

This product is no longer marketed in New Zealand and this data sheet may not be up to date. A more up-to-date data sheet for a product with the same active ingredient may be available on the Medsafe website.

## Data Sheet

### ACB

#### *Acebutolol hydrochloride*

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### Presentation

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ACB 100 capsules each containing the equivalent of 100 mg acebutolol (in the form of the hydrochloride). The size 2 capsules are bi-coloured (opaque yellow/opaque ivory). Their length is approximately 17.5 mm and the diameter of the body is approximately 6 mm.

ACB 200 capsules each containing the equivalent of 200 mg acebutolol (in the form of the hydrochloride). The capsules are bi-coloured (opaque yellow/opaque flesh). Their length is approximately 19 mm and the diameter of the body is approximately 6 mm.

ACB 400 tablets each containing the equivalent of 400 mg acebutolol (in the form of the hydrochloride). The tablets are white, film coated, circular, bi-convex, one face imprinted 'ACB 400' with a plain reverse. The tablet diameter is about 12.7 mm.

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### Uses

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#### *Actions*

ACEBUTOLOL is a beta adrenoreceptor antagonist which is cardioselective, ie. acts preferentially on beta-1 adrenergic receptors in the heart. Its principal effects are to reduce heart rate especially on exercise and to lower blood pressure in hypertensive subjects. ACEBUTOLOL and its equally active metabolite, diacetolol, have anti-arrhythmic activity. Both have partial agonist activity (PAA) also known as intrinsic sympathomimetic activity (ISA). This property ensures that some degree of stimulation of beta-receptors is maintained. Under conditions of rest this tends to balance the negative chronotropic and negative inotropic effects. ACEBUTOLOL blocks the effects of excessive catecholamine stimulation resulting from stress.

#### *Pharmacokinetics*

On oral administration acebutolol is rapidly and almost completely absorbed from ACEBUTOLOL tablets and capsules. Absorption appears to be unaffected by the presence of food in the gut. There is rapid formation of a major equiactive metabolite, diacetolol, which possesses a similar pharmacological profile to acebutolol. Peak plasma concentrations of active material (i.e. acebutolol and diacetolol) are achieved within 2-4 hours, and the plasma elimination half-life of the parent compound, acebutolol, is 3-4 hours and that of diacetolol, which pre-dominates during repeated dosage, is 8-11 hours.

A study comparing the pharmacokinetics of acebutolol in young adults and aged subjects showed no significant differences. Limited data from a further study suggest that maximum plasma concentrations may be increased by up to a factor of two in elderly patients. Because of biliary excretion and direct transfer across the gut wall from the systemic circulation to the gut lumen, more than 50% of an oral dose of ACEBUTOLOL is recovered in the faeces with acebutolol and diacetolol in equal portions; the rest of the dose is recovered in urine, mainly as diacetolol. Both acebutolol and diacetolol are hydrophilic and exhibit poor penetration of the CNS.

#### *Indications*

ACEBUTOLOL is indicated in the following conditions:

1. The management of all grades of hypertension.

2. The management of angina pectoris.
3. The control of tachyarrhythmias.

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## Dosage and Administration

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*ELDERLY:* There are no specific dosage recommendations for the elderly.

### **Hypertension:**

Initial dosage of 400 mg orally once daily at breakfast or 200 mg orally twice daily. If response is not adequate within two weeks, dosage may be increased up to 400 mg orally twice daily. If the hypertension is not adequately controlled consideration should be given to adding a second antihypertensive agent such as a compatible calcium antagonist or a small dose of a thiazide diuretic.

### **Angina Pectoris:**

Initial dosage of 200 mg orally twice daily; patients thus adequately controlled may receive the total dose as 400 mg once daily, at breakfast.

Daily dosage higher than 400 mg should be administered as divided doses. In severe forms up to 300 mg three times daily may be required; up to 1200 mg daily has been used. When given orally an initial dose of 200 mg is recommended and may take up to three hours for maximal antiarrhythmic effect to become apparent. Thereafter 100 mg- 200 mg twice or three times daily is usually needed but may be increased as required if response is not obtained at lower dosage.

### **Cardiac Arrhythmias:**

When given orally an initial dose of 200 mg is recommended and may take up to three hours for maximal antiarrhythmic effect to become apparent. Thereafter 100 mg- 200 mg twice or three times daily is usually needed but may be increased as required if response is not obtained at lower dosage.

