic shock
- uncontrolled heart failure
- sick sinus syndrome
- second-or third-degree heart block
- untreated phaeochromocytoma
- metabolic acidosis
- bradycardia (<45 bpm)
- hypotension
- severe peripheral arterial circulatory disturbances.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Betacard as with other beta-blockers:

- Should not be withdrawn abruptly. The dosage should be withdrawn gradually over a period of 7–14 days, to facilitate a reduction in beta-blocker dosage. Patients should be followed during withdrawal, especially those with ischaemic heart disease.
- When a patient is scheduled for surgery, and a decision is made to discontinue beta-blocker therapy, this should be done at least 24 hours prior to the procedure. The risk-benefit assessment of stopping beta-blockade should be made for each patient. If treatment is continued, an anaesthetic with little negative inotropic activity should be selected to minimise the risk of myocardial depression. The patient may be protected against vagal reactions by intravenous administration of atropine.
- Although contraindicated in uncontrolled heart failure, may be used in patients whose signs of heart failure have been controlled. Caution must be exercised in patients whose cardiac reserve is poor.
- May increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. Betacard is a beta₁-selective beta-blocker; consequently, its use may be considered although utmost caution must be exercised.
- Although contraindicated in severe peripheral arterial circulatory disturbances, may also aggravate less severe peripheral arterial circulatory disturbances.
- Due to its negative effect on conduction time, caution must be exercised if it is given to patients with first-degree heart block.
- May mask the symptoms of hypoglycaemia, in particular, tachycardia.
- May mask the signs of thyrotoxicosis.
- Will reduce heart rate as a result of its pharmacological action. In the rare instances when a treated patient develops symptoms which may be attributable to a slow heart rate and the pulse rate drops to less than 50–55 bpm at rest, the dose should be reduced.
- May cause a more severe reaction to a variety of allergens when given to patients with a history of anaphylactic reaction to such allergens. Such patients may be unresponsive to the usual doses of adrenaline (epinephrine) used to treat the allergic reactions.
- May cause a hypersensitivity reaction including angioedema and urticaria.
- Should be used with caution in the elderly, starting with a lesser dose.

Since Betacard is excreted via the kidneys, dosage should be reduced in patients with a creatinine clearance of below 35 ml/min/1.73 m².

Although cardioselective (beta₁) beta-blockers may have less effect on lung function than non-selective beta-blockers, as with all beta-blockers, these should be avoided in patients with reversible obstructive airways disease, unless there are compelling clinical reasons for their use. Where such reasons exist, Betacard may be used with caution. Occasionally, some increase in airways resistance may occur in asthmatic patients however, and this may usually be reversed by commonly used dosage of bronchodilators such as salbutamol or isoprenaline. The label and patient information leaflet for this product state the

following warning: “If you have ever had asthma or wheezing, you should not take this medicine unless you have discussed these symptoms with the prescribing doctor”. As with other beta-blockers, in patients with a phaeochromocytoma, an alpha-blocker should be given concomitantly.

DRUG INTERACTION

Combined use of beta-blockers and calcium channel blockers with negative inotropic effects, e.g. verapamil and diltiazem, can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or sinoatrial or atrioventricular conduction abnormalities. This may result in severe hypotension, bradycardia and cardiac failure. Neither the beta-blocker nor the calcium channel blocker should be administered intravenously within 48 hours of discontinuing the other. Concomitant therapy with dihydropyridines, e.g. nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency. Digitalis glycosides, in association with beta-blockers, may increase atrioventricular conduction time.

Beta-blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two drugs are co-administered, the beta-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine by beta-blocker therapy, the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped. (See also prescribing information for clonidine.)

Class I anti-arrhythmic drugs (e.g. disopyramide) and amiodarone may have a potentiating effect on atrial-conduction time and induce negative inotropic effect. Concomitant use of sympathomimetic agents, e.g. adrenaline (epinephrine), may counteract the effect of beta-blockers.

