

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.

# PINDOL

## *Pindolol*

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### Presentation

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PINDOL 5 mg contains 5 mg of pindolol base. It is a round, FBE, white-scored 7.1 mm diameter tablet. It is imprinted P/5 on one side and plain on the reverse.

PINDOL 10 mg contains 10 mg of pindolol base. It is round, FBE, white-scored 7.9 mm diameter tablet. It is imprinted P/10 on one side and plain on the reverse.

PINDOL 15 mg contains 15 mg of pindolol base. It is round, FBE; white-scored 8.7 mm diameter tablet. It is imprinted P/15 on one side and plain on the reverse.

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### Uses

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#### **Actions**

PINDOLOL is a potent beta-adrenoceptor antagonist (beta-blocker). It blocks both beta 1- and beta 2-adrenoceptors for more than 24 hours after oral administration. It has negligible membrane-stabilising activity. As a beta-blocker, PINDOLOL protects the heart from beta-adrenoceptor stimulation during physical exercise and mental stress, and also reduces the sympathetic drive to the heart at rest. Its intrinsic sympathomimetic activity (ISA), however, provides the heart with basal stimulation similar to that elicited by normal resting sympathetic activity with the result that heart rate and contractility at rest, and intracardiac conduction are not unduly depressed. The risk of bradycardia is therefore, small, and a normal cardiac output is not reduced.

PINDOLOL is a beta-blocker with clinically relevant vasodilator activity. This results from the partial agonism exerted on beta 2-adrenoceptors in blood vessels. The high vascular resistance of established hypertension is lowered by PINDOLOL; tissue and organ perfusion is not impaired, and may even be improved.

In contrast to the potentially adverse changes in blood lipoprotein profiles seen during treatment with other beta-blockers (a decrease in the HDL/LDL ratio), the ratio of high density lipoproteins (HDL) to low density lipoproteins (LDL) does not change during long term therapy with PINDOLOL, because of its pronounced ISA. This ISA, exerted on bronchial smooth muscle reduces the risk of bronchospasm in non-asthmatic subjects with obstructive lung disease.

The low therapeutic doses of PINDOLOL reflect its high potency and bioavailability. The latter, resulting from near-complete absorption and a negligible hepatic first-pass effect, reduces individual plasma level variations and thus leads to constant therapeutic effects at a given dosage.

#### **Pharmacokinetics**

The rapid, nearly complete absorption ( $\geq 95\%$ ) and the negligible hepatic first-pass effect (13%) of PINDOLOL result in a high bioavailability (87%). Maximum plasma concentration is reached within one hour of oral administration. PINDOLOL has a plasma-protein binding of 40%, a volume of distribution of 2-3 L/kg and a total clearance of 500 mL/min. The elimination half-life of PINDOLOL is 3-4 hours; 30-40% is excreted unchanged in the urine, while 60-70% is excreted via the kidney and liver as inactive metabolites. PINDOLOL crosses the placental barrier and passes in small quantities into breast milk.

#### **Indications**

Arterial hypertension.

Angina pectoris (prevention of attacks).

Sinus and atrial tachycardia, paroxysmal tachycardia, tachycardia in patients with atrial flutter or fibrillation, supraventricular extrasystoles.

Hyperkinetic heart syndrome.

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## Dosage and Administration

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Oral:

The dosage should be adapted to the requirements of the individual patient, and is usually within a range of 5 to 30 mg per day.

Arterial hypertension:

Doses of 5 to 15 mg may be given as a single dose in the morning. Doses of 20 mg should be divided into 2 daily doses. In mild and moderate hypertension, PINDOLOL alone is often sufficient. In more severe or resistant cases, additional therapy with other anti-hypertensive drugs may be necessary.

Angina pectoris and cardiac arrhythmias:

The daily dosage of 10 to 30 mg is generally divided into 2 or 3 single doses.

Hyperkinetic heart syndrome:

7.5 to 20 mg daily.

Patients with impaired kidney or liver function may usually be treated with normal doses. Only in severe cases may a reduction of the daily dose be necessary.

Children:

Experience with PINDOLOL in children is limited.

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## Contraindications

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Bronchial asthma; digitalis-resistant and uncontrolled cardiac failure, cor pulmonale, marked bradycardia, heart block, sick sinus syndrome, 2<sup>nd</sup> and 3<sup>rd</sup> degree and infranodal A-V block, cardiogenic shock.

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## Warnings and Precautions

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Although PINDOLOL produces less depression of resting myocardial function than  $\beta$ -blockers without ISA, patients with incipient or manifest heart failure must be adequately digitalised before treatment with PINDOLOL. Similarly, if PINDOLOL is used for the treatment of acute myocardial infarction, it is necessary to monitor cardiovascular parameters closely.

Because of intrinsic sympathomimetic activity, PINDOLOL generally causes no significant changes in pulmonary function in patients with a tendency to bronchospasm due to non-asthmatic chronic obstructive lung disease. However, as with any  $\beta$ -blocker, a bronchoconstrictor effect can never be completely excluded, and  $\beta$ -blockers should never be administered to patients with a history of bronchial asthma. Should bronchospasm occur, appropriate therapeutic measures should be taken ( $\beta$ 2-stimulant, theophylline derivative).

