SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Propranolol Tablets 10mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Propranolol Hydrochloride 10mg
For excipients see 6.1

3 PHARMACEUTICAL FORM
Film Coated Tablets
Pink, Bi-Convex embossed P10 on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
The control of hypertension.
The management of angina pectoris.
The long term prophylaxis after recovery from acute myocardial infarction.
The control of most forms of cardiac dysrhythmias.
The prophylaxis of migraine.
The management of essential tremor.
The relief of situational anxiety and generalised anxiety symptoms, particularly those of somatic type.
Prophylaxis of upper gastro-intestinal bleeding in patients with portal hypertension and oesophageal varices.
The adjunctive management of thyrotoxicosis and thyrotoxic crisis.
Management of hypertropic obstructive cardiomyopathy.
Management of phaeochromocytoma perioperatively (with alpha blocker).

4.2 Posology and method of administration
Method of Administration:
Tablets are to be taken orally with a drink of water.

Posology:
**Adults:**

**Hypertension:**
A starting dose of 80mg twice a day may be increased at weekly intervals according to response. The usual dose range is 160-320mg per day. Lower doses may be effective when a diuretic or other antihypertensive drugs are given concurrently.

**Angina, Migraine and Essential Tremor:**
Initially, 40mg two or three times daily, increased by the same amount at weekly intervals according to patient response. An adequate response in migraine and essential tremor is usually seen in the range 80-160mg/day and in angina in the range 120-240mg/day.

**Situational and Generalised Anxiety:**
In acute situational anxiety, a dose of 40mg daily may provide short term relief. In generalised anxiety requiring longer term therapy, an adequate response may be expected with 40mg twice daily which, in individual cases, may be increased to 40mg three times daily. Treatment should be continued according to response and patients should be reviewed after six to twelve months treatment.

**Dysrhythmias, Anxiety, Tachycardia, Hypertrophic Obstructive Cardiomyopathy and Thyrotoxicosis:**
10-40mg three or four times a day.

**Post Myocardial Infarction:**
For long-term prevention of sudden cardiac death in patients who have survived the acute phase of myocardial infarct, treatment should start between days 5 and 21 after myocardial infarction, with an initial dose of 40mg four times a day for 2 to 3 days. In order to improve compliance the total daily dosage may thereafter be given as 80mg twice a day.

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

**Phaeochromocytoma:**
Propranolol should be used only with an alpha-receptor blocking drug.

**Pre-operative:**
60mg daily for three days.

**Non-Operable Malignant Cases:**
30mg daily.

**Children:**

**Dysrhythmias, Phaeochromocytoma, Thyrotoxicosis:**
Dosage should be determined individually. The following dosages are intended only as a guide.
0.25 -0.50mg/kg three or four times daily as required.

**Migraine**
Under the age of 12: 20mg two or three times daily.
Over the age of 12: Similar to adult dose.

**Fallot's Tetralogy:**
Propranolol is used mainly to relieve right-ventricular outflow tract shutdown. It is also useful for treatment of associated dysrhythmias and angina. Dosage should be individually determined and the following is only a guide:

Up to 1mg/kg repeated three or four times daily as required.

**Elderly Patients**
The optimum dose should be individually determined according to clinical response.

### 4.3 Contraindications
In patients with second or third degree heart block.
In patients with cardiogenic shock.
If there is a history of bronchospasm.
After prolonged fasting.
In metabolic acidosis (e.g., in some diabetics).
Uncontrolled heart failure.
Sick sinus syndrome (including sino-atrial block).
Printzmetal’s angina (in case of non-selective beta-blockers).
If there is a history of bronchospasm and bronchial asthma.
Untreated phaeochromocytoma.
Bradycardia (<45 –50bpm).
Hypotension.
Hypersensitivity to the substance.
Severe peripheral circulatory disturbances.

