

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Eudemine 50mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50mg diazoxide

Excipient (s) with known effect

Each tablet contains 37.0 mg lactose monohydrate and 46.640 mg sucrose

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

White to off white, round, biconvex, sugar coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Eudemine tablets are used in the treatment of intractable hypoglycaemia.

Diazoxide also causes salt and water retention.

Hypoglycaemia: Diaoxide administered orally is indicated for the treatment of intractable hypoglycaemia with severe symptoms from a variety of causes including: idiopathic hypoglycaemia in infancy, leucine-sensitive or unclassified; functional islet cell tumours both malignant and benign if inoperable, extra-pancreatic neoplasms producing hypoglycaemia; glycogen storage disease; hypoglycaemia of unknown origin.

4.2 Posology and method of administration

Posology

Hypoglycaemia:

In hypoglycaemia, the dosage schedule of Eudemine tablets is determined according to the clinical needs and the response of the individual patient. For both adults and children a starting oral dose of 5mg/kg body weight divided into 2 or 3 equal doses per 24 hours will establish the patient's response and thereafter the dose can be increased until the symptoms and blood glucose level respond satisfactorily. Regular determinations of the blood glucose in the initial days of treatment are essential. The usual maintenance dose is 3 - 8mg/kg/day given in two or three divided doses.

In adults with benign or malignant islet-cell tumours producing large quantities of insulin, high dosages of up to 1,000mg per day have been used.

In children with leucine-sensitive hypoglycaemia, a dosage range of 15- 20mg/kg/day is suggested.

Renal impairment

Reduced doses may be required in patients with impaired renal function.

Method of administration

Oral use

4.3 Contraindications

Hypersensitivity to the active substance, other thiazides, or to any of the excipients listed in section 6.1

In the treatment of hypoglycaemia, Eudemine is contraindicated in all cases which are amenable to surgery or other specific therapy.

4.4 Special warnings and precautions for use

Necrotising enterocolitis neonatal

Cases of necrotising enterocolitis (NEC), including fatal, have been reported in neonates treated with diazoxide (see section 4.8). Patients should be monitored for symptoms such as vomiting, abdominal distention, bloody stools and lethargy, especially those with increased risk factors (such as pre-term neonates). Treatment with diazoxide should be discontinued if NEC is suspected and appropriate clinical management should be initiated.

In the treatment of hypoglycaemia it is necessary that the blood pressure be monitored regularly.

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 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.

Diazoxide should be used with caution in patients with cardiac failure or impaired cardiac reserve in whom sodium and water retention may worsen or precipitate congestive heart failure. A direct effect on myocardium and cardiac function cannot be excluded.

Diazoxide should be used with care in patients with impaired cardiac or cerebral circulation and in patients with aortic coarctation, aortic stenosis, arteriovenous shunt, heart failure or other cardiovascular disorders in which an increase in cardiac output could be detrimental.

Pericardial effusion has been observed in patients without structural heart disease receiving oral diazoxide in the post-marketing setting. Cases have been mostly observed in paediatric patients, including infants. In some cases, resolution of pericardial effusion was observed upon diazoxide discontinuation. Some cases required pericardiocentesis. Pericardial effusion is a serious condition that has the potential to progress to cardiac tamponade. Patients should be observed for signs and symptoms of pericardial effusion.

Diazoxide should be administered with caution to patients with hyperuricaemia or a history of gout, and it is advisable to monitor serum uric acid concentration.

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.

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.

This medicinal product contains lactose and sucrose. Patients with rare hereditary problems of galactose intolerance, fructose intolerance total lactase deficiency, sucrase-isomaltase insufficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs potentiated by diazoxide therapy include: oral diuretics, anti-hypertensive agents and anticoagulants.

Phenytoin levels should be monitored as increased dosage may be needed if administered concurrently with diazoxide.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Eudemine tablets are only to be used in pregnant women when the indicated condition is deemed to put the mother's life at risk.

Prolonged oral therapy with diazoxide during pregnancy has been reported to cause alopecia in the newborn.

Lactation

Eudemine tablets 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 known.