Concomitant use with insulin and oral antidiabetic drugs may lead to the intensification of the blood sugar lowering effects of these drugs. Symptoms of hypoglycaemia, particularly tachycardia, may be masked.

Concomitant use of prostaglandin synthetase-inhibiting drugs, e.g. ibuprofen and indometacin, may decrease the hypotensive effects of beta-blockers.

Caution must be exercised when using anaesthetic agents with Betacard. The anaesthetist should be informed and the choice of anaesthetic should be an agent with as little negative inotropic activity as possible. Use of beta-blockers with anaesthetic drugs may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic agents causing myocardial depression are best avoided.

FERTILITY, PREGNANCY AND LACTATION

Caution should be exercised when Betacard is administered during pregnancy or to a woman who is breast-feeding.

Pregnancy

Betacard crosses the placental barrier and appears in the cord blood. No studies have been performed on the use of Betacard in the first trimester and the possibility of foetal injury cannot be excluded. Betacard has been used under close supervision for the treatment of hypertension in the third trimester. Administration of Betacard to pregnant women in the management of mild to moderate hypertension has been associated with intra-uterine growth retardation.

The use of Betacard in women who are, or may become, pregnant requires that the anticipated benefit be weighed against the possible risks, particularly in the first and second trimesters, since beta-blockers, in general, have been associated with a decrease in placental perfusion which may result in intra-uterine deaths, immature and premature deliveries.

Breast-feeding

There is significant accumulation of Betacard in breast milk.

Neonates born to mothers who are receiving Betacard at parturition or breast-feeding may be at risk of hypoglycaemia and bradycardia.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Betacard has no or negligible influence on the ability to drive and use machines. However, it should be taken into account that occasionally dizziness or fatigue may occur.

UNDESIRABLE EFFECTS

Betacard is well tolerated. In clinical studies, the undesired events reported are usually attributable to the pharmacological actions of atenolol.

The following undesired events, listed by body system, have been reported with the following frequencies: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) including isolated reports, not known (cannot be estimated from the available data).

System Organ Class	Frequency	Undesirable Effect
Blood and lymphatic system disorders	Rare	Purpura, thrombocytopenia

Psychiatric disorders	Uncommon	Sleep disturbances of the type noted with other beta-blockers
	Rare	Mood changes, nightmares, confusion, psychoses and hallucinations
Nervous system disorders	Rare	Dizziness, headache, paraesthesia
Eye disorders	Rare	Dry eyes, visual disturbances
Cardiac disorders	Common	Bradycardia
	Rare	Heart failure deterioration, precipitation of heart block
Vascular disorders	Common	Cold extremities
	Rare	Postural hypotension which may be associated with syncope, intermittent claudication may be increased if already present, in susceptible patients Raynaud's phenomenon
Respiratory, thoracic and mediastinal disorders	Rare	Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints
Gastrointestinal disorders	Common	Gastrointestinal disturbances
	Rare	Dry mouth
Hepatobiliary disorders	Uncommon	Elevations of transaminase levels
	Rare	Hepatic toxicity including intrahepatic cholestasis
Skin and subcutaneous tissue disorders	Rare	Alopecia, psoriasiform skin reactions, exacerbation of psoriasis, skin rashes
	Not known	Hypersensitivity reactions, including angioedema and urticaria
Musculoskeletal and connective tissue disorders	Not known	Lupus-like syndrome
Reproductive system and breast disorders	Rare	Impotence

General disorders and administration site conditions	Common	Fatigue
Investigations	Very rare	An increase in ANA (Antinuclear Antibodies) has been observed, however the clinical relevance of this is not clear

Discontinuance of the drug should be considered if, according to clinical judgement, the well-being of the patient is adversely affected by any of the above reactions.

OVERDOSE

The symptoms of overdosage may include bradycardia, hypotension, acute cardiac insufficiency and bronchospasm.