### 4.4 Special warnings and precautions for use
In patients with ischaemic heart disease, sudden withdrawal of beta-adrenoceptor blocking drugs may result in anginal attacks of increased frequency or severity. Therefore withdrawal of Propranolol in patients with ischaemic heart disease should be gradual, i.e., over 1-2 weeks. If necessary at the same time initiating replacement therapy, to prevent exacerbation of angina pectoris.

In addition, hypertension and arrhythmias may develop. When it has been decided to interrupt a beta-blockade in preparation for surgery, therapy should be discontinued for a least 24-hours. Continuation of beta-blockade reduces the risk of arrhythmias during induction and intubation; however, the risk of hypertension may be increased as well. If treatment is continued, caution should be observed with the use of certain
anaesthetic drugs. The patient may be protected against vagal reactions by intravenous administration of atropine.

In patients with peripheral circulatory disorders (Raynaud’s disease or syndrome, intermittent claudication), beta-blockers should be used with great caution as aggravation of these disorders may occur. If the pulse rate decreases to less than 50-55 beats per minute at rest and the patient experiences symptoms related to the bradycardia, the dosage should be reduced.

In patients with chronic obstructive pulmonary disorders, airway obstructions may be aggravated. Therefore, non-selective beta-blockers should not be used for these patients, and beta-1 selective blockers only with the utmost care.

Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block. Patients with liver or kidney insufficiency may need a lower dosage, depending on the pharmacokinetic profile of the compound. The elderly should be treated with caution, starting with a lower dosage but tolerance is usually good in the elderly.

Beta-blockers may increase the number and the duration of anginal attacks in patients with Printzmetal’s angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. Non-selective beta-blockers should not be used for these patients, and beta-1 selective blockers only with the utmost care.

Patients with anamnestically known psoriasis should take beta-blockers only after careful consideration.

Beta-blockers may increase both the sensitivity towards allergens and the seriousness of anaphylactic reactions.

Particular care is required with patients whose cardiac reserve is poor. Beta-adrenoceptor blocking drugs should be avoided in overt heart failure, although they may be used when signs of failure have been controlled.

Cardiac failure due to thyrotoxicosis may respond to Propranolol alone but if other adverse factors are also present it is important to control signs of failure with digitalis and diuretics.

A reduction in heart rate is a pharmacological effect of Propranolol. In rare cases where symptoms may be attributable to the slow heart rate, the dose may be reduced.

Propranolol modifies the tachycardia of hypoglycaemia and it may prolong the hypoglycaemic response to insulin. Care should be exercised during concomitant use of Propranolol and hypoglycaemic therapy in patients with diabetes mellitus. Hepatic function will deteriorate in patients with portal hypertension and hepatic encephalopathy may develop. It has been suggested that treatment with Propranolol may increase the risk of developing hepatic encephalopathy.

Care is required when transferring patients from Clonidine to a beta-adrenoceptor blocking drug. If the two drugs are given concurrently, Clonidine should not be
discontinued until several days after the withdrawal of the beta-adrenoceptor blocking drug. Care is required with prescribing a beta-adrenoceptor blocking drug with class I antidysrhythmic agent such as Disopyramide. Beta-adrenoceptor blocking drugs should be used with caution in combination with Verapamil where ventricular function is impaired. The combination should not be given to patients with conduction abnormalities, nor should either drug be administered intravenously within 48 hours of discontinuing the other. Care is required during parenteral administration of preparations containing adrenaline to patients receiving beta-adrenoceptor blocking drugs, as in rare instances vasoconstriction, hypertension and bradycardia may occur.

Care is required when administering anaesthetic agents to patients receiving Propranolol. The anaesthetist should always be informed of the use of beta-adrenoceptor blocking drug and the chosen anaesthetic should have as little negative inotropic activity as possible.

Propranolol has been reported to interfere with some laboratory tests, viz estimation of serum bilirubin by the diazo method and determination of catecholamines by fluorescence methods.

