SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Propranolol 10 mg Tablets
Propranolol 40 mg Tablets
Propranolol 80 mg Tablets
Propranolol 160 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg Propranolol Hydrochloride.
Excipients with known effect: Also contains Lactose 60mg

Each tablet contains 40 mg Propranolol Hydrochloride.
Excipients with known effect: Also contains Lactose 101.00 mg

Each tablet contains 80 mg Propranolol Hydrochloride.
Excipients with known effect: Also contains Lactose 93mg

Each tablet contains 160 mg Propranolol Hydrochloride.
Excipients with known effect: Also contains Lactose 120mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet

Pink biconvex film coated tablets embossed with ‘1’ on one side and break line on the other side.

Pink biconvex film coated tablets embossed with ‘2’ on one side and break line on the other side

Pink biconvex film coated tablets embossed with ‘3’ on one side and break line on the other side.

Pink biconvex film coated tablets embossed with ‘4’ on one side and break line on the other side.

The score line is not intended for breaking the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Angina pectoris.
- Hypertension.
- Long-term prophylaxis against myocardial reinfarction after recovery from acute myocardial infarction Hypertrophic obstructive cardiomyopathy.
- Essential tremor.
- Supraventricular cardiac arrhythmia.
- Ventricular cardiac arrythmias.
- Hyperthyroidism and thyrotoxicosis Phaeochromocytoma (with an alpha-blocker).
- Migraine.
- Prophylaxis of upper gastrointestinal bleeding in patients with portal hypertension and oesophageal varices.

4.2 Posology and method of administration

Posology

Adults:

Angina pectoris:

The starting dose is 40 mg two to three times daily, increasing by the same amount at weekly intervals according to the response. The dose may be increased to120 - 240 mg daily.

Migraine:

The starting dose is 40 mg two to three times daily. The dose may be increased to 80mg -160 mg daily.

Essential tremor:

The starting dose is 40 mg two to three times daily. For these indications the dosage and the dose intervals should be adapted to individual patient needs.

Hypertension: Initially 40 mg two or three times daily, which may be increased by 80 mg per day at weekly intervals according to response. The usual dose range is 160-320 mg daily. With concurrent diuretic and/or peripheral vasodilators a further reduction of blood pressure is obtained.

Arrhythmias The starting dose is 10 mg to -40 mg two or three times a day.

Hypertrophic obstructive cardiomyopathy:

Most patients respond within the dosage range of 10-40mg three or four times daily.

Post myocardial infarction: Treatment should be initiated when myocardial infarction has been stabilized with an initial dose of 40 mg 2-3 times daily for two or three days. In order to improve compliance, the total daily dosage may thereafter be given as 80 mg twice a day.

Thyrotoxicosis:
Most patients respond within the dosage range of 10-40 mg three or four times daily.

Hyperthyroidism: The dose is adjusted according to clinical response.

Phaeochromocytoma (used only in conjunction with an alpha-receptor blocking drug): Pre-operatively; 60 mg daily for three days is recommended. In-operable malignant cases, 30 mg daily.

Portal Hypertension: Dosage should be titrated to achieve approximately 25% reduction in heart rate at rest. Dosing should begin with 40 mg twice daily, increasing to 80 mg twice daily depending on heart rate response. If necessary, the dose may be increased incrementally to a maximum of 160 mg twice daily.

Pediatric population:
Arrhythmias: Dosage should be determined according to the cardiac status of the patient and the circumstances necessitating treatment. The dose should be adjusted individually and the following is a guide: Children and adolescents: 0.25-0.5 mg/kg 3-4 times daily, adjusted according to clinical response.

Elderly:
Evidence concerning the relationship between blood level and age is conflicting. Propranolol should be used to treat older people with caution. It is suggested that treatment should start with the lowest dose. The optimum dose should be individually determined according to clinical response.

Hepatic impairment:
The bioavailability of propranolol may be increased in patients with hepatic impairment and dose adjustments may be required. In patients with severe liver disease (e.g. cirrhosis) a low initial dose is recommended (not exceeding 20 mg three times a day) with close monitoring of the response to treatment (such as the effect on heart rate).

