

Product Summary

1. Trade Name of the Medicinal Product

Eudemine Injection

2. **Qualitative and Quantitative Composition**

Neutral glass 20 ml ampoule contains 300mg Diazoxide BP.

3. **Pharmaceutical Form**

Solution.

Clinical Particulars

- 4.1 Therapeutic Indications

Diazoxide is a benzothiadiazine analogue. It is used intravenously for the acute treatment of severe hypertension associated with renal disease.

Hypertensive emergencies:

Eudemine injection is used particularly for the emergency treatment of acute hypertensive crises, especially those occurring in association with acute hypertensive encephalopathy, congestive heart failure, acute glomerular nephritis, eclampsia or pre-eclampsia.

Severe hypertension:

It is also indicated for the control of severe hypertension associated with renal disease. In hypertensive patients requiring such diagnostic procedures as renal biopsy, arteriography or cardiac catheterisation, Eudemine injection may be given to facilitate the procedure and reduce the danger of haemorrhage due to hypertension. Eudemine injection is also indicated in patients who have failed to respond to other hypotensive agents.

- 4.2 **Posology and Method of Administration**

Diazoxide should never be mixed with other drugs and should not be diluted.

HYPERTENSIVE EMERGENCIES AND SEVERE HYPERTENSION: In the treatment of hypertension, Eudemine injection is administered by the intravenous route only and it should never be given intramuscularly or subcutaneously.

ADULTS: A full dose of 300 mg in 20 ml will be required by most patients. However, an adequate fall in blood pressure in some patients may be obtained

with as little as 150 mg. Patients must be recumbent during the injection which must be rapid and not exceed 30 seconds. Eudemine injection should not be administered in a bolus dose of 300 mg since single intravenous doses of 300 mg have been associated with myocardial and cerebral infarction.

CHILDREN: On the rare occasions that Eudemine injection is indicated for hypertension in children, the dosage should be based on a level of 5 mg per Kg body weight.

A response occurs within five minutes and usually persists for a least four hours. One injection is usually effective, but further injections may be required, particularly in hypertensive crises or in accelerating disease refractory to other hypotensive agents. Up to four ampoules may be given in 24 hours.

An initial dose of 600 mg is recommended only in life-threatening situations. Once the blood pressure is controlled by Eudemine injection, treatment with anti-hypertensive agents designed for maintenance can be initiated. It appears that if hypertensive patients treated with Eudemine injection are allowed an unrestricted sodium intake then the subsequent response to oral hypotensive agents will be improved.

ROUTE OF ADMINISTRATION: Intravenous injection.

4.3 Contra-Indications

There are no absolute contraindications to Eudemine for the control of hypertension but it should be used with discretion. Agents which can be given by infusion, such as hydralazine or labetalol, should have been shown to be ineffective before a bolus injection of diazoxide is given. Hypersensitivity to any component of the preparation or to other thiazides.

4.4 Special Warnings and Precautions for Use

Eudemine injection may cause hyperglycaemia and therefore in the treatment of hypertension, therapy with Eudemine necessitates regular monitoring of the blood glucose levels.

Eudemine injection should be used with care in patients who have impaired cerebral or cardiac circulation, ie. in patients in whom abrupt reduction in blood pressure might be detrimental. Prolonged hypotension should be avoided so as not to aggravate pre-existing renal failure.

Retention of sodium and water is likely to necessitate therapy with an oral diuretic such as frusemide or ethacrynic acid. The dosage of either of the diuretics mentioned may be up to 1g daily. It must be appreciated that if diuretics are employed then both the hypotensive and the hyperglycaemic activities of diazoxide will be potentiated and it is likely that the dosage of diazoxide will require adjustment downwards. In patients with severe renal failure it is desirable to maintain, with diuretic therapy, urinary volumes in

excess of 1 litre daily. Hypokalaemia should be avoided by adequate potassium replacement.

Whenever Eudemine is given over a prolonged period regular haematological examinations are indicated to exclude changes in white blood cell and platelet counts. Also in children, there should be regular assessment of growth, bone and psychological maturation.

With Eudemine injection the high alkalinity of the solution necessitates that great care is taken to ensure that the injection is given directly into a vein without leakage into surrounding tissues.

