

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Famotidine 20 mg Film Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 20 mg famotidine

Excipient with known effect:

Each tablet contains 3.42 mg lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film Coated Tablet

White, film coated, D shaped, biconvex tablets marked with 'G' on one side and 'FD/20' on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Famotidine tablets are indicated for the following conditions;

Duodenal ulcers

Prevention of relapses of duodenal ulceration

Benign gastric ulcers

Zollinger-Ellison syndrome

Symptomatic treatment of mild to moderate reflux oesophagitis.

4.2 Posology and method of administration

Posology

Adults

Duodenal ulcers – The initial recommended dose is 40 mg of famotidine to be taken at night. Healing generally occurs in most patients within 4 weeks. This period, however, may be shortened if an endoscopic examination reveals that the ulcer has healed. However, in those patients whose ulcers have not healed within this 4 week period, treatment should continue for a further 4 weeks.

Prevention of relapses of duodenal ulceration – To prevent ulcers from reoccurring the recommended dose is 20 mg of famotidine to be taken at night.

Benign gastric ulcers – The recommended dose of 40 mg of famotidine to be taken at night. Treatment should continue for between 4-8 weeks unless earlier healing is revealed by endoscopy.

Zollinger-Ellison syndrome – Patients who are not receiving any antisecretory therapy should be started on a dose of 20 mg of famotidine every 6 hours. The 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.

If the desired inhibition of acid secretion cannot be attained with a daily dosage of 800 mg, alternative treatment should be considered to regulate acid secretion, since no long term experience with dosages of more than 800 mg of famotidine/day have been recorded.

Treatment should be continued for as long as necessary. Patients who have been receiving other H₂-receptor antagonist treatment may be switched directly to famotidine treatment at a higher dosage than the initial dosage that is usually recommended. The starting dosage will depend on the severity of the disease and the dosage of the last dose of H₂-antagonist previously used.

Symptomatic treatment of mild to moderate oesophagitis – The recommended dose in case of mild oesophagitis is 20 mg of famotidine twice daily, in case of mild to moderate oesophagitis the recommended dose is 40 mg twice daily. Generally treatment should be conducted for 6 weeks. If the condition has not improved, treatment should be continued for a further 6 weeks.

Elderly

The dosage regimen recommended for elderly patients is the same as for adults.

Use in impaired renal function.

Famotidine is primarily eliminated via the kidneys. For patients with impaired renal function in whom creatinine clearance is less than 30ml/min, the daily dosage of famotidine should be reduced by 50%. Caution is advised in patients with renal impairment.

Dialysis patients should also take dosages that are reduced by 50%. Famotidine 20 mg tablets should be administered at the end of dialysis or thereafter since some of the active ingredient is removed via dialysis

Paediatric population

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

Method of administration

For oral use.

Famotidine tablets can be taken with or without food (see section 5.2).

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to other H₂-receptor antagonists.

Cross sensitivity in this class of compounds has been observed. Therefore, famotidine 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

The presence of gastric malignancy should be excluded prior to the use of famotidine for the treatment of gastric ulcers. Symptomatic responses of gastric ulcers following treatment with famotidine do not preclude the presence of gastric malignancy.

Renal dysfunction

As famotidine is excreted primarily via the kidneys, caution should be exercised when treating patients who are suffering from impaired renal function. A reduction in daily dosage to 20 mg at night should be considered if creatinine clearance falls below 10 ml/min (see section 4.2).

Paediatric population

The safety and efficacy for the use of famotidine in children has not been established.

Use in the elderly

When Famotidine 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

This medicine 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 Interaction with other medicinal products and other forms of interaction

No clinically important drug interactions have been identified.

Famotidine does not interact with the cytochrome P450 drug metabolising enzyme system. Compounds metabolised by this system, which have been tested in man have included warfarin, theophylline, phenytoin, diazepam, propranolol, aminopyrine and antipyrine.

Indocyanide 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 stabilised 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 administered two hours before administering famotidine.

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

Concomitant use of famotidine and antacids may reduce the famotidine absorption and lead to lower plasma levels of famotidine. Therefore, famotidine should be administered 1-2 hours before taking an antacid.

Concomitant use of sucralfate inhibits the absorption of famotidine. Therefore, sucralfate should as a rule not be administered within two hours of the famotidine dose.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breast-feeding

Famotidine is secreted in human breast milk. Therefore breast-feeding mothers should either stop taking famotidine or stop breast-feeding.

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

Famotidine has been demonstrated to be generally well-tolerated.

Adverse reactions are ranked under the heading of frequency, the most frequent first, using the following convention: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$), including isolated cases and not known (cannot be estimated from the available data).