Renal impairment:

Concentrations of propranolol may increase in patients with significant renal impairment and haemodialysis. Caution should be exercised when starting treatment and selecting the initial dose.

As with other beta-adrenoceptor blocking agents, treatment should not be discontinued abruptly. The dosage should be withdrawn gradually over a period of 7 to 14 days. Either the equivalent dosage of another beta-adrenoceptor blocker may be substituted or the withdrawal of propranolol should be gradual. Patients should be followed during withdrawal especially those with ischaemic heart disease. The risk/benefit of stopping beta blockade should be made for each patient.

Method of administration:
The tablets should preferably be administered before meals.
For oral administration.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Propranolol must not be used if there is a history of bronchial asthma or bronchospasm. The product label states the following warning: “Do not take Propranolol if you have a history of asthma or wheezing”. A similar warning appears in the patient information leaflet. Bronchospasm can usually be reversed by beta2 agonist bronchodilators such as salbutamol. Large doses of the beta2 agonist bronchodilator may be required to overcome the beta blockade produced by propranolol and the dose should be titrated according to the clinical response; both intravenous and inhalational administration should be considered. The use of intravenous aminophylline and/or the use of ipratropium (given by nebuliser) may also be considered. Glucagon (1 to 2 mg given intravenously) has also been reported to produce a bronchodilator effect in asthmatic patients. Oxygen or artificial ventilation may be required in severe cases.
  Propranolol, as with other beta-blockers must not be used in patients with any of the following conditions:

  - Cardiac decompensation which is not adequately treated.
  - Sick sinus syndrome/SA-block.
  - History of bronchospasm or bronchial asthma, chronic obstructive pulmonary disease.
  - Metabolic acidosis.
  - Second and third-degree heart block.

- Patients prone to hypoglycaemia, e.g. due to prolonged fasting or restricted counter regulatory reserve.
- Cardiogenic shock.
- Untreated phaeochromocytoma.
- Severe bradycardia
- Severe hypotension
- Severe peripheral arterial disturbances
- Uncontrolled heart failure or Prinzmetal's angina

- Propranolol must not be used in patients prone to hypoglycaemia, i.e., patients after prolonged fasting or patients with restricted counter-regulatory reserves. Patients with restricted counter regulatory reserves may have reduced autonomic and hormonal responses to hypoglycaemia which includes glycogenolysis, gluconeogenesis and /or impaired modulation of insulin secretion. Patients at risk for an inadequate response to hypoglycaemia includes individuals with malnutrition, prolonged fasting, starvation, chronic liver disease, diabetes and concomitant use of drugs which block the full response to catecholamines.

4.4 Special warnings and precautions for use

Propranolol as with other beta-blockers:

- Although contraindicated in uncontrolled heart failure (see section 4.3), may be used in patients whose signs of heart failure have been controlled. Caution must be exercised in patients whose cardiac reserve is poor.
- Should not be used in combination with calcium channel blockers with negative inotropic effects (e.g. verapamil, diltiazem), as it can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or SA or AV 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.
- Although contraindicated in severe peripheral circulatory disturbances (see section 4.3), 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.
- Propranolol may block/modify the signs and symptoms of the hypoglycaemia (especially tachycardia). Propranolol may occasionally cause hypoglycaemia even in non-diabetics patients, such as neonates, infants, children, elderly patients, patients on hemodialysis or patients suffering from chronic liver disease and patients suffering from overdose.

Severe hypoglycaemia associated with propranolol has rarely presented with seizures and/or coma in isolated patients. Caution must be exercised in the concurrent use of propranolol and hypoglycemic therapy in diabetic patients. Propranolol may prolong the hypoglycaemic response to insulin (see section 4.3).

- Propranolol may mask signs of thyrotoxicosis.
- Should not be used in untreated phaeochromocytoma. However, in patients with phaeochromocytoma, an alpha-blocker may be given concomitantly.
- Will reduce heart rate as a result of its pharmacological action.; In the rare instances when a treated patient develops symptoms may be attributable to slow heart rate, the dose may 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 used to treat the allergic reactions.

