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 film-coated tablet contains 1.44 mg lactose monohydrate.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets

Beige, round biconvex film-coated tablets marked ‘93’ on one side and ‘896’ on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Prevention of recurrent duodenal ulcers
- Duodenal ulcer
- Benign gastric ulcer
- Zollinger-Ellison syndrome
- Symptomatic treatment of mild reflux oesophagitis

4.2 Posology and method of administration

Posology

Adults and the elderly

Duodenal ulcers and benign gastric ulcers
40 mg of famotidine once before going to sleep.

Prophylactic treatment of recurrent duodenal ulcers
20 mg of famotidine in the evening.

Zollinger-Ellison syndrome

If no preceding treatment with medicines which inhibit secretion has been conducted, the therapy of the Zollinger-Ellison syndrome should be initiated with 20 mg famotidine (equivalent to 1 famotidine 20 mg film coated tablet) every 6 hours. For further treatment doses have to be adjusted according to the extent of acid secretion and the patient's clinical response until acid secretion has been reduced to an acceptable level (e.g. <10 mEq/h the hour before the next famotidine dose).

If a dosage of 800 mg/d does not result in sufficient inhibition of acid secretion, an alternative therapy for the regulation of acid secretion should be considered, because there are no experiences with the long-term application of doses higher than 800 mg famotidine/d.

The therapy should be continued as long as it is clinically necessary.

Patients who have been previously treated with other H_2-receptor-antagonists can change immediately to a higher initial dose than that recommended for new patients. The initial dose is dependent on the severity of the clinical picture and on the dose of medication taken prior to the change of medicine.

Symptomatic treatment of mild reflux oesophagitis
A daily dose of twice 20 mg famotidine is recommended.

Renal impairment
Famotidine is mainly excreted via the kidneys. In patients with impaired kidney function whose creatinine clearance amounts to less than 30 ml/min (serum creatinine above 3.0 mg/100 ml) a reduction of the daily dose to 50% is recommended.

For patients under dialysis a reduction of the daily dose to 50% is recommended as well. Famotidine 20 mg film-coated tablets should be given at the end or after dialysis, because part of the active ingredient will be removed in the course of dialysis.

Method and duration of administration
Famotidine 20 mg film-coated tablets should be swallowed whole with some liquid. The film-coated tablets may be taken independently of meals.

Prophylactic treatment of recurrent duodenal ulcers
With regards to the maintenance therapy for preventing the recurrence of duodenal ulceration, the recommended maintenance dose of 20 mg has been continued effectively in clinical studies of 12 months duration.

Duodenal ulcers and benign gastric ulcers
The treatment of duodenal ulcers and benign gastric ulcers should be conducted for 4 to 8 weeks. The period of time can be shorter if a healing of the ulcer can be endoscopically proved. In case the ulcers do not endoscopically heal after 4 weeks the treatment should be continued for another 4 weeks.

Zollinger-Ellison syndrome
The treatment should be continued as long as it is clinically necessary

Symptomatic treatment of mild reflux oesophagitis
Generally, treatment should be conducted for 6 weeks, if necessary 12 weeks.

Paediatric population
The safety and efficacy of famotidine 20 mg film-coated tablets in children has not been established. Therefore, children should not be treated with famotidine 20 mg film-coated tablets.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients with a history of hypersensitivity to other H_2-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 famotidine. Symptomatic response of gastric ulcer to famotidine therapy does not preclude the presence of gastric malignancy.

Renal impairment
Since famotidine 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 30 ml/min (see section 4.2).

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.

In patients with duodenal and benign gastric ulcers the *H. pylori*-status should be determined. For *H. pylori*-positive patients removal of the bacterium *H. pylori* by means of eradication therapy should be striven for whenever possible.

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.

Lactose
This medicinal product 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 drug interactions of clinical importance have been identified.

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

Co-administration of posaconazole oral suspension with famotidine should be avoided if possible, since famotidine may reduce the absorption of posaconazole oral suspension during concomitant use.

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.

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

If famotidine, atazanavir and ritonavir are co-administered, a dose of 20 mg famotidine should not be exceeded. If a higher dose of famotidine is required (e.g. famotidine 40 mg) dose adjustment of atazanavir and ritonavir may be considered. Co-administration of famotidine, atazanavir, ritonavir and tenofovir should be avoided. If the combination of famotidine, atazanavir, ritonavir and tenefovir is judged unavoidable, close clinical monitoring is recommended.

