1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS:

S3

PROPRIETARY NAME AND DOSAGE FORM:

TRANDATE Tablets 100 mg

TRANDATE Tablets 200 mg

COMPOSITION:

Tablets containing either 100 mg labetalol hydrochloride or 200 mg labetalol hydrochloride.

PHARMACOLOGICAL CLASSIFICATION:

Category A.7.1.3 Vascular medicines, vasodilators, other hypotensives.

PHARMACOLOGICAL ACTION:

TRANDATE lowers the blood pressure primarily by blocking alpha-adrenoceptors in peripheral arterioles and thereby reducing the peripheral resistance.

It also exhibits beta-adrenergic blocking activity and is able to inhibit the re-uptake of norepinephrine into nerve terminals. Labetalol is approximately one tenth as potent as phentolamine in its ability to block alpha-receptors, and it is approximately one third as potent as propranolol in blocking beta-receptors.

Labetalol possesses no intrinsic sympathomimetic activity. Labetalol is well absorbed when administered orally. A considerable fraction of the drug is metabolized in the first circulation through the liver. Its half-life in plasma is approximately 5 hours, and about 5% of the drug is excreted in the urine unchanged.

INDICATIONS:

TRANDATE TABLETS are indicated for the treatment of all grades of hypertension (mild, moderate and severe), including hypertension in pregnancy after the twentieth week when oral antihypertensive therapy is desirable.

CONTRA-INDICATIONS:

The safety of TRANDATE in the first twenty weeks of pregnancy has not been established and TRANDATE should not be used during this period of pregnancy.

WARNINGS:

Labetalol has been associated with jaundice (both hepatic and cholestatic). It is therefore recommended that treatment with labetalol should be stopped immediately, should a patient develop jaundice, since the latter has been shown to be reversible on stopping the drug.

DOSAGE AND DIRECTIONS FOR USE:

The recommended starting dose for all patients is 200 mg two times daily. A satisfactory reduction in blood pressure is achieved at this dose level in some patients, especially those already on diuretic therapy, but higher doses are usually necessary for optimal responses.

ADJUSTMENT OF DOSAGE:

If the fall in blood pressure achieved is less than optimal within two weeks the dose should be increased to a total amount of 600 mg. TRANDATE should be taken as 400 mg in the morning (2 x 200 mg tablets) and 200 mg in the early evening. Satisfactory control of blood pressure is achieved in most patients at this dose level but some, particularly those with more severe hypertension, need the higher doses indicated below.

Start at 200 mg two times a day i.e. 400 mg daily.

If necessary, increase to 600 mg daily in divided doses.

If necessary, increase to 800 mg daily in divided doses.

If necessary, increase to 1000 mg daily in divided doses.

If necessary, increase to 1200 mg daily in divided doses.

It is important to follow these dosage instructions and to increase the dosage gradually in order to avoid side-effects.

DOSAGE RANGE:

Effective total daily doses of TRANDATE may be expected within the following ranges:

In mild to moderate hypertension - 300 mg to 800 mg daily.

In moderate to severe hypertension - 800 to 1200 mg daily.

In severe hypertension - 1200 mg to 2400 mg daily.

If it is necessary to reduce the blood pressure rapidly in severe hypertension TRANDATE INJECTION (Reg. No J/7.1.3/54) is indicated.

Hypertension in pregnancy (after the twentieth week of pregnancy): the dosage range is 200 mg - 1200 mg daily. Close supervision is essential.

GENERAL INSTRUCTIONS:

TRANDATE TABLETS should preferably be taken after food. They are usually taken two times daily but have also been shown to be effective and well tolerated when administered three or four times daily.

USE WITH OTHER AGENTS:

Diuretics usually increase the antihypertensive action of TRANDATE. If TRANDATE TABLETS are prescribed together with another antihypertensive drug an additive effect may be expected in patients who are responsive to both drugs. When transferring patients from other drugs TRANDATE TABLETS should be introduced as recommended above and the dosage of the

existing therapy progressively decreased. Concurrent administration of beta-blockers with TRANDATE is unnecessary in uncomplicated hypertension.

In patients with co-existing angina pectoris beta-blockers may be used concurrently, if need be, with caution, in sufficient doses to control the angina.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Symptoms of postural hypotension may occur if the initial dosage is too high or if the dose is increased too rapidly but are uncommon, except at very high doses, if the drug is used as recommended. Patients with difficulties at first, usually tolerate the drug well after a few weeks treatment.

Nasal stuffiness, vivid dreams and failure of ejaculation have been reported in a few patients. Epigastric pain has occurred in some individuals on high doses of the drug.

Prickly scalp, headache, nausea, lethargy, tiredness and cramp have also been reported but are usually transient and disappear after a week or so.

Heart failure should be controlled with digitalis and diuretic therapy before treatment is initiated. TRANDATE should not normally be given to patients with digitalis-resistant heart failure or atrio-ventricular block. Caution must be observed if TRANDATE is used to treat asthmatic patients or individuals prone to bronchospasm. Any resultant bronchospasm may be controlled by an inhaled selectively-acting bronchodilator; the required dose may be greater than the normal anti-asthmatic dose. If further treatment is required intravenous atropine 1 mg should be given. It is not necessary to discontinue TRANDATE TABLETS in patients requiring anaesthesia but they should be given atropine prior to induction; the effect of halothane on blood pressure may be enhanced by TRANDATE.

Labetalol hydrochloride should be used with caution in patients suffering from diabetes mellitus. This statement is based on the fact that a slight increase in blood sugar level occurs following

the administration of labetalol hydrochloride, and the possibility of interactions with TRANDATE and insulin or oral antidiabetic agents.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Overdosage with TRANDATE causes excessive hypotension, which is posture sensitive, and sometimes, excessive bradycardia. Patients should be laid supine and their legs raised if necessary to improve the blood supply to the brain. Atropine 1 to 2 mg should be given intravenously to relieve bradycardia.

Massive overdosage with TRANDATE in man has not been reported, but profound cardiovascular effects are to be expected. Atropine should be given to minimise bradycardia. Gastric lavage or induced emesis is warranted for a few hours after oral ingestion of the drug. If further measures are required to obtain adequate circulatory function, intravenous noradrenaline may be preferable to isoprenaline, the established pharmacological treatment for excessive cardiac beta-blockade.

The former drug, infused into anaesthetised dogs overdosed with TRANDATE, has been found in Allen and Hanburys Research Laboratories to be more effective than isoprenaline for re-establishing circulatory function. The recommended starting dose of noradrenaline in patients is 5 to 10 micrograms by intravenous injection repeated as required according to the response. Alternatively noradrenaline may be infused at a rate of 5 micrograms per minute until a satisfactory response is achieved.

IDENTIFICATION:

Circular, orange-coloured, film-coated biconvex tablet marked "TRANDATE 100" on one face for the 100 mg tablet or "TRANDATE 200" on one face for the 200 mg tablet.

PRESENTATION:

100 mg and 200 mg tablets in packs of 30 and 60.

STORAGE INSTRUCTIONS:

Store below 30°C.

Keep out of reach of children.

REGISTRATION NUMBERS:

J/7.1.3/52

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NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pharmacare Limited

Healthcare Park

Woodlands Drive

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