Abrupt withdrawal of beta-blockers is to be avoided. The dosage should be withdrawn gradually over a period of 7 to 14 days. 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 48 hours prior to the procedure. The risk/benefit of stopping beta blockade should be made for each patient.

Since the half-life may be increased in patients with significant hepatic or renal impairment, caution must be exercised when starting treatment and selecting the initial dose.

Propranolol must be used with caution in patients with decompensated cirrhosis (see section 4.2).

In patients with portal hypertension, liver function may deteriorate and hepatic encephalopathy may develop. There have been reports suggesting that treatment with propranolol may increase the risk of developing hepatic encephalopathy (see section 4.2).

In patients with chronic obstructive pulmonary disease, non-selective beta blockers such as propranolol may aggravate the obstructive condition. Therefore propranolol should not be used in this condition (see section 4.3).

Isolated reports of myasthenia gravis like syndrome or exacerbation of myasthenia gravis have been reported in patients administered propranolol.

Interference with laboratory tests:

Propranolol has been reported to interfere with the estimation of serum bilirubin by the diazo method and with the determination of catecholamines by methods using fluorescence.

Important information regarding the ingredients of this medicine

Lactose:
This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium: This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

Combined use of beta-blockers and calcium channel blockers with negative inotropic effects (e.g. verapamil, diltiazem) can lead to an exaggeration of these effects, particularly in patients with impaired ventricular function and/or SA or AV 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 use of sympathomimetic agents e.g., adrenaline, may counteract the effect of beta-blockers. Caution must be exercised in the parenteral administration of preparations containing adrenaline to patients taking beta-blockers as, in rare cases, vasoconstriction, hypertension and bradycardia may result.

Beta-agonist bronchodilators:

Non-cardioselective beta-blockers oppose the bronchodilator effects of beta-agonist bronchodilators, propranolol is contraindicated in patients with asthma (see section 4.3).

Fingolimod:
Potentiation of bradycardia effects with possible fatal outcomes. Treatment with Fingolimod should not be initiated in patients receiving beta blockers. In case of combination, appropriate monitoring for treatment initiation, at least overnight monitoring is recommended.

Barbiturates:
The plasma levels and the effects of beta-blockers are reduced by the barbiturates. Barbiturates are potent liver enzyme inducers which may increase the metabolism of propranolol.

Propafenone:

Plasma propranolol levels can be raised up to 100% by propafenone. This probably was because propranolol is partially metabolized by the same enzyme like propafenone (CYP2D6). This combination is also not advisable because propafenone has negative inotropic effects.

Warfarin:
Propranolol may cause a reduction in clearance and an increase in plasma concentrations of warfarin.

MAO inhibitors:

Concomitant use of MAO inhibitors (except MAO-B inhibitors) with antihypertensive agents may diminish the antihypertensive effect and lead to hypertensive reactions.

Glycosides:
Digitalis glycosides used in association with beta-blockers may increase atrio-ventricular conduction time.

Combination to be used with caution, dose adjustment may be required

Amiodarone:
A few case reports suggest that patients treated with amiodarone can have severe sinus bradycardia when treated concomitantly with propranolol. Amiodarone has an extremely long half-life (about 50 days), which means that interactions may occur long after discontinuation of therapy.

Class I antiarrhythmic drugs (disopyramide, quinidine):
Class I antiarrhythmic drugs and beta-blockers have additive negative inotropic effects which may result in hypotension and severe hemodynamic side effects in patients with impaired left ventricular function.

Non-steroidal anti-inflammatory / anti-rheumatic drugs (NSAIDs):
Anti-inflammatory drugs of NSAID-type counter the antihypertensive effect of beta-blockers. It has been studied mainly in indomethacin. In a study on diclofenac no such interaction could be detected. Data for COX-2 inhibitors are missing.

Cimetidine:
Concomitant use of cimetidine of hydralazine will increase plasma levels of propranolol, probably by inhibiting its first pass metabolism. There may be a risk of e.g. bradycardia with oral dosing.