The product label will carry the following warning:
Do not take this medicine if you have a history of wheezing or asthma.

4.5 Interaction with other medicinal products and other forms of interaction
Not recommended association:

Calcium antagonists:
Verapamil and to a lesser extent diltiazem: Negative influence on contractility and auriculo-ventricular conduction.

Clonidine:
Beta-blockers increase the risk of “rebound hypertension”. When clonidine is used in conjunction with non-selective beta-blockers, such as propranolol, treatment with clonidine should be continued for some time after treatment when the beta-blocker has been discontinued.

Monamineoxidase Inhibitors (exception MOA-B Inhibitors)

Precautions for use:

Class 1 anti-arrrhythmic drugs (e.g. disopyramide, quinidine) and amiodarone:
May have potentiating effect on atrial-conduction time and induce negative inotropic effect.

Insulin and oral antidiabetic drugs:
May intensify blood sugar lowering effect (especially non-selective beta-blockers).

Beta-adrenergic blockade may prevent the appearance of signs of hypoglycaemia (tachycardia).
Anaesthetic drugs:
Attenuation of the reflex tachycardia and increase the risk of hypotension.

Continuation of beta-blockades reduce the risk of arrhythmia during induction and intubation. The anaesthesiologist should be informed when the patient is receiving a beta-blocking agent. Anaesthetic agents causing myocardial depression such as cyclopropane and trichlorethylene are best avoided.

Cimetidine, hydralazine and alcohol:
Induce increased plasma levels of hepatically metabolised beta-blockers.

Take into account:

Calcium antagonists:
The risk of hypotension may be increased with dihydropyridine derivates such as nifedipine. In patients with latent cardiac insufficiency, treatment with beta-blocking agents may lead to cardiac failure.

Prostaglandin synthetase inhibiting drugs:
May decrease the hypotensive effects of beta-blockers.

Sympathomimetic agents:
May counteract the effects of beta blockers.

Concomitant administration of tricyclic antidepressants, barbiturates and phenothiazines, as well as other antihypertensive agents, may increase the blood pressure lowering effect.

Parenteral administration of preparations containing adrenaline to patients taking beta-adrenoceptor blocking drugs may, in rare cases, result in vasoconstriction, hypertension and bradycardia. Propranolol may prolong the hypoglycaemic response to insulin.

Beta-adrenoceptor blocking drugs may enhance the negative inotropic action of verapamil, class I antidysrhythmic agents such as disopyramide and certain anaesthetic agents.

Digitalis glycosides:
Association with beta-blockers may increase auriculo-ventricular conduction.

4.6 Pregnancy and lactation
The safety of Propranolol in pregnancy has not been established and its use should be avoided unless the potential benefits are likely to outweigh the possible risk to the foetus.

Beta-blockers reduce placental perfusion, which may result in intrauterine foetal death, immature and premature deliveries. In addition, adverse affects (especially hypoglycaemia and bradycardia) may occur in foetus and neonate.
There is an increased risk of cardiac and pulmonary complications in the neonate in the postnatal period.

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

4.7 Effects on ability to drive and use machines

Although symptoms such as dizziness and fatigue have occasionally been reported in association with the use of beta-blockers, the ability to drive and to use machines is usually unaffected by Propranolol therapy.

4.8 Undesirable effects

Propranolol is generally well tolerated. Minor side effects, which are often transient, include nausea, vomiting, diarrhoea, sleep disturbances, lassitude and muscle fatigue. Bradycardia and hypotension are usually a sign of overdosage, but may rarely be due to intolerance of the drug. Cold extremities and Raynaud's phenomenon have been reported and there have been rare reports of blood dyscrasias during therapy with Propranolol.

Bronchospasm may occur, particularly in patients with a history of asthma or hay fever.

Skin rashes and/or dry eyes have been reported in association with the use of beta-adrenoceptor blocking drugs. If these symptoms are not attributable to some other cause, the drug should be withdrawn.

