

CERUPT

[Diacerein]

50mg Capsules

DESCRIPTION:

CERUPT (Diacerein) is an anthraquinone derivative that is used in osteoarthritis.

QUALITATIVE & QUANTITATIVE COMPOSITION:

CERUPT (Diacerein) is available for oral administration as:

CERUPT Capsules 50mg

Each capsule contains:

Diacerein 50mg

(Product Specs.: Sigma)

CLINICAL PHARMACOLOGY:

MECHANISM OF ACTION:

Diacerein is thought to act via inhibition of interleukin-1 synthesis. Interleukin-1 (IL-1) plays a fundamental role in osteoarthritis (OA) pathophysiology and cartilage destruction. Hence, by inhibiting IL-1 **CERUPT** (Diacerein) retards all pathological prepossess initiated in OA.

Diacerein also has a role in 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 and devoid of any irritant effect on the stomach. It differs from the well known class of NSAIDs in its mechanisms of action. Action onset is slow and becoming significant after about 45 Days.

PHARMACOKINETICS:

After oral administration, Diacerein is hydrolyzed before entering the systemic circulation and is absorbed, metabolized and excreted as rhein and its conjugate. 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 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.

Metabolism:

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

Excretion:

The elimination half-life from plasma is about 5 to 7 Hours. Excretion is mainly renal 20% as rhein and 80% as conjugates of rhein (glucuronide and sulphate). Following oral administration of doses of 50mg-100mg, about, 50% of the total dose of diacerein is recovered in the urine as rhein.

Special Population:

Renal insufficiency:

In patient with severe renal insufficiency (Creatinine Clearance <30mL/min), elimination half-life is increased and renal clearance becomes halved.

THERAPEUTIC INDICATION:

CERUPT (Diacerein) is indicated for the treatment of symptoms in patients with osteoarthritis of the hip or knee, with delayed effect. Treatment with diacerein is not recommended in patients with rapidly progressive hip osteoarthritis, as they may have a weaker response to diacerein.

DOSAGE & ADMINISTRATION:

CERUPT (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 **CERUPT** (Diacerein) is 50mg 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 should be started with 50mg once a day with meals for 4 weeks followed by the increase of dose to 50mg twice a day.

Elderly Patient:

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

Patient with Renal Insufficiency:

Patient with severe renal insufficiency (Creatinine Clearance <30mL/min) the daily dose should be halved.

CONTRAINDICATIONS:

Diacerein is contraindicated in patient with:

- Known hypersensitivity to the active substance or any of the excipients.
- Inflammatory organic bowel disease (ulcerative colitis, Crohn's disease)
- Intestinal obstruction or partial obstruction.

- Painful abdominal syndrome.
- Patients with current or/history of liver disease.
- Children under the age of 15 years.
- Diacerein is not recommended in patients older than 65 years.

PRECAUTIONS:

- Intake of diacerein frequently leads to diarrhoea that can consequently lead to dehydration and hypokalaemia. Patients should be advised to stop diacerein treatment in case of diarrhoea and contact their physician to discuss treatment alternatives.
- Caution should be exercised in patients receiving diuretics, because dehydration and hypokalaemia may occur. Particular caution should also be exercised in case of hypokalaemia in patients treated with cardiac glycosides (digitoxin, digoxin).
- Concomitant intake of laxatives should be avoided.

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Hepatotoxicity:

Elevated serum hepatic enzyme levels and symptomatic acute hepatic injury have been reported with diacerein in the post-marketing phase.

Before treatment with diacerein is initiated, the patient should be questioned about possible comorbid conditions and past or concurrent liver disease and screened for major causes of active hepatic disease. A diagnosis of liver disease is a contraindication to diacerein use.

Signs of hepatic injury should be monitored and caution should be exercised when diacerein is used concomitantly with other medicinal products associated with hepatic injury. Patients should be advised to limit their alcohol intake while on treatment with diacerein.

Treatment with diacerein should be stopped if elevation of hepatic enzymes or suspected signs or symptoms of liver damage are detected. Patients should be advised about the signs and symptoms of hepatotoxicity and must be advised to immediately contact their physician in case of appearance of symptoms suggestive of liver damage.

Pregnancy and Lactation:

CERUPT (Diacerein) is contraindicated in pregnancy and during lactation.

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 (eg. Excess fibers or phytates).

Antacids (Aluminium, Calcium and Magnesium Salts, Oxides or Hydroxide):

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.

Diuretics:

Intake of diacerein can lead to diarrhoea and hypokalaemia. Caution must be exercised in the concomitant administration of diuretics (high-ceiling loop and thiazides) and/or cardiac glycosides (digitoxin, digoxin), as the risk of arrhythmia is increased.

ADVERSE REACTION:

Gastrointestinal Disorders:

Very Common: accelerated intestinal transit, diarrhoea, abdominal pain.

Common: frequent bowel movements, flatulence.

As a rule, these effects abate with continuing treatment. In some cases, diarrhoea was severe with complications such as dehydration and disorders of fluid and electrolyte balance.

Rare: intense yellow coloration of urine (having no clinical significance), pigmentation of rectocolic mucosa.

Hepatobiliary Disorders:

Uncommon: cases of elevated hepatic enzymes in serum.

Skin and Subcutaneous Tissue Disorders:

Common: pruritus, rash, eczema.

OVERDOSAGE:

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

INSTRUCTIONS:

- Store below 30°C.
- Protect from light & moisture.
- Keep out of reach of children.

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

HOW SUPPLIED:

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

غواہ: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایت: دوا کو دیکھ کر ہی استعمال نہ کریں۔ اس کی ضرورت ہوگی۔
دیکھ کر ہی استعمال کریں۔
صرف دوا کے لئے استعمال کریں۔

**SIGMA
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