SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

OSIREC 4 g/60 ml rectal suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Etkin madde:

Each rectal suspension contains 4 g mesalazine in 60 ml of suspension.

Excipient with known effect: sodium benzoate (E211)

For the full list of excipient, see section 6.1.

3. PHARMACEUTICAL FORM

Rectal suspension.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Therapy and prophylaxis of acute attacks of mild ulcerative colitis, especially in the rectum and sigmoid colon and also in the descending colon.

4.2. Posology and method of administration

Posology

Adults:

Unless otherwise recommended, the contents of one bottle of rectal suspension (60 g suspension) is administered to the intestine at once before bedtime.

The best results are achieved if the bowels are emptied before administration of the OSIREC.

OSIREC should be used regularly and continuously because a successful recovery can only be achieved in this way.

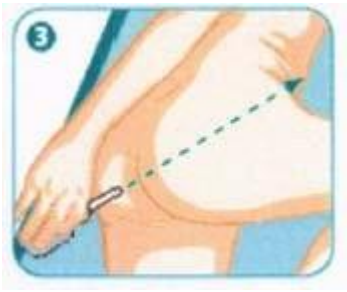
Method of administration:

Preparation:

- Shake the bottle for 30 seconds.
- Remove the protective cap.
- Hold the bottle at the top and bottom

Right position for the administration:

- Lie down comfortably on the left side with the left leg stretched out and the right leg bent. With this position, OSIREC is easier to apply and will be more effective.



Administration:

- Insert the deep into the rectum keeping bottle tipped downwards slightly.
- Slowly squeeze the bottle until empty.
- Slowly withdraw the applicator from the rectum.
- Lie on the left side for at least 30 minutes to allow the contents of the suspension to spread.
- If possible, retain the enema all night.

Additional information on special populations:

Impaired kidney/liver function:

Caution is recommended in patients with impaired hepatic function.

Mesalazine should not be used in patients with impaired renal function. Mesalazine-induced renal toxicity should be considered if renal function deteriorates during treatment.

It is contraindicated in patients with severe kidney and liver failure.

Pediatric population:

There is very little experience and a limited number of documents that mesalazine has an impact on children.

Geriatric population:

The posology and method of administration given for adults also apply to the geriatric population.

4.3. Contraindications

OSIREC is contraindicated in cases of,

- Severe impairment of renal or hepatic function.
- Hypersensitivity to the active substance, salicylates or any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use

Blood tests (differential blood count; liver function parameters such as ALT or AST; serum creatinine) and urinary status (dip-sticks) should be determined prior to and during treatment, at the discretion of the treating physician.

As a guideline, follow-up tests are recommended 14 days after commencement of treatment, then a further two to three tests at intervals of 4 weeks.

If the findings are normal, follow-up tests should be carried out every 3 months. If additional symptoms occur, tests should be performed immediately.

Patients with pulmonary disease, in particular asthma, should be very carefully monitored during a course of treatment.

Patients with a history of adverse drug reactions to preparations containing sulphasalazine should be kept under close medical surveillance on commencement of a course of treatment with Osirec suspensions. Should the rectal suspension cause acute intolerance reactions such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

This medicine contains sodium benzoate, which may be mildly irritant to the skin, eyes and mucous membranes.

This medicine contains potassium metabisulfite therefore, it can rarely cause severe hypersensitivity reactions and bronchospasm.

4.5. Interaction with other medicinal products and other forms of interaction

Specific interaction studies have not been performed.

In patients who are concomitantly treated with azathioprine, 6-mercaptopurine or thioquanine, a possible increase in the myelosuppressive effects of azathioprine, 6-mercaptopurine or thioquanine should be taken into account.

There is weak evidence that mesalazine might decrease the anticoagulant effect of warfarin.

4.6. Pregnancy and lactation

General advice

The pregnancy category is B.

Women with childbearing potential/Contraception

No effect of Mesalazine on women with childbearing potential or any interaction with drugs used for contraception.

Pregnancy

There are no adequate data from the use of Osirec in pregnant women. However, data on a limited number of exposed pregnancies indicate no adverse effect of mesalazine on the pregnancy or on the health of the foetus/newborn child. To date no other relevant epidemiologic data are available. In one single case after long-term use of a high döşe mesalazine (2-4g, orally) during pregnancy, renal failure in a neonate was reported.

Animal studies on oral mesalazine do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/fetal development, parturition or postnatal development.

Osirec should only be used during pregnancy if the potential benefit outweighs the possible risk.

Breastfeeding

N-acetyl-5-aminosalicylic acid and to a lesser degree mesalazine are excreted in breast milk. Only limited experience during lactation in women is available to date. Hypersensitivity reactions such as diarrhoea cannot be excluded.

Therefore, Osirec should only be used during breast-feeding if the potential benefit outweighs the possible risk. If the infant develops diarrhoea, breast-feeding should be discontinued.

Fertility

The effect on reproductive ability/fertility in humans is unknown.