The following undesirable effects may occur: a slowed AV-conduction or increase of an existing AV-block, hypotension, heart failure, paraesthesia of the extremities, increase of an existing intermittent claudication.

Headaches, impaired vision, hallucinations, psychoses, confusion, impotence, dizziness, depression and nightmares may also occur.

Beta-blockers may mask the symptoms of thyrotoxicosis or hypoglycaemia. The frequency of hypoglycaemia is not known. Seizures have been linked to hypoglycaemia. An increase in Anti Nuclear Antibodies has been seen; its clinical relevance is not clear.

4.9 Overdose

Symptoms of overdose are:
Bradycardia, hypotension, bronchospasm and acute cardiac insufficiency.
After ingestion of an overdose or in case of hypersensitivity, the patient should be kept under close supervision and be treated in an intensive-care ward.

Absorption of any drug material still present in the gastro-intestinal tract can be prevented by gastric lavage, administration of activated charcoal and a laxative. Artificial respiration may be required. Bradycardia or extensive vagal reactions should be treated by administering atropine or methylatropine.

Hypotension and shock should be treated with plasma/plasma substitutes and, if necessary, catecholamines. The beta-blocking effect can be counteracted by slow intravenous administration of isoprenaline hydrochloride, starting with a dose of approximately 5 microgram/minute, or dobutamine, starting with a dose of 2.5 microgram/minute, until required effect has been obtained. In refractory cases isoprenaline can be combined with dopamine. If this does not produce the desired effect either, intravenous administration of 8-10mg glucagon may be considered. If required, the injection should be repeated within one hour to be followed – if required – by an IV infusion of glucagon at an administration rate of 1-3mg/hour. Administration of calcium ions or the use of cardiac pacemaker may also be considered. In patients intoxicated with hydrophilic beta-blocking agents haemodialysis or hemoperfusion may be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Propranolol is a beta-adrenergic receptor blocking agent and a member of Division I (non-cardioselective), Group II (possessing membrane-stabilising activity) class of beta-blocking agents. By blocking beta-receptor sites, Propanolol decreases the inotropic, chronotropic, and vasodilator responses to beta-adrenergic stimulation. The mechanisms of Propranolol's antimigraine and antihypertensive effects have not been established although factors contributing to the latter effects may possibly include a decrease in cardiac output, inhibition of renin release and a decrease in sympathetic outflow from the vasomotor centres in the brain.

5.2 Pharmacokinetic properties
Propranolol is almost completely absorbed from the gastro-intestinal tract and undergoes considerable first-pass metabolism in the liver. Peak plasma concentrations occur about two hours after administration and the plasma half-life is about 3 to 6 hours. Propranolol is highly bound to plasma proteins. Before excretion in the urine, Propranolol is virtually completely metabolised and one of the metabolites, 4-Hydroxy-Propranolol appears to exhibit beta-adrenergic blocking activity. Other urinary metabolites of Propranolol include naphthoxylactic acid, isopropylamine and propranolol glycol.
5.3 Preclinical safety data
There is no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Tablet Core:
Lactose, talc, stearic acid, magnesium stearate.

Film Coating:
Carmine (E120), Titanium dioxide (E171), hypromellose and macrogol.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special Precautions for Storage
Bottles
Do not store above 25°C. Keep the container tightly closed in order to protect from moisture.

Blisters
Do not store above 25°C. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container
Securitainers: 20, 28, 50, 56 and 500 tablets
Blister pack: 28 Tablets.
The Securitainer is made up of High Density Polypropylene body and Low Density Polyethylene cap.
The blister pack is made up of Aluminium foil and PVC/PVDC foil.
6.6 Special precautions for disposal
No special instructions necessary.

7 MARKETING AUTHORISATION HOLDER
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First Floor,
2 Victoria Road,
Harpenden,
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A15 4EA,
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