ULCERAN TABLET 40MG
PACKAGE INSERT

1. NAME OF THE MEDICINAL PRODUCT
Ulceran Tablet 40mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Ulceran tablets 40mg contain 40mg of famotidine.

Excipient with known effect: lactose.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Film-coated Tablet
Ulceran tablets 40mg are brown, round, biconvex, film-coated tablets with diameter of nucleus 9.5mm

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
Ulceran tablets are indicated for the treatment of the following conditions:
- Duodenal and benign gastric ulcer.
- Prophylaxis of recurrent duodenal ulceration
- Management of Zollinger-Ellison syndrome
- Other conditions where reduction of gastric acid is indicated: bleeding from upper gastrointestinal tract

4.2. Posology and method of administration
Method of administration
Ulceran tablets are for oral administration only. They should be swallowed whole with a little water.

Posology
For the treatment of an acute duodenal ulcer the recommended dosage is one tablet 40mg before retiring. The duration of treatment is 4 to 8 weeks. This period can be shortened if healing of the ulcer is confirmed by endoscopy. Healing of the ulcers occurs in the vast majority of patients within 4 weeks. When after 4 weeks of treatment no healing has been achieved a further period of 4 weeks is recommended. For the prophylaxis of recurrent duodenal ulcers the recommended dosage is 20mg before retiring.

In benign gastric ulcers the recommended dosage is one tablet 40mg before retiring. Duration of treatment is 6-8 weeks. This period can be shortened if healing of the ulcers is confirmed by endoscopy.

In patients with very high gastric acid secretion (e.g. Zollinger Ellison Syndrome) the initial dosage is one tablet 20mg every 6 hours. The further dosage should be adjusted to the clinical response of the patient. 480mg/day up to a year have been used without significant side effects or loss of efficacy.

Patients already receiving another H_2 Antagonist can be switched over to Famotidine on a higher initial dosage than the above recommended.

Dosage in patients with impaired kidney functions:
Dosage adjustment is required for patients with moderate to severe renal insufficiency. Since CNS adverse effects have been reported in patients with moderate to severe renal insufficiency, to avoid excess accumulation of the drug, the dose of famotidine may be reduced to half the recommended dose or the dosing interval may be prolonged to 36 - 48 hours as indicated by the patient's clinical response.

Famotidine is mainly excreted in the urine. Therefore dosage should be reduced in patients with impaired renal function (creatinine clearance under 30ml/min or blood creatinine of 3mg/100ml) to 20mg/day instead of 40mg/day.

4.3. Contraindications

Hypersensitivity to famotidine or to any of the excipients listed in section 6.1.
Since cross-sensitivity has been documented in this class, Ulceran should not be administered to patients with a history of hypersensitivity to other H_2-receptor antagonists.

4.4. Special warnings and precautions for use

Since cross sensitivity has been observed among H2-receptor antagonists, Ulceran should not be administered to patients with a history of hypersensitivity to other drugs in this class.

Gastric neoplasm

Before starting treatment of gastric ulcer with Ulceran, the possibility of malignant gastric tumour should be excluded. The symptomatic response of a gastric ulcer to famotidine therapy does not exclude the possible existence of a malignant tumour.

Do not administer Ulceran tablets in cases of minor gastro-intestinal complaints.

In patients with duodenal ulcers and benign gastric ulcers the H. Pylori status should be determined. Wherever possible, patients with H. Pylori should undergo eradication therapy to eliminate the bacteria.

Renal insufficiency

Since famotidine is secreted mainly via the kidneys, caution should be exercised when treating patients with renal insufficiency. A reduction in the daily dose should be considered if creatinine clearance falls below 10 ml/min (see section 4.2 Posology and Method of administration).

Paediatric population

The safety and efficacy of Ulceran in children has not been established, and should therefore not be used.

Use in the elderly

When Ulceran was administered to elderly patients in clinical trials, no increase in the incidence or change in the type of drug-related side effects was observed. No dosage adjustment is required based on age alone. As elderly patients are more likely to have decreased clearance of famotidine, care should be taken in dose selection and it may be useful to monitor renal function.