4.7. Effects on ability to drive and use machines

Osirec Rectal Suspension has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

Side effects were evaluated according to the following frequency data:

Very common (≥1/10)
Common (≥1/100 - <1/10)
Not common (≥1/1000 - 1/100)
Rare (≥1/10.000 - 1/1000)
Very rare (<1/10.000)

Blood and lymphatic system disorders

Very rare: Altered blood counts (aplastic anaemia, agranulocytosis, pancytopenia, neutropenia, leukopenia, thrombocytopenia)

Immune system disorders

Very rare: Hypersensitivity reactions such as allergic exanthema, drug fever, lupus erythematosus syndrome, pancolitis

Nervous system disorders

Rare: Headache, dizziness
Very rare: Peripheral neuropathy

Cardiac disorders

Rare: Myocarditis, Pericarditis

Gastrointestinal disorders

Rare: Abdominal pain, diarrhoea, flatulence, nausea, vomiting, constipation
Very rare: Acute pancreatitis

Respiratory, thoracic and mediastinal disorders

Very rare: Allergic and fibrotic lung reactions (including dyspnoea, cough, bronchospasm, alveolitis, pulmonary eosinophilia, lung infiltration, pneumonitis)

Hepatobiliary disorders

Very rare: Changes in liver function parameters (increase in transaminases and cholestasis parameters), hepatitis, cholestatic hepatitis

Skin and subcutaneous tissue disorders

Very rare: Alopecia

Musculoskeletal and connective tissue disorders

Very rare: Myalgia, arthralgia

Renal and urinary disorders

Very rare: Impairment of renal function including acute and chronic interstitial nephritis and renal insufficiency

Reproductive system disorders
Very rare: Oligospermia (reversible)

Reporting of suspected adverse reactions
Reporting of suspected reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9. Overdose
There are rare data on overdosage (e.g., intended suicide with high oral doses of mesalazine), which do not indicate renal or hepatic toxicity. There is no specific antidote and treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Aminosalicylic acid and similar agents

ATC code: A07EC02

The mechanism of the anti-inflammatory action is unknown. The results of in vitro studies indicate that inhibition of lipoxygenase may play a role.

Effects on prostaglandin concentrations in the intestinal mucosa have also been demonstrated. Mesalazine (5-Aminosalicylic acid/5-ASA) may also function as a radical scavenger of reactive oxygen compounds.

On reaching the intestinal lumen, rectally administered mesalazine has largely local effects on the intestinal mucosa and submucosal tissue.

5.2. Pharmacokinetic properties

Absorbtion:

Mesalazine absorption is highest in proximal gut regions and lowest in distal gut areas.

In a study of patients with ulcerative colitis in remission under steady-state conditions, peak plasma concentrations (0.92 micrograms/ml 5-ASA and 1.62 micrograms/ml N-Ac-5-ASA) were reached after approximately 11-12 hours.

Steady-state plasma concentrations in children with chronic inflammatory bowel disease treated with mesalazine; 0.5-2.8 micrograms/ml 5-ASA and 0.9-4.1 micrograms/ml N-Ac-5-ASA.

Distribution:

An imaging study in patients with mild to moderate acute ulcerative colitis has shown that at the beginning of treatment and after 12 weeks, the rectal suspension is distributed throughout the rest of the colon, mostly the rectum, sigmoid colon, and less.

Biotransformation:

Mesalazine is metabolised both pre-systemically by the intestinal mucosa and in the liver to the pharmacologically inactive N-acetyl-5-aminosalicylic acid (N-Ac-5-ASA). The acetylation seems to be independent of the acetylator phenotype of the patient. Some acetylation also occurs through the action of colonic bacteria. Protein binding of mesalazine and N-Ac-5-ASA is 43% and 78%, respectively.

Elimination:

Mesalazine and its metabolite N-Ac-5-ASA are eliminated via the faeces (major part), renally (varies between 20 and 50%, dependent on kind of application, pharmaceutical preparation and route of mesalazine release, respectively), and biliary (minor part). Renal excretion predominantly occurs as N-Ac-5-ASA. About 1 % of total orally administered mesalazine dose is excreted into the breast milk mainly as N-Ac-5-ASA.

5.3. Preclinical safety data

With the exception of a local tolerance study in dogs, which demonstrated good rectal tolerance, no preclinical studies have been performed with Mesalazine rectal preparations.
Preclinical data on mesalazine reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity, carcinogenicity (rat) or toxicity to reproduction. Kidney toxicity (renal papillary necrosis and epithelial damage in the proximal convoluted tubule or the whole nephron) has been seen in repeat-dose toxicity studies with high oral doses of mesalazine. The clinical relevance of this finding is unknown.

6. Pharmaceutical particulars

6.1. List of excipients

Osirec contains the following excipients: Carbomer 974 P, disodium edetate, potassium acetate (E261), potassium metabisulphite (E224), purified water, sodium benzoate (E211), xanthan gum (E415).

6.2. Incompatibilities

None known.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store at room temperature below 25 ° C. Store it in its original packaging and protect it from light.

6.5. Nature and contents of container

Packed in a cardboard box containing 7 round white accordion-shaped LDPE bottle with blue protective caps.

6.6. Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

MCG Pharma İlaç San. ve Tic. Ltd. Şti
Macun Dist. Batı Bulv. ATB Business Center
No:1/129 Yenimahalle/ANKARA
Phone: 0 312 397 27 27
e-mail: info@pharmamcg.com

8. Marketing authorization number(s)

2019/356

9. Date of first authorisation/renewal of the authorisation

31st July 2019

10. Date of revision of the text