

APO-PINDOLOL

1. APO-PINDOLOL (5mg, 10mg and 15mg tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pindolol 5mg, 10mg or 15mg

Excipient(s) of known effect

Apo-Pindolol does not contain gluten.

Apo-Pindolol contains lactose.

If you have been told by your doctor that you have intolerance to some sugars contact your doctor before taking this medicinal product.

Contains 135 mg of lactose monohydrate per 50 mg and 85 mg of lactose monohydrate per 100 mg.

This should be taken into account in patients with diabetes mellitus.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Apo-Pindolol 5mg tablets are white, round, 6.4 mm in diameter, flat faced with bevelled edges, identified APO over P5 on one side. Each tablet contains 5mg pindolol and typically weighs 80mg.

Apo-Pindolol 10mg tablets are white, round, 7.9 mm in diameter, biconvex, identified APO over P10 on one side. Each tablet contains 10mg pindolol and typically weighs 160mg.

Apo-Pindolol 15mg tablets are white, round, 8.7 mm in diameter, flat faced with bevelled edges, identified APO over P15 on one side. Each tablet contains 15mg pindolol and typically weighs 240mg.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- Arterial hypertension
- Prophylaxis of angina pectoris
- Cardiac arrhythmias (sinus and atrial tachycardia, paroxysmal tachycardia, tachycardia in patients with atrial flutter or fibrillation, supraventricular extrasystoles)
- Hyperkinetic heart syndrome

4.2 Dose and method of administration

Dose

Dosage should be adapted to the requirements of the individual person.

Hypertension:

The usual dosage is 15mg/day. Up to 15mg may be given as a single daily dose usually in the morning. Doses above 15mg should be divided into two daily doses.

In mild and moderate hypertension pindolol alone may be sufficient. In more severe or in resistant cases addition of other antihypertensive drugs may be required.

Angina pectoris and cardiac arrhythmias:

10 to 30mg daily generally divided into two or three single doses.

Hyperkinetic heart syndrome:

7.5 to 20mg daily.

Patients with kidney or liver impairment may usually be treated with the normal dose. In severe cases a reduction of the daily dose may be necessary

Method of administration

The tablets are to be administered orally.

4.3 Contraindications

- Sick sinus syndrome (SSS)
- Second or third degree A-V block
- Uncontrolled cardiac failure
- Cardiogenic shock
- Cor pulmonale
- Heart block
- Bronchial asthma
- Anaesthesia with agents that produce myocardial depression e.g. ether

4.4 Special warnings and precautions for use

Cardiac failure:

Special caution should be exercised when administering pindolol alone to patients presenting a history of heart failure. Concomitant administration with digoxin may reduce, but not abolish, the inotropic action of digoxin, and there may be additive effects of decreased A-V nodal conduction. Patients without a previous history of cardiac disease who develop signs of heart failure should be fully digitalised and/or given a diuretic. If cardiac failure persists, pindolol should be withdrawn.

Thyrotoxicosis:

Beta-blocker therapy may mask the signs of hyperthyroidism. Acute manifestations such as thyroid storm may develop upon abrupt withdrawal.

Withdrawal:

Abrupt cessation of pindolol therapy should be avoided. Although rebound hypersensitivity to beta-adrenoceptor stimulation is less likely to occur than with abrupt withdrawal of β -blockers lacking ISA activity, pindolol should be withdrawn gradually over one to two weeks, if possible.

Bradycardia:

Pindolol causes less sinus bradycardia at rest than other beta-blockers, but if excessive bradycardia occurs, the dosage of pindolol should be reduced or the patient treated appropriately (see Overdosage).

Diabetes mellitus:

Pindolol should be administered with care to patients prone to spontaneous hypoglycaemia or those receiving antidiabetic therapy since hypoglycaemia may be precipitated during fasting. Attendant symptoms of tachycardia and tremor may be masked but dizziness and sweating are unaffected and can serve as warning signs of hypoglycaemia.