It is essential to monitor cardiovascular function closely during general anaesthesia in patients treated with a  $\beta$ -blocker.

PINDOLOL is less likely to cause a rebound supersensitivity to  $\beta$ -adrenoceptor stimulation following abrupt cessation of chronic therapy than are  $\beta$ -blockers without ISA. However, interruption of therapy is considered necessary, it is advisable to reduce the dose of PINDOLOL progressively. If patients with phaeochromocytoma are treated with a beta-blocker an alpha-blocker should always be co-administered.

Beta-blocker treatment is often associated with an aggravation of the symptoms of pre-existing peripheral vascular disease. However, because of its sympathomimetic effects mediated at the vascular beta-2 receptors (vasodilation) peripheral vascular side effects (cold extremities) are only rarely encountered during PINDOLOL therapy.

In severe renal failure, further impairment of renal function has only been rarely observed during the therapy with PINDOLOL.

Care must be exercised when beta-blockers are administered to patients receiving antidiabetic therapy, since hypoglycaemia may occur during prolonged fasting and some of its symptoms (tachycardia, tremor) are masked. However, patients can be trained to recognise sweating as the principal symptom of hypoglycaemia during beta-blocker therapy.

Experimental studies in animals provide no evidence of a teratogenic effect of PINDOLOL. In the treatment of pregnant women presenting with hypertension, the drug has been shown to be effective and well tolerated without causing unfavourable effects in the foetus except, on rare occasions, bradycardia or hypoglycaemia in the newborn as a possible consequence of  $\beta$ -adrenoceptor blockade. PINDOLOL passes in small quantities into breast milk, but it is unlikely to affect the infant when therapeutic doses are used.

Because dizziness or fatigue may occur during initiation of treatment with beta-adrenoceptor blocking drugs, patients driving vehicles or operating machinery should exercise caution until they have determined their individual reaction to the treatment.

PINDOLOL should be kept out of reach of children.

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## Adverse Effects

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PINDOLOL is generally well tolerated. The side effects include: tiredness, dizziness, muscle cramps, tremor, gastrointestinal disturbances (mainly nausea), headache, sleep disturbances (similar to those observed with other beta-blockers). These side effects are, in most cases, mild and transient. Skin reactions and psychic symptoms (depression, hallucinations), necessitating interruption of therapy are rarely observed (see also Warnings and Precautions).

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## Interactions

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Antidiabetics:

(See under Warnings and Precautions.)

Calcium-channel blocking agents:

Experience has shown that the concomitant use of oral  $\beta$ -blockers and calcium antagonists of the dihydropyridine type can be useful in hypertension or angina pectoris. However, because of their potential effect on the cardiac conduction system and contractility, the IV route must be avoided. Oral treatment requires careful monitoring, especially when the  $\beta$ -blocker is combined with a verapamil-type calcium antagonist.

Cimetidine:

May increase the plasma levels of  $\beta$ -blockers, possibly by interference with hepatic metabolism.

Clonidine:

When therapy is discontinued in patients receiving a  $\beta$ -blocker and clonidine concurrently, the  $\beta$ -blockers should be gradually discontinued several days before clonidine is discontinued, in order to reduce the potential risk of a clonidine withdrawal hypertensive crisis.

MAO inhibitors:

Concurrent use with  $\beta$ -blockers is not recommended. Possibly significant hypertension may theoretically occur up to 14 days following discontinuation of the MAO inhibitor.

Nonsteroidal anti-inflammatory drugs (NSAIDs):

The effect of many antihypertensive agents, including  $\beta$ -blockers, may be reduced when they are used concurrently with these drugs, possibly as a result of the inhibition of renal prostaglandin synthesis and sodium and fluid retention caused by NSAIDs.

Phenothiazines:

Concurrent use with  $\beta$ -blockers may result in an increased plasma concentration of either drug.

Reserpine:

Concurrent use may result in an additive and possibly excessive  $\beta$ -adrenergic blockade.

Sympathomimetics with  $\beta$ -adrenergic stimulant activity and xanthines:

Concurrent use with  $\beta$ -blockers may result in mutual inhibition of therapeutic effects; in addition,  $\beta$ -blockers may decrease theophylline clearance.

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## Overdosage

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Overdosage with PINDOLOL usually requires no special treatment. If, in severe cases of bradycardia, therapy is required, 0.5-1.0 mg (or more) atropine sulphate should be given IV. Alternatively, in order to stimulate the beta-adrenergic receptors, isoprenaline hydrochloride may be given by slow IV infusion beginning with approx. 5 mcg/min until the desired effect is achieved.

In refractory cases the intravenous administration of 8 to 10 mg glucagon hydrochloride may be effective; the injection may be repeated and followed, if necessary, by an intravenous infusion of 1 to 3 mg/hour. The patient must be continuously monitored during these procedures.

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## Pharmaceutical Precautions

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Store 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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PINDOL 5 mg comes in packs of 100 and 500.

PINDOL 10 mg comes in packs of 100.

PINDOL 15 mg comes in packs of 100.

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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