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## Contraindications

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1. Bronchial asthma or other obstructive lung disorders.
2. Uncontrolled heart failure.
3. Cardiogenic shock is an absolute contraindication to beta-blockade and caution is required in patients with blood pressures of the order of 100/60 mm Hg or below.
4. Sick-sinus syndrome.
5. Grade 2 and 3 A-V block and infranodal A-V block.
6. Severe bradycardia.
7. ACEBUTOLOL should not be used with verapamil or within several days of verapamil therapy (and vice versa).

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## Warnings and Precautions

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Renal impairment is not a contraindication to the use of ACEBUTOLOL which has both renal and non-renal excretory pathways. Some caution should be exercised when administering

high doses to patients with severe renal failure as cumulation could possibly occur in these circumstances. Caution should be exercised in patients with obstructive airways disease and particularly if ACEBUTOLOL is to be administered intravenously in asthmatic subjects. Bronchospasm is usually at least partially reversible by the use of a suitable agonist.

Chronic oral toxicity studies in animals have not indicated a carcinogenic potential for either acebutolol or its active metabolite, diacetolol. Acebutolol and diacetolol were also shown to be devoid of mutagenic potential in the Ames Test. Animal studies have not shown a teratogenic hazard.

Pregnancy:

ACEBUTOLOL should not be administered to female patients during the first trimester of pregnancy unless the physician considers it essential. Beta-blockers administered in late pregnancy may give rise to bradycardia of the foetus.

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## Adverse Effects

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ACEBUTOLOL possesses antihypertensive effects but these are unlikely to be noted in normotensive subjects. Those common to beta-blockade; bradycardia, gastrointestinal effects, cold extremities and lethargy have been met with infrequently. The low lipid solubility and lack of cumulation in CNS tissues of acebutolol and its active metabolite reduces the likelihood of sleep disturbances, depression or other central effects and such occurrences are rare.

Rashes and dry eyes may occur but are rare. Discontinuation of the drug should be considered if the occurrence of rash or dry eyes is otherwise not explicable. Isolated cases of pleurisy, hyper-sensitivity pneumonitis, pulmonary granulomas and pleuropulmonary fibrosis have been reported in patients taking acebutolol. Acebutolol has occasionally been associated with the development of antinuclear antibodies (ANA) and, rarely, myalgia and arthralgia. Significantly high ANA titres are rarely achieved at the recommended dose and both ANA and any related symptoms are reversible when the drug is discontinued.

Cessation of therapy with a beta-blocker should be gradual.

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## Interactions

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(See also Contraindications).

In patients with labile and insulin-dependent diabetes the dosage of the hypoglycaemic agent may need to be reduced.

Cross reactions due to displacement of other drugs from plasma protein binding sites are unlikely due to the low degree of plasma protein binding exhibited by acebutolol and diacetolol. If a beta adrenoceptor antagonist is used concurrently with clonidine the latter should not be withdrawn until several days after the former is discontinued. Acebutolol has been reported to interfere with the hypoglycaemic effect of glibenclamide.

ACEBUTOLOL therapy should be brought to the attention of the anaesthetist prior to general anaesthesia. If treatment is continued, special care should be taken when using anaesthetic agents such as ether, cyclopropane and trichlorethylene.

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## Overdosage

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In the rare event of excessive bradycardia or hypotension, 1 mg atropine sulphate administered intravenously should be given without delay. If this is insufficient it should be

followed by a slow intravenous injection of isoprenaline (5 mcg per minute) with constant monitoring until a response occurs. In severe cases of self poisoning with circulatory collapse unresponsive to atropine and catecholamines the intravenous injection of glucagon 10 – 20 mg may produce a dramatic improvement. Cardiac pacing may be employed if bradycardia becomes severe.

ACEBUTOLOL is dialysable.

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## Pharmaceutical Precautions

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ACEBUTOLOL capsules and tablets should be stored in a dry place below 25°C.

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## Medicine Classification

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Prescription Medicine.

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## Package Quantities

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Containers of 100 x 100 mg capsules.

Containers of 100 x 200 mg capsules.

Containers of 100 x 400 mg tablets.

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## Further Information

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## Name and Address

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## Date of Preparation

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2 February 2009