Respiratory diseases:

Pindolol generally causes no significant changes in pulmonary function in patients prone to non-allergic bronchospasm (e.g. chronic bronchitis, emphysema) because of its ISA activity. However, if a bronchoconstrictor effect occurs it can be controlled using a beta-agonist and/or theophylline.

Impaired renal function:

In patients with severe renal disease, haemodynamic changes following beta-blockade may impair renal function further.

Surgery:

Prior to patients undergoing elective surgery, pindolol should be withdrawn cautiously with at least 72 hours between the last dose and anaesthesia. In emergency surgery, untoward effects of beta-blockade may be reversed by administration of a beta-agonist such as isoprenaline.

Use in children:

Apo-Pindolol should not be administered to children.

4.5 Interactions with other medicines and other forms of interactions

Anti-arrhythmic medicines:

Modifications to dosage levels of Class 1 anti-arrhythmic agents such as lignocaine, disopyramide, quinidine, phenytoin and procainamide may be necessary if concomitant administration with pindolol is intended.

Anti-diabetics:

See special warnings and precautions for use.

Anti-hypertensive medicines:

The combination of pindolol with other β -blockers and calcium antagonists, such as verapamil and diltiazem, should be used with caution for patients presenting impaired ventricular function, and should be avoided if possible for patients presenting conduction abnormalities. Additive hypotensive effects may result when calcium channel blockers and pindolol are used concomitantly.

Cimetidine:

The pindolol plasma levels may be increased possibly due to interference with hepatic metabolism.

Clonidine:

When therapy is discontinued in patients receiving a β -blocker and clonidine concurrently, the β -blocker 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. Significant hypertension may occur up to fourteen days following discontinuation of the MAO-inhibitors.

Nonsteroidal anti-inflammatory medicines:

These medicines may counter the antihypertensive effects of pindolol by promoting sodium and fluid retention through inhibition of renal prostaglandin synthesis.

Phenothiazines:

Concurrent use with β -blockers may result in an increased plasma concentration of either medication.

Reserpine:

Concurrent use may result in an additive and possibly excessive β -adrenergic blockade.

Sympathomimetics with β -adrenergic stimulant activity and Xanthines:

Concurrent use with β -blockers may result in mutual inhibition of therapeutic effects. β -blockers may decrease theophylline clearance.

4.6 Fertility, pregnancy and lactation

Fertility

NIL

Pregnancy

Category C:

Pindolol may cause bradycardia in the foetus and new-born infant. During later stages of the pregnancy pindolol should only be given if the benefits to the mother justify the potential risk to the foetus.

Experimental studies in animals with pindolol give no evidence of teratogenicity. However the effects on the human foetus and pregnant uterus are yet not fully known and pindolol should only be administered under compelling circumstances.

Lactation

Pindolol can pass into breast milk and the drug should not be given to lactating women unless the expected benefit outweighs the potential risk.

4.7 Effects on ability to drive and use machines

Because dizziness or fatigue may occur during initiation of treatment with pindolol, patients driving vehicles or operating machinery should exercise caution until they have determined their reaction to the drug.

4.8 Undesirable effects

Pindolol is generally well tolerated.

The most common adverse reaction to pindolol therapy include dizziness, sleep disturbances, headache, weakness, fatigue and gastrointestinal complaints like nausea and vomiting (usually mild and transient).

The less common and more specific reactions include:

Nervous system:

Tremor and paraesthesia.

Gastrointestinal:

Diarrhoea, abdominal discomfort.

Respiratory:

Shortness of breath and/or dyspnoea, wheezing and bronchospasm in susceptible patients.

Psychiatric:

Hallucinations and depression necessitating interruption of the therapy are observed very rarely.

Dermatological:

Erythematous rashes, pruritus, allergic psoriasiform rashes.

Musculoskeletal:

Muscle cramps, aching legs, cold extremities.

Ocular:

Keratitis and conjunctivitis.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Symptoms:

Overdosage may cause bradycardia, nausea, vomiting, orthostatic disturbances and collapse.

Treatment:

No special treatment is normally required.