4.8 Undesirable effects

With oral therapy, nausea is common in the first two or three weeks and may require relief with an anti-nauseant. Prolonged therapy has given rise to reports of hypertrichosis lanuginosa, anorexia and hyperuricaemia.

Extra-pyramidal side-effects have been reported with oral diazoxide. It was found that extra-pyramidal effects such as parkinsonian tremor, cogwheel rigidity and oculogyric crisis could be easily suppressed by intravenous injection of an antiparkinsonian drug such as procyclidine and that they could be prevented by maintenance therapy with such a drug given orally.

Other adverse effects of Eudemine tablets which have been reported are listed below.

Blood and lymphatic system disorders

Leucopenia, thrombocytopenia, decreased haemoglobin and / or haematocrit, eosinophilia, bleeding

Immune system disorders

Hypogammaglobulinaemia, hypersensitivity reactions such as rash, fever and leucopenia, decreased immunoglobulins (IgG) in infants,

Endocrine disorder

Hirsutism, galactorrhoea, pancreatitis, increased serum androgens

Metabolism and nutrition disorders

Hyperuricaemia (after prolonged therapy), hyperosmolar non-ketotic coma, inappropriate hyperglycaemia including ketoacidosis

Psychiatric disorders

Anorexia (after prolonged therapy), decreased libido

Nervous system disorders

Extra-pyramidal side-effects such as parkinsonian tremor, cogwheel rigidity and oculogyric crisis, headache, dizziness

Eye disorders

Blurred vision, transient cataracts, subconjunctival haemorrhage, ring scotoma, diplopia, lacrimation.

Ear and labyrinth disorders

Tinnitus

Cardiac disorders

Cardiomegaly, cardiac failure, arrhythmias, pericardial effusion (see section 4.4)

Vascular disorders

Inappropriate hypotension

Respiratory, thoracic and mediastinal disorders

Dyspnoea, pulmonary hypertension

Gastrointestinal disorders

Nausea, vomiting, abdominal pain, diarrhoea, ileus, constipation, dysgeusia
Not known: necrotising enterocolitis neonatal

Hepatobiliary disorders

Increased AST and alkaline phosphate

Skin and subcutaneous tissue disorders

Pruritis, dermatitis, lichenoid eruption

Musculoskeletal and connective tissue disorders

Musculoskeletal pain

Renal and urinary disorders

Azotemia, decreased creatinine clearance, reversible nephritic syndrome, haematuria and albuminuria.

Congenital, familial and genetic disorders

Hypertrichosis lanuginosa (after prolonged therapy)

General disorders and administration site disorders

Voice changes and abnormal faces in children (on long term therapy), sodium retention, fluids retention.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme on the MHRA website (www.mhra.gov.uk/yellowcard) or search for MHRA yellow card in the Google Play or Apple app store.

4.9 Overdose

Excessive dosage of diazoxide can result in hyperglycaemia. Severe hyperglycaemia may be corrected by giving insulin and less severe hyperglycaemia may respond to oral hypoglycaemics. Hypotension may be managed with intravenous fluids and in severe cases may require sympathomimetics.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drug for the treatment of hypoglycaemia. ATC Code: V03AH01.

5.2 Pharmacokinetic properties

None stated.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The tablet core consists of:

Lactose

Maize starch

Maize starch, pre-gelatinised

Magnesium stearate

Purified water

The tablet coating consists of:

Sugar (mineral water grade)

Gelatin coarse powder 200 bloom

Purified water

Opaglos AG-7350

Opaglos AG-7350 consists of:

Purified water

Carnauba wax (E903)

Beeswax, white (E901)

Polysorbate 20 (E432)

Sorbic acid (E200)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25°C

6.5 Nature and contents of container

Plastic containers with tamper evident closure containing 100 tablets.

6.6 Special precautions for disposal

No special requirements

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

RPH Pharmaceuticals AB
Box 603
101 32 Stockholm
Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PL 36301/0021

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 December 1992 / 17 December 1997

10 DATE OF REVISION OF THE TEXT

21/11/2025