

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pepcid 40 mg Film-coated Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 40 mg of famotidine.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Brown, round-cornered, square tablets, engraved 'MSD 964' on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Duodenal ulcer.

Prevention of relapses of duodenal ulceration.

Benign gastric ulcer.

Hypersecretory conditions such as Zollinger–Ellison syndrome.

Healing of oesophageal erosion or ulceration associated with gastro–oesophageal reflux disease.

Symptomatic relief of gastro–oesophageal reflux disease.

Prevention of relapse of symptoms and erosions or ulcerations associated with gastro–oesophageal reflux disease.

4.2 Posology and method of administration

It is unnecessary to time the dose in relation to meals: bioavailability is not clinically affected by food in the stomach. In all cases the clinical response of the patient should be taken into consideration.

In benign gastric and duodenal ulceration, the dose of 'Pepcid' is one 40 mg tablet at night.

Duodenal ulcer

The recommended initial dose is one 40 mg tablet of 'Pepcid' at night. Treatment should continue for four to eight weeks. In most patients, healing occurs on this regimen within four weeks. In those patients whose ulcers have not healed completely after four weeks, a further four–week period of treatment is recommended.

Maintenance therapy: For preventing the recurrence of duodenal ulceration, the reduced dose of 20 mg of 'Pepcid' at night is recommended. This 20 mg maintenance dose has been continued effectively in clinical studies for 12 months.

Benign gastric ulcer

The recommended dose is one 40 mg tablet of 'Pepcid' at night. Treatment should continue for four to eight weeks unless endoscopy reveals earlier healing. Patients with a suspected gastric ulcer should have gastric carcinoma excluded (*see section 4.4*).

Zollinger–Ellison syndrome

Patients without prior antisecretory therapy should be started on 20 mg of 'Pepcid' every six hours. Dosage should then be adjusted to individual response: doses up to 800 mg daily have been used up to one year without the development of significant adverse effects or tachyphylaxis. Patients who have been receiving another H₂ antagonist may be switched directly to 'Pepcid' at a dose higher than that recommended for new cases. This starting dose will depend on the severity of the condition and the last dose of H₂ antagonist previously used.

Gastro–oesophageal reflux disease

For the treatment of oesophageal erosion or ulceration associated with gastro–oesophageal reflux disease, the recommended dosage is 40 mg of famotidine twice daily, which may be given for six to twelve weeks.

The recommended dosage for the symptomatic relief of gastro–oesophageal reflux disease is 20 mg of famotidine twice daily, which may be given for six to twelve weeks. Most patients experience improvement after two weeks.

Maintenance therapy: For the prevention of recurrence of symptoms and erosions or ulcerations associated with gastro–oesophageal reflux disease, the recommended dosage is 20 mg of famotidine twice daily. As with all chronic therapy, patients should be kept under regular surveillance.

Use in the elderly: 'Pepcid' should be used with caution in elderly patients. The recommended dosage in most elderly patients is the same as in younger patients for all indications (*see above*). No change in the incidence or type of drug–related side effects were seen in treated elderly patients.

Use in impaired renal function: Since 'Pepcid' is excreted primarily by the kidney, caution should be observed in patients with severe renal impairment.

The dose should be reduced to 20 mg *nocte* when creatinine clearance falls below 10 ml/min.

Currently, no clinical data are available regarding dosage recommendations for patients undergoing haemodialysis.

Paediatric use

The efficacy and safety of 'Pepcid' in children have not been established.

4.3 Contraindications

Hypersensitivity to any component of this product. Cross sensitivity in this class of compounds has been observed. Therefore 'Pepcid' should not be administered to patients with a history of hypersensitivity to other H₂-receptor antagonists.

4.4 Special warnings and precautions for use**GASTRIC NEOPLASM**

Gastric malignancy should be excluded prior to initiation of therapy of gastric ulcer with 'Pepcid'. Symptomatic response of gastric ulcer to 'Pepcid' therapy does not preclude the presence of gastric malignancy.

RENAL DYSFUNCTION

Since 'Pepcid' is excreted primarily by the kidney, caution should be observed in patients with impaired renal function. A reduction in daily dosage should be considered if creatinine clearance falls below 10 mL/min (see Dosage and administration).

PEDIATRIC

The efficacy and safety of 'Pepcid' in children have not been established.

USE IN THE ELDERLY

When 'Pepcid' 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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions of clinical importance have been identified.

'Pepcid' 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 famotidine 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.

The absorption of ketoconazole and itraconazole could be reduced. Ketoconazole should be given 2 hours before famotidine administration.

Antacids may decrease the absorption of famotidine and lead to lower plasma concentrations of famotidine. Famotidine should therefore be taken 1 - 2 hours before the application of an antacid.

The administration of probenecid can delay the elimination of famotidine. Concomitant use of probenecid and famotidine should be avoided.

The concomitant use of sucralfate should be avoided within two hours of the famotidine dose.

4.6 Fertility, pregnancy and lactation

Pregnancy: 'Pepcid' is not recommended for use in pregnancy, and should be prescribed only if clearly needed. Before a decision is made to use 'Pepcid' during pregnancy, the physician should weigh the potential benefits from the drug against the possible risks involved.