<p><u>Blood and lymphatic system disorders</u></p> <p><i>Very rare</i></p>	<p>Thrombocytopenia, leucopenia, agranulocytosis, pancytopenia, neutropenia.</p>
<p><u>Immune system disorders</u></p> <p><i>Very rare</i></p>	<p>Hypersensitivity reactions (anaphylaxis, angioneurotic oedema, bronchospasm).</p>
<p><u>Metabolism and nutrition disorders</u></p> <p><i>Uncommon</i></p>	<p>Anorexia.</p>
<p><u>Psychiatric disorders</u></p> <p><i>Very rare</i></p>	<p>Reversible psychological disturbances including hallucinations, disorientation, confusion, anxiety disorders, agitation, depression, insomnia, reduced libido.</p>
<p><u>Nervous system disorders</u></p> <p><i>Common</i></p> <p><i>Uncommon</i></p> <p><i>Very rare</i></p>	<p>Headache, dizziness.</p> <p>Taste disorder.</p> <p>Paraesthesia, somnolence, convulsions, grand mal seizures (particularly in patients with impaired renal function).</p>
<p><u>Cardiac disorders</u></p> <p><i>Very rare</i></p>	<p>Atrioventricular block with H₂-receptor antagonists administered intravenously, arrhythmias, QT prolongation (especially in patients with impaired renal function)</p>
<p><u>Respiratory, thoracic and mediastinal disorders</u></p> <p><i>Very rare</i></p>	<p>Interstitial pneumonia, sometimes fatal.</p>

<p><u>Gastrointestinal disorders</u></p> <p><i>Common</i></p> <p><i>Uncommon</i></p>	<p>Constipation, diarrhoea.</p> <p>Dry mouth, nausea and/or vomiting, flatulence, abdominal discomfort or distension.</p>
<p><u>Hepatobiliary disorders</u></p> <p><i>Very rare</i></p>	<p>Liver enzyme abnormalities, hepatitis, cholestatic jaundice.</p> <p>Isolated cases of worsening of existing hepatic disease.</p>
<p><u>Skin and subcutaneous tissue disorders</u></p> <p><i>Uncommon</i></p> <p><i>Very rare</i></p>	<p>Rash, pruritus, urticaria.</p> <p>Alopecia, Stevens-Johnson syndrome/toxic epidermal necrolysis sometimes fatal.</p>
<p><u>Musculoskeletal and connective tissue disorders</u></p> <p><i>Very rare</i></p>	<p>Arthralgia, muscle cramps.</p>
<p><u>Reproductive system and breast disorders</u></p> <p><i>Very rare</i></p>	<p>Impotence.</p>
<p><u>General disorders and administration site conditions</u></p> <p><i>Uncommon</i></p> <p><i>Very rare</i></p>	<p>Fatigue.</p> <p>Chest tightness.</p>

<p><u>Investigations</u></p> <p><i>Rare</i></p>	<p>Increase in laboratory values (transaminases, gamma GT, alkaline phosphatase, bilirubin).</p>
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Adverse effects – Causal relationship unknown

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

4.9 Overdose

The adverse reactions in overdose cases are similar to the adverse reactions encountered in normal clinical experiences (see section 4.8).

In the event of overdose the usual measures to remove unabsorbed material from the gastrointestinal tract, clinical monitoring and supportive therapy should be employed.

Patients suffering from Zollinger-Ellison syndrome have tolerated doses of up to 800 mg/day. These patients have been treated for more than a year without the development of any significant adverse effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), H₂-receptor antagonists, ATC code: A02BA03

Clinical efficacy and safety

In healthy volunteers, single oral doses of famotidine (5 mg to 40 mg) produced dose-related inhibition of basal and pentagastrin, betazole or insulin-stimulated gastric secretion. In addition, pepsin levels were also reduced and there was a decrease in the volume of the basal gastric juice and the gastric juice secreted on stimulation. Similar inhibitory effects on gastric secretion were also noted in patients with benign gastric or duodenal ulceration.

In contrast to control subjects on cimetidine 300 mg or on placebo, inhibition of gastric secretion persisted in volunteers given a second pentagastrin challenge 5-7 hours after the initial dose of famotidine.

A single oral dose of 40 mg of famotidine, given at 9 pm was effective for more than 12 hours after administration and had some continuing effect through the breakfast meal. The duration of action of the 80 mg dose of famotidine administered at 9 pm was no longer than the 40 mg dose.

In several studies, 10 mg and 20 mg doses of famotidine increased basal serum gastrin levels, however the levels remained unchanged in others. Gastric emptying, and hepatic and portal blood flows were unaltered by famotidine. In addition, famotidine did not cause changes in endocrine function.

5.2 Pharmacokinetic properties

Absorption

The drug is rapidly absorbed and takes effect within an hour of oral administration, reaching dose-related peak plasma concentrations within 1-3 hours. Oral bioavailability is not affected by the presence of food in the stomach. Repeated doses do not lead to accumulation of the drug.

Distribution

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

Biotransformation

The drug is metabolised in the liver, with formation of the inactive sulfoxide metabolite.

Elimination

Famotidine is excreted mainly unchanged in the urine (25-60%); a small amount of the drug may be excreted as the sulfoxide.

Linearity/non-linearity

Famotidine displays linear kinetics.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Cellulose, microcrystalline

Starch, pregelatinised

Talc

Magnesium stearate

Film-coating:

Lactose monohydrate

Hypromellose

Titanium dioxide (E171)

Triacetin

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

Polyvinylchloride aluminium foil blisters packed into cartons containing 10, 20, 28, 30, 50, 56, 60, 90 or 100 tablets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7 MARKETING AUTHORISATION HOLDER

Generics [UK] Limited t/a Mylan
Station Close
Potters Bar
Hertfordshire
EN6 1TL
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 04569/0422

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

Date of first authorisation: 2 July 2001
Date of last renewal: 2 July 2006

10 DATE OF REVISION OF THE TEXT

13/02/2019