The very rapid, almost complete protein binding of diazoxide requires cautious dosage to be used in patients whose plasma proteins may be lower than normal.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs potentiated by diazoxide therapy include diuretics, anti-hypertensive agents and anticoagulants. Phenytoin may reduce the effects of diazoxide.

The risk of hyperglycaemia may be increased by concurrent administration of corticosteroids or oestrogen-progestogen combinations.

4.6 Pregnancy and lactation

Eudemine injection should only be used in pregnant women when the indicated condition is deemed to be life-threatening to the mother.

Eudemine should not be given to nursing mothers as the safety of diazoxide during lactation has not been established.

4.7 Effects on Ability to Drive and Use Machines

None stated.

4.8 Undesirable Effects

In the treatment of hypertension the hyperglycaemia induced by diazoxide is generally inevitable. Each injection of diazoxide usually means a transient rise in blood sugar of about 10 %. Fortunately the hyperglycaemia in hypertensive patients can be readily controlled with tolbutamide, or exceptionally with insulin.

A hypotensive effect in normotensive patients is of minor importance and rarely requires any specific therapy. An oral diuretic may be indicated to control sodium and water retention.

With Eudemine injection reflex tachycardia is not uncommon in the first few minutes after injection and is more frequent in digitalised patients. Orthostatic

hypotension is unlikely but it may occur in those recently treated with adrenergic blocking agents. When it is used during labour for the treatment of toxemia, the smooth muscle relaxant effect can cause delay in the second stage. This should be counteracted with oxytocic agents.

Other adverse effects of Eudemine injection which have been reported are hyperosmolar non-ketonic coma, cardiomegaly, leucopenia, thrombocytopenia, and hirsutism.

4.9 Overdose

Excessive dosage of Eudemine injection can result in hyperglycaemia which will respond to insulin and/or to hypotension which will necessitate maintenance of blood volume with intravenous fluids.

Pharmacological Properties

5.1 Pharmacodynamic Properties

Eudemine is a peripheral vasodilator and has qualitatively the same effect on blood vessels as benzothiazine compounds, but the effect is more rapid and profound. Unlike benzothiazines, Eudemine is non-diuretic and causes retention of sodium and water. It causes a prompt increase in blood glucose by a direct inhibitory action on the secretion of insulin by the beta cells in the Islets of Langerhans.

5.2 Pharmacokinetic Properties

Eudemine injection is administered to adults as a rapid intravenous injection at doses of 150mg to 300mg initially for the treatment of severe hypertension or hypertensive crises. Approximately 90% of Eudemine is bound to plasma proteins. Eudemine crosses the placenta and can cause hyperbilirubinaemia and altered carbohydrate metabolism in the foetus and new-born. Eudemine is eliminated from the body primarily through glomerular filtration. Its long serum half-life (20-30 hours) reflects the fact that 90% of the drug in serum is bound to albumin and protected from filtration. In patients with impaired renal function, the serum half-life increases with decreasing creatinine clearance. The serum half-life is at least 3 times longer than its hypotensive action, and, when dosage is repeated at intervals of 4 to 12 hours, there is extensive accumulation in the body.

5.3 Preclinical Safety Data

No further data of relevance.

Pharmaceutical Particulars

6.1 List of Excipients

Sodium hydroxide BP
Water for injection

6.2 Incompatibilities

None stated.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Protect from light.
Store below 25°C.

**Clean SPC fragment
for Section 6.5**

6.5. Nature and Contents of Container

20 ml One Point Cut (OPC) clear glass ampoule, Type I Ph.Eur. Borosilicate glass, with white snap ring, in packs of 5, containing 300 mg Diazoxide BP.

6.6 Instruction for Use/Handling

It is particularly important that Eudemine ampoules are protected from light. Eudemine injection must never be mixed with other drugs, and must not be diluted.

Administrative Data

7. Marketing Authorisation Holder

Goldshield group plc
NLA Tower
12-16 Addiscombe Road
Croydon
CR0 0XT

8. Marketing Authorisation Number

PL 10972/0043

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/04/2008

10 DATE OF REVISION OF THE TEXT

11/11/2011