General treatment should include: close supervision; treatment in an intensive care ward; the use of gastric lavage; activated charcoal and a laxative to prevent absorption of any drug still present in the gastrointestinal tract; the use of plasma or plasma substitutes to treat hypotension and shock. The possible uses of haemodialysis or haemoperfusion may be considered.

Excessive bradycardia can be countered with atropine 1–2 mg intravenously and/or a cardiac pacemaker. If necessary, this may be followed by a bolus dose of glucagon 10 mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon 1–10 mg/hour depending on response. If no response to glucagon occurs or if glucagon is unavailable, a beta-adrenoceptor stimulant such as dobutamine 2.5 to 10 micrograms/kg/minute by intravenous infusion may be given. Dobutamine, because of its positive inotropic effect could also be used to treat hypotension and acute cardiac insufficiency. It is likely that these doses would be inadequate to reverse the cardiac effects of beta-blocker blockade if a large overdose has been taken. The dose of dobutamine should therefore be increased if necessary to achieve the required response according to the clinical condition of the patient.

Bronchospasm can usually be reversed by bronchodilators.

PHARMACOLOGICAL PROPERTIES

- **Pharmacodynamic properties**

Pharmacotherapeutic group: Beta-blocking agents, plain, selective, ATC code: CO7A B03.

Mechanism of action

Atenolol is a beta-blocker which is beta₁-selective, (i.e. acts preferentially on beta₁-adrenergic receptors in the heart). Selectivity decreases with increasing dose.

Atenolol is without intrinsic sympathomimetic and membrane-stabilising activities and as with other beta-blockers, has negative inotropic effects (and is therefore contraindicated in uncontrolled heart failure).

As with other beta-blockers, the mode of action of atenolol in the treatment of hypertension is unclear.

It is probably the action of atenolol in reducing cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina.

It is unlikely that any additional ancillary properties possessed by S (-) atenolol, in comparison with the racemic mixture, will give rise to different therapeutic effects.

Clinical efficacy and safety

Betacard is effective and well-tolerated in most ethnic populations although the response may be less in black patients.

Betacard is effective for at least 24 hours after a single oral dose. The drug facilitates compliance by its acceptability to patients and simplicity of dosing. The narrow dose range and early patient response ensure that the effect of the drug in individual patients is quickly demonstrated. Betacard is compatible with diuretics, other hypotensive agents and antianginals. Since it acts preferentially on beta-receptors in the heart, Betacard may, with care, be used successfully in the treatment of patients with respiratory disease, who cannot tolerate non-selective beta-blockers.

Early intervention with Betacard in acute myocardial infarction reduces infarct size and decreases morbidity and mortality. Fewer patients with a threatened infarction progress to frank infarction; the incidence of ventricular arrhythmias is decreased and marked pain relief may result in reduced need of opiate analgesics. Early mortality is decreased.

Betacard is an additional treatment to standard coronary care.

- **Pharmacokinetic properties**

Absorption

Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40–50%) with peak plasma concentrations occurring 2–4 hours after dosing. The atenolol blood levels are consistent and subject to little variability. There is no significant hepatic metabolism of atenolol and more than 90% of that absorbed reaches the systemic circulation unaltered.

Distribution

Atenolol penetrates tissues poorly due to its low lipid solubility and its concentration in brain tissue is low. Plasma protein binding is low (approximately 3%).

Elimination

The plasma half-life is about 6 hours but this may rise in severe renal impairment since the kidney is the major route of elimination.

- **Preclinical safety data**

Atenolol is a drug on which extensive clinical experience has been obtained. Relevant information for the prescriber is provided elsewhere in the Prescribing Information.

Expiry date

Do not use later than the date of expiry.

Storage

KEEP IN COOL DRY PLACE, PROTECTED FROM LIGHT

Presentation

BETACARD-100 is available in Blister strip of 14 Tablets

MARKETED BY



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IN/BETACARD 100mg/JUL-17/02/PI