Trandate tablets.

DATA SHEET

TRANDATE Tablets

LABETALOL HYDROCHLORIDE

TRANDATE TABLETS 100mg ▼

TRANDATE TABLETS 200mg ▼

Presentation

(a) Trandate Tablets 100mg; Circular, orange coloured, film-coated bi-convex tablets, each containing labetalol hydrochloride 100mg, marked TRANDATE 100AH on one face.

(b) Trandate Tablets 200mg; Circular, orange coloured, film-coated bi-convex tablets, each containing labetalol hydrochloride 200mg, marked TRANDATE 200AH on one face.

Labetalol hydrochloride is 2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenyl-propylamino) ethyl] benzamide hydrochloride.

Uses

Indications:

Trandate Tablets are indicated for the treatment of all grades of hypertension (mild, moderate and severe) when oral antihypertensive therapy is desirable.

Mode of Action:

The mode of action of Trandate is different from that of any other currently available antihypertensive agent. Trandate lowers the blood pressure primarily by blocking alpha-adrenoceptors in peripheral arterioles and thereby reducing the peripheral resistance.

The drug differs, however, from simple alpha-adrenoceptor blockers in that it concurrently blocks beta-adrenoceptors, notably in the heart. This beta-blockade protects the heart from the reflex sympathetic drive normally induced by peripheral vasodilatation and so the reduction in blood pressure is achieved without cardiac stimulation. Conversely increased reflex activity modulates the beta-blocking effect of the drug on the heart and the cardiac output is not significantly reduced at rest or after moderate exercise. Increases in systolic pressure during exercise are, however, reduced after Trandate; corresponding changes in the diastolic pressure are essentially normal. All these effects would be expected to benefit hypertensive patients.

Trandate is rather less active at alpha-adrenoceptors than at beta-adrenoceptors and this ratio of alpha- and beta-blocking activities is thought to be important for its unique effectiveness and lack of side effects. The resultant effect is that adequate vasodilatation is achieved with incomplete blockade of the alpha-adrenoceptors in the arterioles, while the barostatic reflexes remain sufficiently active to avoid side effects associated with postural hypotension in most patients.

The acute and chronic haemodynamic effects of Trandate are quite different from those of beta-blocking drugs currently used to treat hypertension. Anti-hypertensive doses of these drugs reduce the cardiac output in most patients, but the peripheral resistance is not greatly different from the pre-treatment levels after their blood pressure has been reduced; given acutely, beta-blockers reduce the cardiac output but not the blood pressure because of a reflexly mediated increase in peripheral resistance.
Trandate, given acutely or continuously, reduces the blood pressure primarily by reducing the peripheral resistance; the cardiac output is maintained at rest and during moderate exercise. This is clearly a more desirable mechanism for reducing the blood pressure in essential hypertension because circulatory function is more nearly normal in treated patients and blood flow to essential organs, notably the kidney, is more likely to be satisfactorily maintained.
Trandate does not enter the central nervous system of animals in quantity and would not therefore be expected to enter the brain in man. For this reason the sedation often encountered with centrally acting antihypertensives does not occur in patients treated with Trandate.

Dosage and Administration

Adults:

Initial Dosage:

The recommended starting dose for all patients is 100mg three 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 after one or two weeks, the dose should be increased to 200mg three or four times daily. 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.
It is important to follow these dosage instructions and to increase the dosage gradually in order to avoid side effects.

Dosage Range:

Effective doses of Trandate may be expected within the following ranges:
In mild to moderate hypertension – 300mg to 800mg daily.
In moderately severe hypertension – 600mg to 1200mg daily.
In severe hypertension – 1200mg to 2400mg daily.
If it is necessary to reduce the blood pressure rapidly in very severe hypertension, Trandate Injection is indicated (see Data Sheet for Trandate Injection).

Children:

Not applicable.

General Instructions:

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

Use with other Agents:

Hypertension is usually controlled by Trandate alone. Diuretic therapy is not usually necessary in patients receiving Trandate Tablets, but may be introduced

or continued if required. Diuretics usually increase the antihypertensive action of Trandate.
If Trandate Tablets are prescribed together with another antihypertensive drug, such as methyldopa or clonidine, 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, in sufficient doses to control the angina.

Contra-indications, Warnings, etc.

Contra-indications:

There are no known absolute contra-indications to the use of Trandate Tablets.

Precautions:

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 such as salbutamol; the required dose may be greater than the normal anti-asthmatic dose. If further treatment is required, intravenous atropine 1mg should be given.
It is not necessary to discontinue Trandate Tablets in patients requiring anaesthesia but they should be given intravenous atropine prior to induction; the effect of halothane on blood pressure may be enhanced by Trandate.
Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side Effects:

Trandate is usually well tolerated.

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.
Headache, nausea, lethargy, tiredness and cramp have also been reported but are usually transient and disappear after a week or so.
Seldom has it been necessary to discontinue treatment with Trandate.

Overdosage:

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 1-2mg 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 adrenaline 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 & Hanburys Research laboratories to be more effective than isoprenaline for re-establishing circulatory function. The recommended starting dose of adrenaline in patients is 5-10 micrograms by intravenous injection repeated as required according to the response. Alternatively adrenaline may be infused at a rate of 5 micrograms per minute until a satisfactory response is achieved.

Pharmaceutical Precautions

No special storage precautions are required.

Legal Category

S62 (prescription only).

Package Quantities

Trandate Tablets 100mg:	Containers of 50 and 250
Trandate Tablets 200mg:	Containers of 50 and 250

Further Information

Trandate does not adversely affect renal function and is a particularly suitable drug for use in hypertensive patients with renal disease. The metabolites of Trandate are excreted in the faeces as well as in the urine and so the drug is unlikely to accumulate in the body even in renal failure.
The half-life of Trandate in plasma is about four hours. Only about 50% of Trandate in the blood is protein bound.
Trandate fluoresces in alkaline solution at an excitation wavelength of 334nm and a fluorescence wavelength of 412nm and may therefore interfere with the assays of certain fluorescent substances.

Product Licence Numbers

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PL 0045/0107

Product Licence Holder

Allen & Hanburys Ltd., London E2 6LA

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