General

In case of long-term treatment with high dosage, monitoring of blood count and liver function is recommended.
In case of long-standing ulcer disease, abrupt withdrawal after symptom relief should be avoided.

Ulceran tablets contains lactose.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

No drug interactions of clinical importance have been identified.

During concomitant use of drugs where the absorption of the drug is affected by the amount of gastric juice, a possible effect on the absorption should be taken into consideration. The absorption of ketoconazole and itraconazole could be reduced. Ketoconazole should be given two hours before Ulceran administration.

Probenecid inhibits renal tubular secretion of famotidine, and has been shown to cause a 50% increase in plasma levels of famotidine. Therefore, concomitant use of probenecid and famotidine should be avoided.

Concomitant use of Ulceran and antacids could reduce the famotidine uptake and cause lower plasma levels of famotidine. Therefore, Ulceran should be administered 1-2 hours before antacids.

Concomitant use of sucralfate inhibits absorption of Ulceran. Therefore, sucralfate should not be administered within 2 hours after Ulceran.

Ulceran does not interact with the cytochrome P450-linked drug metabolizing enzyme system. Compounds metabolized by this system which have been tested in man have included warfarin, theophylline, phenytoin, diazepam, propranolol, aminopyrine and antipyrine. Indocyanine green as an index of hepatic blood flow and/or hepatic drug extraction has been tested and no significant effects have been found.

Studies in patients stabilized on phenprocoumon therapy have shown no pharmacokinetic interaction with Ulceran and no effect on the pharmacokinetic or anticoagulant activity of phenprocoumon.

In addition, studies with famotidine have shown no augmentation of expected blood alcohol levels resulting from alcohol ingestion.

Alterations of gastric pH may affect the bioavailability of certain drugs resulting in a decrease in the absorption of atazanavir.

Risk of loss of efficacy of calcium carbonate when co-administered as phosphate binder with Ulceran in hemodialysis patients.

4.6. Fertility, pregnancy and lactation

Pregnancy

Ulceran is not recommended for use in pregnancy. It should be prescribed only if use is essential, and the physician should weigh the potential benefits against the potential risks.

Breast-feeding

Famotidine is excreted in breast milk. Patients who are breast-feeding should either stop breast-feeding or stop taking Ulceran.

4.7. Effects on ability to drive and use machines

As dizziness and fatigue may occur, patients should make sure they are not affected before driving or operating machines.

4.8. Undesirable effects

Ulceran is generally well tolerated.

Nervous system disorders

Common: Headache, dizziness
Uncommon: Taste disorder
Very rare: Paraethesia, somnolence, epileptic seizures, convulsions; grand mal seizures (particularly in patients with impaired renal function)

Psychiatric disorders

Very rare: Reversible psychic disturbances including Hallucinations, disorientation, reduce libido, insomnia, depression, anxiety, agitation, confusion and hallucination.

Musculoskeletal and connective tissue and bone disorders

Very rare: arthralgia, muscle cramps.

Gastrointestinal disorders

Common: Constipation, diarrhoea
Uncommon: Nausea, vomiting, abdominal discomfort or distension, flatulence, dry mouth

Hepato-biliary disorders
Rare: Intrahepatic cholestasis (visible sign: jaundice)
Very rare: abnormalities of liver enzymes (transaminases, gamma GT, alkaline phosphatase, bilirubin), cholestatic jaundice.

Blood and lymphatic system disorders
Very rare: pancytopenia, leukopenia, thrombocytopenia, agranulocytosis, neutropenia.

Metabolism and nutrition disorders
Uncommon: Loss of appetite (anorexia)

Cardiac disorders
Very rare: A-V block with H_2 receptor antagonists administered intravenously

Reproductive system and breast disorders
Rare: impotence
Adverse Effects - Causal Relationship Unknown

Rare cases of gynecomastia, have been reported, however, in controlled clinical trials the incidences were not greater than those seen with placebo.

