Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Antarol Tablets 40mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 40 mg of Propranolol Hydrochloride.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets.
Pink film-coated tablets embossed P/40 on one face and the Antigen logo on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

1) The control of hypertension.
2) The management of angina pectoris.
3) The long-term prophylaxis after recovery from acute myocardial infarction.
4) The control of cardiac dysrhythmias.
5) The prophylaxis of migraine.
6) As an adjunct in the control of the symptoms of anxiety, essential tremor, tachycardia (including that with thyrotoxicosis).
7) The management of phaeochromocytoma (Antarol should only be started in the presence of effective alpha blockade).
8) The prophylaxis of upper gastrointestinal bleeding in patients with portal hypertension and oesophageal varices.

4.2 Posology and method of adminstration

Antarol Tablets are for oral administration.

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. With concurrent diuretic or other antihypertensive drugs, a further reduction of blood pressure is obtained.

Angina, anxiety, migraine and essential tremor: A starting dose of 40mg two or three times daily may be increased by the same amount at weekly intervals according to patient response.
An adequate response in anxiety, migraine and essential tremor is usually seen in the range 80 - 160mg/day and in angina in the range 120 - 240mg/day.

Dysrhythmias, anxiety, tachycardia and thyrotoxicosis: A dosage range of 10 - 40mg three or four times a day usually achieves the required response.

Post-myocardial infarction: Treatment should start between days 5 and 21 after myocardial infarction, with an initial dose of 40mg four times a day for 2 or 3 days. In order to improve compliance, the total daily dosage may thereafter be

given as 80mg twice a day.

Phaeochromocytoma: (Used only with an alpha-receptor blocking drug). Pre-operative: 60mg daily for three days is recommended. Non-operable malignant cases: 30mg daily.

Portal hypertension/oesophageal varices: Dosage should be titrated to achieve approximately 25% reduction in resting heart rate. Dosing should begin with 40mg twice 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.

Elderly:

Some older patients tend to be more susceptible to the effects of beta blockade; reduced dosages should be used initially.

Children:

The usual dose range is 0.25 to 0.5mg/kg three or four times daily.

4.3 Contraindications

1) Second and third degree AV block.
2) Severe bradycardia.
3) Uncontrolled or digitalis/diuretic refractory heart failure.
4) Cardiogenic shock
5) Use in patients with asthma or a history of asthma.
6) Metabolic acidosis (e.g. diabetic ketoacidosis).
7) Prolonged fasting.
8) Severe peripheral arterial disease.

4.4 Special warnings and precautions for use

Sudden withdrawal of beta-adrenoceptor blocking agents from patients with ischaemic heart disease may result in the appearance of anginal attacks of increased frequency and severity or in deterioration in cardiac state. Discontinuation of therapy should be gradual.

Propranolol should only be used with caution in patients with controlled congestive cardiac failure. Evidence of recrudescence of the condition should be regarded as a signal to discontinue therapy.

When propranolol is administered to patients with renal failure, the interval between doses may need to be increased or the dosage reduced to avoid accumulation of the drug. In patients with significant hepatic or renal impairment care should be taken when starting treatment and selecting the initial dose.

Some ocular changes (conjunctivitis and ‘dry eye’) and/or skin rashes (including a psoriasiform type) have been reported in association with the use of beta-adrenoceptor blockers. Until their significance is known, it is recommended that consideration be given to discontinuing such therapy if these effects appear.

The initial treatment of severe malignant hypertension should be so designed as to avoid sudden reduction in diastolic blood pressure with impairment of autoregulatory mechanisms. Caution must be exercised when using anaesthetic agents with “Antarol”. The anaesthetist should be informed and the choice of anaesthetic should be an agent with as little negative inotropic activity as possible.

4.5 Interaction with other medicinal products and other forms of interaction

Propranolol should only be used with caution in patients who are receiving concomitant myocardial depressants such as chloroform, or anti-arrhythmic agents such as lignocaine, quinidine, procainamide, or beta-adrenoceptor stimulants such as isoprenaline, or alpha-adrenoceptor stimulants such as noradrenaline, adrenaline.

Adrenergic neurone blocking agents such as guanethidine and reserpine, diuretics and other antihypertensive agents, including the vasodilator group will have an additive effect on the hypotensive action of the drug.

Propranolol may mask the symptoms of thyrotoxicosis and of hypoglycaemia by inhibition of sympathetic nerve functions. It may also affect carbohydrate metabolism per se. The effects of hypoglycaemic agents may be increased particularly by the non-cardioselective beta-blockers.

If propranolol and clonidine are given concomitantly, the clonidine should not be discontinued until several days after withdrawal of the beta-blocker.

In the event that a patient receiving propranolol requires anaesthesia, the anaesthetist should be informed of the use of the medication prior to the use of a general anaesthetic to permit his taking the necessary precautions.

Concurrent use with verapamil should be avoided, as the effects of beta-blockers and verapamil may be additive with respect to both conduction and contraction.

4.6 Pregnancy and lactation

Propranolol should not be given during pregnancy or lactation unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

Symptoms such as light-headedness and fatigue have occasionally been reported in association with use of beta-blockers and patients should be advised not to drive or to operate machinery if affected.

4.8 Undesirable effects

Possible side-effects include nausea, vomiting, diarrhoea, bradycardia, hypotension, cold extremities, depression and sleep disturbances. Bronchospasm may occur, particularly in susceptible individuals. Some ocular changes (conjunctivitis and ‘dry eye’) and/or skin rashes have been reported in association with the use of beta-adrenoceptor blockers.
(See Special warnings and precautions for use).

4.9 Overdose

If overdosage is recent, the stomach should be emptied by gastric aspiration/lavage. Excessive bradycardia and hypotension may respond to atropine 1 - 2mg intravenously, if necessary followed by a bolus dose of glucagon 10mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon at the rate of 1 - 10mg/hour depending on response. If there is no response to glucagon, or if glucagon is not available, a beta-adrenoceptor stimulant such as isoprenaline 25 micrograms initially or orciprenaline 0.5mg may be given by slow intravenous injection.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Propranolol is a beta-adrenergic receptor blocking agent.

5.2 Pharmacokinetic properties

Propranolol is almost completely absorbed from the gastro-intestinal tract and undergoes extensive first-pass metabolism in the liver. Plasma half-life is about 3 to 6 hours. Metabolites are excreted in the urine with some unchanged propranolol.

5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Maize starch
Povidone
Colloidal anhydrous silica
Magnesium stearate

Film-coating:
Methylcellulose
Ethylcellulose
Diethyl phthalate
Opaspray K-I-1340 containing hypromellose, titanium dioxide (E171) and carmine (E120)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

5 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original container.

6.5 Nature and contents of container

Polypropylene tablet containers with tamper evident polypropylene caps.
Pack size: 100, 250, 500 and 1,000 tablets.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Antigen Pharmaceuticals Ltd.
Roscrea
County Tipperary

8 MARKETING AUTHORISATION NUMBER

PA 73/73/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st November 1982

Date of last renewal: 1st November 2002

10 DATE OF REVISION OF THE TEXT

November 2005