Alcohol:
Concomitant use of alcohol may increase the plasma levels of propranolol

Anaesthetics:
Concomitant use of beta-adrenergic antagonists and anaesthetics may attenuate reflex tachycardia and increase the risk of hypotension (see section 4.4). As a general rule, avoid sudden withdrawal of beta-blocker treatment. The anaesthesiologist should be informed when the patient is receiving beta-adrenergic antagonists. Anaesthetic agents causing myocardial depression are best avoided.

Epinephrine (adrenaline):
A number of reports are available for severe hypertension and bradycardia in patients treated with propranolol and epinephrine. These clinical observations have been confirmed by studies in healthy volunteers. It has also been suggested that the intravascular administration of epinephrine may trigger these reactions

Fluvoxamine:
Fluvoxamine inhibits oxidative metabolism and increases plasma concentrations of propranolol. This may result in severe bradycardia.

Centrally-acting antihypertensives (clonidine, moxonidine, methyldopa):
Concomitant use of centrally acting antihypertensive drugs may worsen heart failure by a decrease in the central sympathetic tonus (reduction of heart rate and cardiac output, vasodilation). Abrupt withdrawal, particularly if prior to beta-blocker discontinuation, may increase risk of “rebound hypertension”. If the two drugs are co administered, the beta-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine with beta blocker therapy the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped.

Rifampicin:
The metabolism of propranolol may be increased by potent liver enzyme inducer rifampicin.

Alpha blockers:
Concomitant use with alpha blockers increases the risk of hypotension, especially orthostatic hypotension, and tachycardia and palpitations

Concomitant therapy with dihydropyridine calcium channel blockers: e.g., nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.

Chlorpromazine:

Concomitant administration of chlorpromazine with propranolol may result in an increase in plasma levels of both drugs. This may lead to enhanced antipsychotic effect for chlorpromazine and an increased antihypertensive effect for propranolol.

Lidocaine:
Administration of propranolol during infusion of lidocaine may increase the plasma concentration of lidocaine by approximately 30%. Patients already receiving propranolol tend to have higher lidocaine levels than controls. The combination should be avoided.

Antimigraine drugs:
Simultaneous administration of rizatriptan and propranolol can caused an increased rizatriptan AUC and C_{max} by approximately 70-80%. The increased rizatriptan exposure is presumed to be caused by inhibition of first-passage metabolism of rizatriptan through inhibition of monoamine oxidase-A. If both drugs are to be used, a rizatriptan dose of 5mg has been recommended.

Caution must be exercised if ergotamine, dihydroergotamine or related compounds are given in combination with propranolol since vasospastic reactions have been reported in few patients.

Theophylline:
Propranolol reduces the metabolic clearance of theophylline by about 30% at a dosage of 120 mg / day and 50% at doses of 720 mg / day.

Insulin and oral antidiabetic drugs:
Propranolol modifies the tachycardia of hypoglycaemia. Caution must be exercised in the concurrent use of propranolol and hypoglycaemic therapy in diabetic patients. Propranolol may prolong the hypoglycaemic response to insulin (see sections 4.3 and 4.4).

Tobacco:
Tobacco smoking can reduce the beneficial effects of the beta-blockers on heart rate and blood pressure.

Laboratory tests:
Interference with laboratory tests - Propranolol has been reported to interfere with the estimation of serum bilirubin by the diazo method and with the determination of catecholamines by methods using fluorescence.

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

Pharmacokinetic studies have shown that the following agents may interact with propranolol due to effects on enzyme systems in the liver which metabolise propranolol and these agents: quinidine, propafenone, rifampicin, theophylline, warfarin, thioridazine and dihydropyridine calcium channel blockers such as nifedipine, nisoldipine, nicardipine, isradipine and lacidipine.

Owing to the fact that blood concentrations of either agent may be affected, dosage adjustments may be needed according to clinical judgement (see also the interaction above concerning the concomitant therapy with dihydropyridine calcium channel blockers).