Although there is no experience with 'Pepcid' in human pregnancy, animal studies have shown that famotidine crosses

the placental barrier without teratogenic effect, but some delay in maturation was seen in animals at high doses.

Breast-feeding mothers: 'Pepcid' is secreted in human milk, therefore breast-feeding mothers should either stop breast-feeding or stop taking the drug.

4.7 Effects on ability to drive and use machines

Some patients have experienced adverse reactions such as dizziness and headache while taking famotidine. Patients should be informed that they should avoid driving vehicles or operating machinery or doing activities which require prompt vigilance if they experience these symptoms. (see section 4.8).

4.8 Undesirable effects

'Pepcid' has been demonstrated to be generally well-tolerated.

[Very Common (>1/10) Common (>1/100, <1/10) Uncommon (>1/1000, <1/100) Rare (>1/10,000, <1/1,000) Very rare (<1/10,000) including isolated cases Not known (cannot be estimated from the available data)]

Cardiac disorders:

Very rare: AV block with H₂ receptor antagonists administered intravenously, prolonged QT interval in patients with impaired renal function

Blood and lymphatic disorders:

Very rare: leukopenia; thrombocytopenia; neutropenia; agranulocytosis; pancytopenia

Nervous system disorders:

Common: headache; dizziness

Uncommon: taste disorder

Very rare: convulsions; grand mal seizures (particularly in patients with impaired renal function); paresthesia; somnolence

Respiratory, thoracic, and mediastinal disorders:

Very rare: interstitial pneumonia sometimes fatal

Gastrointestinal disorders:

Common: constipation; diarrhea

Uncommon: dry mouth; nausea and/or vomiting; abdominal discomfort or distension; flatulence;

Skin and subcutaneous tissue disorders:

Uncommon: rash; pruritus; urticaria

Very rare: alopecia; Stevens Johnson syndrome/toxic epidermal necrolysis sometimes fatal

Musculoskeletal and connective tissue disorders:

Very rare: arthralgia; muscle cramps

Metabolism and nutrition disorders:

Uncommon: anorexia

General disorders and administration site conditions:

Uncommon: fatigue

Very rare: chest tightness, alopecia

Immune system disorders:

Very rare: hypersensitivity reactions (anaphylaxis, angioneurotic oedema, bronchospasm)

Hepatobiliary disorders:

Very rare: liver enzyme abnormalities; hepatitis; cholestatic jaundice

Reproductive system and breast disorders:

Very rare: impotence

Psychiatric disorders:

Very rare: reversible psychic disturbances including depression, anxiety disorders, agitation, disorientation, confusion, and hallucinations; insomnia; reduced libido

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.

4.9 Overdose

The adverse reactions in overdose cases are similar to the adverse reactions encountered in normal clinical experience (see Side Effects).

There is no experience to date with overdosage. The usual measures to remove unabsorbed material from the gastro-intestinal tract, clinical monitoring, and supportive therapy should be employed.

Patients with Zollinger-Ellison syndrome have tolerated doses up to 800 mg daily for more than a year without the development of significant adverse effects.

5 PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Mode of action: 'Pepcid' is a highly specific and potent competitive H₂-receptor antagonist. It has a rapid onset of action. Although the plasma half-life of famotidine in patients is approximately 3.0 hours, 'Pepcid' has a long duration of action, and a single 40 mg dose has been shown to reduce gastric acid secretion for at least 10 hours.

'Pepcid' reduces the acid and pepsin content, as well as the volume of basal, nocturnal and stimulated gastric secretion.

In clinical studies, a single dose of 'Pepcid' at night relieved the pain associated with peptic ulcer, usually within a week, and suppressed gastric secretion.

5.2 Pharmacokinetic properties

'Pepcid' is a chemically novel competitive H₂-receptor antagonist with a guanidinothiazole ring. 'Pepcid' is rapidly absorbed, with dose-related peak plasma concentrations reached in one to three hours. When used as recommended, there was no accumulation effect with repeated doses.

Protein binding in the plasma is relatively low (15-20%). The plasma half-life after a single oral dose or multiple repeated doses (for 5 days) was approximately 3 hours.

Metabolism of the drug occurs in the liver, with formation of the inactive sulphoxide metabolite.

Approximately 25-30% of the oral dosage is excreted in the urine, mainly as unchanged drug. A small amount may be excreted as the sulphoxide.

5.3 Preclinical safety data

Studies in animals and human volunteers have not shown anti-androgenic effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Magnesium stearate (E572)
Microcrystalline cellulose (E460)
Pregelatinised maize starch
Talc
Red iron oxide (E172)

Film coating

Hyprolose (E463)
Hypromellose (E464)
Talc
Red iron oxide (E172)
Titanium dioxide (E171)
Yellow iron oxide (E172)
Carnauba wax (E903)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Opacified PVC-aluminium blister packs of 2 and 4 tablets and calendar packs of 28 tablets.
Amber, glass, high density polyethylene or polypropylene bottles of 50 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Merck Sharp & Dohme Ltd
Hertford Road
Hoddesdon
Hertfordshire EN11 9BU
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0035/069/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 06 October 2007

10 DATE OF REVISION OF THE TEXT

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