Diora™

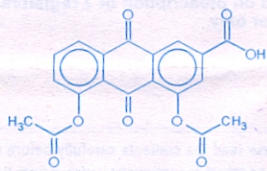
[Diacerein]

ڈائیورا

Capsules 50mg

DESCRIPTION

Diora (Diacerein) is an anthraquinone derivative that is used in osteoarthritis. It acts via inhibition of interleukin-1β. Chemically, Diacerein is 9, 10-Dihydro-4, 5-dihydroxy-9, 10-dioxo-2-anthroic acid diacetate having molecular formula of $C_{19}H_{12}O_8$ and the structural formula is:



Diacerein

QUALITATIVE & QUANTITATIVE COMPOSITION

Diora (Diacerein) is available for oral administration as:
Diora Capsules 50mg
Each capsule contains:
Diacerein ... 50mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Diacerein is thought to act via inhibition of interleukin-1 synthesis, reduction of collagenolytic activity, inhibition of phagocytosis and macrophage migration. Diacerein stimulates production of proteoglycans, glycosaminoglycans and hyaluronic acid. Diacerein has moderate anti-inflammatory activity at high doses. It differs from the well-known class of NSAIDs in its mechanism of action. Action onset is slow and becoming significant after about 45 days.

Pharmacokinetics

After oral administration, Diacerein undergoes a hepatic first-pass effect and is totally deacetylated to the sulphoconjugated metabolite, rhein.The pharmacokinetics parameters of single doses ranging from 50mg to 200mg are dose-independent.

Absorption

After oral administration of single dose of 50mg, the peak plasma levels are 3mg/L of free rhein. The values of t_{max} are 1.8 to 2 hours after administration to fasting healthy volunteers. The simultaneous intake of a standard meal induces a delay in the absorption process and prolongs the t_{max} together which results in a higher bioavailability (increase of about 25% in the AUC). It is advisable to take the drug with meals.

Distribution

Nearly all the non-conjugated rhein (more than 99%) is highly bound to plasma proteins, mainly in high affinity binding to albumin and is not displaced by the usual drugs at their therapeutic concentrations. The mean distribution volume is steady state; Vss/F was approximately 17.1 liters.

Metabolism

Diacerein is rapidly metabolized (mainly pre-systematically) to rhein and this is conjugated to different extents.

Excretion

The elimination half-life from plasma is about 5 to 7 hours. Following oral administration of doses of 50mg-100mg, about, 50% of the total dose of Diacerein is recovered in the urine as rhein, mainly (>90%) as the sulpho and gluco-conjugated forms of rhein.

Special population

Renal insufficiency

In patients with severe renal insufficiency (creatinine clearance <30mL/min), there is a highly significant increase in AUC and elimination half-life with simultaneous decline in renal clearance of rhein.

Hepatic insufficiency

In cirrhotic patients with mild to moderate hepatic insufficiency, no significant changes were observed in any of the pharmacokinetic parameters of rhein as determined from plasma or urine concentration.

THERAPEUTIC INDICATIONS

Diora (Diacerein) is indicated for the treatment of degenerative joint diseases (osteoarthritis and related diseases) and also the symptomatic relief in long - term treatment of osteoarthritis.

DOSAGE & ADMINISTRATION

Diora (Diacerein) should be swallowed whole without chewing, with a glass of water. It should be taken with food (Take with or immediately after meals).

Adults (aged over 15 years)

The recommended usual dose of Diora (Diacerein) is one capsule taken orally twice a day with the main meals for prolonged periods (not less than 6 months). However, as Diacerein may cause acceleration in intestinal transit time during the first 2 weeks of treatment, it is recommended that treatment be started with one capsule of Diacerein per day taken orally with meals for 4 weeks followed by the increase of dose to 2 capsules per day.

Elderly Patients

No change in the usual recommended dose is necessary in elderly subjects.

Patients with renal insufficiency

Patients with moderate renal insufficiency the daily dose should be decreased by 50% of the recommended dose for adults.

Patients with hepatic insufficiency

No significant deviations were observed in any pharmacokinetics parameters in patients with mild to moderate hepatic insufficiency and therefore no dose adjustments is required in these patients.

ADVERSE REACTIONS

Accelerated intestinal transit is the most frequent side effect associated with Diacerein treatment. Other adverse effects are diarrhea, epigastric pain and disturbances, nausea, vomiting, pruritus, cutaneous eruptions and eczema. The intake of Diacerein may sometimes result in intense yellow coloration of urine and is no clinical significance. Pigmentation of rectocolic mucosa has been observed rarely.

CONTRAINDICATIONS

Diacerein is contraindicated in patients with:

- Inflammatory organic colopathy (ulcerative retocolitis, Crohn's disease).
- Intestinal obstruction or partial obstruction.
- Painful abdominal syndrome.
- Known hypersensitivity to the active substances or to any of the excipients.
- Patients with severe hepatic insufficiency.

Children

The safety and efficacy on the product have not been established in this age group, therefore its use is not recommended below 15 years.

Pregnancy and Nursing mothers

Diacerein should not be administered during pregnancy. In addition, Diacerein should not be prescribed to lactating women due to reports that small amounts of Diacerein derivatives pass into the maternal milk.

PRECAUTIONS

- As the incidence of collateral effect, such as accelerated intestinal transit time, is directly proportional to the amount of unabsorbed Diacerein, the intake of the product in a fasting state or after very small amounts of food could cause an increased incidence of collateral effects.
- Avoid concomitant use of laxatives with caution when administering Diacerein

Drug Interactions

Fibre or Phytates:

Diacerein must not be administered at the same time as drugs that modify intestinal transit and / or the quality of the intestinal content (e.g., excess fibers or phytates).

Antacids (aluminium, calcium and magnesium salts, oxides or hydroxides):

Concomitant administration of Diacerein with antacids leads to decreased absorption of Diacerein by gastrointestinal tract. Antacids should be taken separately from Diacerein, allowing for an interval of greater than 2 hours.

Antibiotics and / or Chemotherapy:

Treatment with Diacerein may cause an increase in enterocolic events in patients undergoing antibiotic and/ or chemotherapy which could affect the intestinal flora.

OVERDOSAGE

Profuse diarrheoa may occur in the event of overdose. Symptomatic treatment should then be instituted and electrolyte disorders and dehydration corrected if necessary.

STORAGE

Store at 25°C (Excursions permitted between 15°C to 30°C).

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Diora (Diacerein) Capsules 50mg are available in blister packs of 30's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:

Getz pharma (PVT) LIMITED
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