Immune system disorders
Very rare: Hypersensitivity (anaphylaxis, angioneurotic angioedema, bronchospasm)

Skin and subcutaneous tissue disorders
Uncommon: rash, urticarial, pruritus
Very rare: Stevens Johnson syndrome/toxic epidermal necrolysis, alopecia

Respiratory, thoracic and mediastinal disorders
Very rare: Interstitial pneumonia sometimes fatal

General disorders and administration site conditions
Uncommon: fatigue
Very rare: Chest tightness

4.9. Overdose
There has not been any report of over dosage. The procedure in such a case is to remove unabsorbed material from the gastro-intestinal tract, clinically monitor the patient and therapy should be symptomatic and supportive.
Patients suffering from Zollinger-Ellison syndrome have tolerated a dosage of 800 mg daily for more than a year without the development of significant adverse effects.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), Histamine H2-receptor antagonists, ATC code: A02BA03.

Famotidine is an effective competitive H2 receptor antagonist, the effect of which is particularly clearly concentrated on H2 receptors. It reduces the concentration and amount of acid and pepsin of the gastric juices in the basal and stimulated secretion.

The effect of oral administration of famotidine is rapid. The effect of Famotidine is long lasting when recommended doses are used, and it is effective with relatively low concentrations in the blood. The duration of effect, plasma

concentration and secretion in the urine are dose dependent.

Oral administration of Famotidine leads to the antacid effect starting within an hour of administration. The peak effect is dose dependent and it is achieved within 1-3 hours of administration.

5.2. Pharmacokinetic properties

Absorption

Famotidine is rapidly absorbed. Peak plasma concentration is dose dependent and is achieved within 1-3 hours of administration. The kinetics of Famotidine are linear. The bioavailability of oral famotidine is 40-45% on average. Food contained in the stomach will not affect the bioavailability. First pass metabolism of famotidine is minor. Repeat administration will not cause accumulation of the drug in the body.

Distribution

The binding of Famotidine in plasma proteins is relatively small (15-20%). The plasma half-life is about 3 hours both after oral single doses and during repeated administration (5 days).

Biotransformation

Up to 30-35 % of famotidine is metabolised in the liver to an inactive sulfoxide metabolite.

Elimination

When administered orally, an average of 65-70% of the absorbed Famotidine is excreted in the urine. About 25-30% of the total oral dose is excreted unchanged in the urine. The renal clearance of famotidine is 250-450 ml/min, so consequently, excretion also takes place through tubular secretion. A small proportion may be secreted as sulfoxide.

5.3. Preclinical safety data

No further relevant data.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Magnesium stearate

Colloidal Anhydrous Silica

Croscarmellose Sodium

Microcrystalline cellulose

Lactose Monohydrate

Coating: Opadry Buff OY-3606 [titanium dioxide (E171), Hypromellose, polyethylene glycol 400, iron oxide yellow (E172), iron oxide red (172), iron oxide black (E172)], polyethylene glycol 6000

Incompatibilities

None known.

6.2. Shelf life

5 years

6.3. Special precautions for storage

Store at a temperature not exceeding 25°C protected from light in a dry place

6.4. Nature and contents of container

Polyvinylchloride - aluminium blisters with a patient information leaflet in a carton are available.
40mg: 500 tablets/pack are available.

6.5. Special precautions for disposal and other handling

None

7. PRODUCT REGISTRATION HOLDER

Komedic Sdn. Bhd., No. 4 Jalan PJS 11/14, Bandar Sunway, 46150 Petaling Jaya, Selangor, Malaysia

8. MANUFACTURER

MEDOCHEMIE LTD, (Central Factory), 1-10 Constantinoupoleos street, 3011 Limassol, Cyprus

9. MARKETING AUTHORISATION NUMBER

MAL19900020AZ

10. DATE OF REVISION OF THE TEXT

06/2023