4.6 Fertility, pregnancy and lactation

Pregnancy

As with all drugs Propranolol should not be given during pregnancy unless its use is essential. There is no evidence of teratogenicity with propranolol. However beta-blockers reduce placental perfusion, which may result in intra uterine foetal death, immature and premature deliveries. In addition, adverse effects (especially hypoglycaemia and bradycardia in the neonate and bradycardia in the foetus) may occur. There is an increased risk of cardiac and pulmonary complications in the neonate in the post-natal period.

Breast-feeding

Most beta adrenoceptor blocking drugs, particularly lipophilic compounds, will pass into breast milk although to a variable extent. Breast-feeding is therefore not recommended following administration of these compounds.

Fertility

No relevant data on effect of fertility in humans is available.

4.7 Effects on ability to drive and use machines

Regular medical follow up is required during treatment with this medicinal product. Because reactions differ between individuals the ability to react can be affected to such an extent that the ability to drive, operate machines or work without a secure footing is impaired. This effect is greater at the start of treatment, when the dose is increased, following a treatment switch and in conjunction with alcohol. It should be taken into account that occasionally dizziness or fatigue may occur.

4.8 Undesirable effects

Summary of the safety profile
Propranolol is usually well tolerated. In clinical studies the undesired events reported are usually attributable to the pharmacological actions of propranolol.

Side effects are mostly related to the pharmacological effect. Most common are fatigue, including muscle weakness reported in between 3-5%.

Adverse reactions related to propranolol are listed below by system organ class and frequency. Frequencies are defined as:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000); Frequency not known (cannot be estimated from the available data).

The following undesired events, listed by body system, have been reported:

Blood and lymphatic system disorders
Rare: thrombocytopenia,
Frequency not known: agranulocytosis

Immune system disorders
Rare: angioedema.

Endocrine disorders
Frequency not known: masking signs of thyrotoxicosis.

Metabolic and nutritional disorders
Very rare : hypoglycaemia in neonates, infants, children, elderly patients, patients on haemodialysis, patients on concomitant antidiabetic therapy, patients with prolonged fasting and patients with chronic liver disease has been reported. Changes in lipid metabolism (changes in blood concentrations of triglycerides and cholesterol). Severe hypoglycemia may rarely lead to seizures or coma.

Psychiatric disorders
Common: Sleep disturbances, nightmares.
Rare: Hallucinations, psychoses, mood changes
Frequency not known: depression

Nervous system disorders
Rare: confusion, memory loss, dizziness, paraesthesia.
Very rare: Isolated reports of myasthenia gravis like syndrome or exacerbation of myasthenia gravis have been reported.
Frequency not known: headache, seizure linked to hypoglycaemia

Eye disorders
Rare: visual disturbances, dry eyes
Frequency not known: conjunctivitis

Cardiac disorders
Common: bradycardia
Rare: Heart failure deterioration, precipitation of heart block, postural hypotension which may be associated with syncope,
Frequency not known: worsening of attacks of angina pectoris

Vascular disorders
Common: cold extremities, Raynaud's syndrome
Rare: exacerbation of intermittent claudication,

Respiratory thoracic and mediastinal disorders
Common: breathlessness
Rare: Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints, sometimes with fatal outcome.
Frequency not known: dyspnoea.

Gastrointestinal disorders
Uncommon: diarrhoea, nausea, vomiting
Frequency not known: constipation, dry mouth

Skin and subcutaneous tissue disorders
Rare: alopecia, purpura, psoriasiform skin reactions, exacerbation of psoriasis, skin rashes
Very rare: isolated cases of hyperhidrosis has been reported.

Musculoskeletal system and connective tissue disorders
Frequency not known: arthralgia

Renal and urinary disorders
Frequency not known: reduced renal blood flow and GFR

Reproductive system and breast disorders
Frequency not known: impotence

General disorders and administration site conditions
Common: fatigue and/or lassitude (often transient)
Rare: Dizziness

Investigations:

Very rare: An increase in ANA (antinuclear antibodies) has been observed with many beta blockers, however the clinical relevance of this is not clear.

