Trandate injection.

Contributors

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DATA SHEET

TRANDATE Injection

LABETALOL HYDROCHLORIDE

TRANDATE INJECTION ▼

LABETALOL HYDROCHLORIDE

Presentation

Trandate Injection: 20ml ampoules each containing 100mg (5mg/ml) labetalol hydrochloride in an aqueous colourless solution.
Labetalol hydrochloride is 2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenyl-propylamino) ethyl] benzamide hydrochloride.

Uses

Indications:

Trandate Injection is indicated when rapid control of blood pressure is essential in severely hypertensive patients.

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.
Unlike diazoxide, intravenous labetalol reduces blood pressure without producing tachycardia or increasing plasma renin levels.

Dosage and Administration

Adults:

Trandate Injection is intended for intravenous use in hospitalised patients. The plasma concentrations achieved after intravenous doses of Trandate in severe hypertension are substantially greater than those following oral administration of the drug and provide the greater degree of blockade of alpha-adrenoceptors necessary to control the more severe disease. Patients should, therefore, always receive the drug whilst in the supine position.
If it is essential to reduce the blood pressure quickly, as, for example, in hypertensive encephalopathy, a dose of 50mg of Trandate should be given by intravenous injection over a period of at least one minute. If necessary, doses of 50mg may be repeated at 5-minute intervals until a satisfactory response occurs. The total dose should not exceed 200mg. After bolus injection, the maximum effect usually occurs within 5 minutes and the effective duration of action is usually about 6 hours but may be as long as 18 hours.
An alternative method for administering Trandate is intravenous infusion of a solution made by diluting the contents of two ampoules (200mg) to 200ml with sodium chloride and dextrose injection BP. The resultant infusion solution contains 1mg/ml of Trandate. It should be administered using a paediatric giving set fitted with a 50ml graduated burette to facilitate accurate dosage. The rate of infusion of Trandate should be about 2mg (2ml of infusion solution) per minute, until a satisfactory response is obtained; the infusion should then be stopped. The effective dose is usually in the range 50–200mg, depending on the severity of the hypertension. For most patients, it is unnecessary to administer more than 200mg but doses up to 300mg may be required, especially in patients with phaeochromocytoma. The rate of infusion may be adjusted according to the response, at the discretion of the physician. The blood pressure should be monitored throughout the infusion.
It is desirable to monitor the heart rate after injection and during infusion. In most patients, there is a small decrease in the heart rate; severe bradycardia is unusual but may be controlled by injecting atropine 1–2mg intravenously. Respiratory function should be observed particularly in patients with any known impairment.
Patients should be in the supine position when they receive Trandate Injection. Raising the patient into the upright position within three hours of intravenous Trandate administration should be avoided since excessive postural hypotension may occur.

Once the blood pressure has been adequately reduced, maintenance therapy with Trandate Tablets should be instituted with a starting dose of 200mg three times daily. (See Trandate Tablets Data Sheet for further details.)
Trandate Injection has been administered to patients with uncontrolled hypertension already receiving other hypotensive agents, including beta-blocking drugs, without adverse effects.

Children:

Not applicable.

Contra-indications, Warnings, etc.

Contra-indications:

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

Precautions:

Trandate Injection 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 therapy 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 Injection is usually well tolerated. Excessive postural hypotension may occur if patients are allowed to assume the upright position within three hours of receiving Trandate Injection.

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. 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

Protect from light.

Legal Category
S62 (prescription only).

Package Quantities
Trandate Injection 20ml ampoules: Boxes of 5.

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.

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Product Licence Holder
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