In case of severe bradycardia atropine sulphate 0.5 to 1 mg or more should be given IV. Should bronchospasm occur, therapy with a β_2 -stimulant or therapy with aminophylline may be considered. If necessary, isoprenaline hydrochloride may be given by slow IV infusion beginning with 5 μ g/min to stimulate the beta adrenergic receptors. In refractory cases the intravenous administration of 5-8mg glucagon hydrochloride may be considered with the injection being repeated after 1 hour, followed by IV infusion of 1-3mg/hour as necessary.

Patients must be continuously monitored during these procedures.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta blocking agents, non-selective

ATC code: C07AA03 for 15mg, not yet assigned for 5mg and 10mg

Actions

Pindolol is a competitive nonselective beta-adrenoreceptor antagonist with intrinsic sympathomimetic activity but insignificant membrane stabilising activity.

The mechanism of the hypertensive effect of pindolol has not been established. Among the factors that may be involved are: competitive ability to antagonise catecholamine-induced tachycardia at the beta-receptor sites in the heart, thus decreasing cardiac output; a reduction in total peripheral resistance; inhibition of the vasomotor centres; inhibition of renin release by the kidneys.

The mechanism of the anti-anginal effect of pindolol has not been established. Pindolol may reduce the oxygen requirement of the heart at any level of effort by blocking catecholamine-induced increases in the heart rate, systolic blood pressure and the velocity and extent of myocardial contraction. However, oxygen requirements may be increased by such actions as increases in left ventricular fibre length, end diastolic pressure and the systolic ejection period. When the net effect is beneficial in anginal patients, it manifests itself during exercise or stress by delaying the onset of pain and reducing the incidence and severity of anginal attacks.

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.

5.2 Pharmacokinetic properties

Pindolol is almost completely absorbed (95%) from the small intestine, with peak plasma concentrations being recorded between one and two hours after oral administration. It is highly bioavailable (approximately 90% of an oral dose) since it is not subject to significant hepatic first-pass effect. Establishment of therapeutic blood levels is therefore rapid. Food taken immediately after administration of pindolol does not alter the rate of absorption significantly.

Pindolol is 40% bound to plasma proteins. The apparent volume of distribution varies from two to three L/kg with a total clearance of 500mL/min. Pindolol crosses the placental barrier and is excreted in small quantities into breast milk.

Pindolol is partially metabolised in the by the liver with approximately 40% of an oral dose being excreted unchanged in the urine. The remaining 60% is excreted in the urine and faeces as inactive metabolites. The principal metabolites of pindolol consist of the conjugated glucuronide and phenolic derivatives of pindolol conjugated with sulphuric or glucuronic acid.

The elimination half-life averages 3.3 hours but this can be prolonged in uraemic patients and in the elderly. Haemodynamic affects can persist for up to 12 to 24 hours.

5.3 Preclinical safety data

NIL

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Apo-Pindolol tablets contain the following excipients:

- Croscarmellose sodium
- Magnesium Stearate
- Microcrystalline Cellulose
- Lactose Monohydrate

6.2 Incompatibilities

NIL

6.3 Shelf life

4 years from the date of manufacture.

6.4 Special precautions for storage

Store at or below 25°C. Protect from heat, light and moisture.
Keep container tightly closed.

6.5 Nature and contents of container

Apo-Pindolol 5mg tablet is available in HDPE plastic bottle of 100 tablets.

Apo-Pindolol 10mg tablet is available in HDPE plastic bottle of 100 tablets.

Apo-Pindolol 15mg tablet is available in HDPE plastic bottle of 100 tablets

Not all pack types or pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Apotex NZ Ltd
32 Hillside Road
Glenfield
Private Bag 102-995
North Shore Mail Centre
Auckland
Telephone: (09) 444 2073
Fax: (09) 444 2951
Email: NZcustomerservice@apotex.com

9. DATE OF FIRST APPROVAL

March 1991

10. DATE OF REVISION OF THE TEXT

08 February 2017

Summary Table of Changes

Section changed	Summary of new information
Whole data sheet	Reformatted as per Medsafe new guideline for data sheet.
6.4	Change storage condition from 30°C to 25°C.