Discontinuance of the drug should be considered if, according to clinical judgement, the wellbeing of the patient is adversely affected by any of the above reactions. Cessation of therapy with a beta-blocker should be gradual (see section 4.4). In the rare event of intolerance manifested as bradycardia and hypotension, the drug should be withdrawn and, if necessary, treatment for overdosage instituted (see section 4.9).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Toxicity:
Propranolol is known to cause severe toxicity when used in overdose. Patients should be informed of the signs of overdose and advised to seek urgent medical assistance if an overdose of propranolol has been taken.

Clinical features:
Cardiac
Bradycardia, hypotension, pulmonary oedema, syncope and cardiogenic shock may develop. QRS complex prolongation, ventricular tachycardia, first to third degree AV block, ventricular fibrillation or asystole may also occur. Development of cardiovascular complications is more likely if other cardioactive drugs, especially calcium channel blockers, digoxin, cyclic antidepressants or neuroleptics have also been ingested. Older patients and those with underlying ischaemic heart disease are at risk of developing severe cardiovascular compromise.

CNS
Drowsiness, confusion, seizures, hallucinations, dilated pupils and in severe cases coma may occur. Neurological signs such as coma or absence of pupil reactivity are unreliable prognostic indicators during resuscitation.

Other features

Bronchospasm, hyperkalaemia and occasionally CNS-mediated respiratory depression may occur.

Management:

In cases of overdose or extreme falls in the heart rate or blood pressure, treatment with propranolol must be stopped. Management should include general symptomatic and supportive measures including a clear airway and monitoring of vital signs until stable. In symptomatic patients, or patients with an abnormal ECG, early discussion with critical care should be considered.

Consult national clinical guidance for further information on the management of overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta blocking agents, non-selective (beta blocker)
ATC code: C07AA05

Propranolol is a competitive antagonist at both the $beta_1$- and $beta_2$ adrenoceptors. It has no agonist activity at the beta adrenoceptor, but has membrane stabilising activity at concentrations exceeding 1 to 3 mg/litre, though such concentrations are rarely achieved during oral therapy.

Competitive beta blockade has been demonstrated in man by a parallel shift to the right in the dose-heart rate response curve to beta agonists such as isoprenaline.

Propranolol as with other beta-blockers, has negative inotropic effects, and is therefore contraindicated in uncontrolled heart failure.

Propranolol is a racemic mixture and the active form is the S (-) isomer of propranolol. With the exception of inhibition of the conversion of thyroxine to triiodothyronine, it is unlikely that any additional ancillary properties possessed by R (+) propranolol, in comparison with the racemic mixture, will give rise to different therapeutic effects.

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

5.2 Pharmacokinetic properties

Following intravenous administration the plasma half-life of propranolol is about 2 hours and the ratio of metabolites to parent drug in the blood is lower than after oral administration. In particular 4-hydroxypropranolol is not present after intravenous administration.

Propranolol is completely absorbed after oral administration and peak plasma concentrations occur 1 to 2 hours after dosing in fasting patients. The liver removes up to 90% of an oral dose with an elimination half-life of 3 to 6 hours. Propranolol is widely and rapidly distributed throughout the body with highest levels occurring in the lungs, liver, kidney, brain and heart. Propranolol is highly protein bound (80 to 95%).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, local tolerance, genotoxicity, carcinogenic potential and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Povidone
Sodium starch glycolate
Magnesium stearate
Hydroxypropylmethyl cellulose
Polyethylene glycol 400
Titanium dioxide (E171)
Opaspray M-1-1300B Pink

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister pack comprising of PVC/PVDC white opaque 250/40 gsm; Aluminium Foil 20 microns.

Blister pack comprising of PVC/PVDC white opaque 250/90 gsm; Aluminium Foil 20 microns.

Pack size of 28, 56 Tablets.

6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories
Unit 3 Canalside
Northbridge road
Berkhamsted HP4 1EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0326
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PL 17907/0329

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Date of First Authorisation - 03 April 2002
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22/05/2026