Co–administration of famotidine with the tyrosine kinase inhibitors (TKIs) dasatinib, erlotinib, gefitinib, pazopanib may decrease plasma concentrations of TKIs resulting in lower efficacy, therefore co-administration of famotidine with these TKIs is not recommended. For further specific recommendations, please refer to the product information of individual TKI medicinal products.

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 detectable in human milk. Nursing mothers should either stop this drug or stop nursing.

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

Tabulated list of adverse reactions

Frequencies are defined as common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	Common	Uncommon	Rare	Very rare
Blood and lymphatic system disorders				leukopenia, thrombocytopenia, neutropenia, agranulocytosis, pancytopenia
Immune system disorders				hypersensitivity reactions (anaphylaxis, angioneurotic oedema, bronchospasm)
Metabolism and nutrition disorders		anorexia		
Psychiatric disorders				reversible psychic disturbances including depression, anxiety disorders, agitation, disorientation, confusion, hallucinations, insomnia
Nervous system disorders	headache, dizziness			convulsions, grand mal seizures (particularly in patients with impaired renal function), paresthesia, drowsiness, somnolence

System Organ Class	Common	Uncommon	Rare	Very rare
Respiratory, thoracic and mediastinal disorders				interstitial pneumonia sometimes fatal
Gastrointestinal disorders	constipation, diarrhoea	dry mouth, nausea and/or vomiting, abdominal discomfort or distension, flatulence, dysgeusia		
Hepatobiliary disorders				liver enzyme abnormalities, hepatitis, cholestatic jaundice
Skin and subcutaneous tissue disorders		rash, pruritus, urticaria		alopecia, Stevens Johnson syndrome/toxic epidermal necrolysis sometimes fatal
Musculoskeletal and connective tissue disorders			arthralgia	muscle cramps
Reproductive system and breast disorders				Impotence, reduced libido
General disorders and administration site conditions		fatigue		chest tightness
Investigations			increase in laboratory values (transaminases, gamma-GT, alkaline phosphatase, bilirubin)	

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 or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

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

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

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: histamine H_2-receptor antagonist, guanylthiazole derivative, ATC-classification: A02BA03

Mechanism of action
Famotidine is a competitive histamine H_2-receptor antagonist which leads to an inhibition of acid secretion mediated by H_2-receptors. Beside the acidity the pepsin content and the volume of basal gastric juice as well as that formed after stimulation is reduced. A pharmacological effect on the CNS, immunological, cardiovascular or respiratory parameters could not be observed.

Pharmacodynamic effects, clinical efficacy and safety
After oral administration the effect begins within one hour and reaches its maximum after 1 - 3 hours.

Single oral doses of 20 and 40 mg reliably inhibited basal nocturnal acid secretion. Mean gastric acid secretion was inhibited over at least 10 hours by 86 to 94%. The same doses administered in the morning suppressed the acid secretion stimulated by food 3 - 5 hours after administration by, on average, 76 to 84% and 8 - 10 hours after ingestion by 25 to 30%. However, the duration of action of the 20 mg dose in some subjects lasted 6 - 8 hours. Repeated doses did not lead to an accumulation of active constituent.

The nocturnal basal intragastric pH value was elevated by evening administration of 20 and 40 mg famotidine to an average of 5 and 6.4 respectively. If famotidine was taken after breakfast the pH value after 3 and after 8 hours was increased on the 20 mg as well as the 40 mg dose of famotidine to about 5.

Fasting and postprandial serum gastrin concentrations were not influenced by famotidine or only very slightly. Emptying of the stomach and exocrine pancreatic function were not affected by famotidine. The same applies to hepatic and portal blood flow. Famotidine had no effect on endocrinological functions either. Hormone concentrations of prolactin, cortisone, thyroxine (T4) and testosterone remained unchanged on treatment with famotidine.

5.2 Pharmacokinetic properties

Famotidine kinetics is linear.

Absorption
Famotidine is quickly absorbed after oral administration.

Distribution
Peak plasma concentrations are achieved in approximately 1-3.5 hours after administration of famotidine. Peak plasma concentrations are approximately 0.04 – 0.06 µg/ml, after administration of 20 mg famotidine and 0.075 to 0.1 µg/ml after administration of 40 mg famotidine. Repeated administration does not lead to an accumulation of the active ingredient. Famotidine absorption is not influenced by concomitant food intake.

To a limited extent, famotidine is found in the cerebrospinal fluid. The plasma/fluid ratio 4 hours after administering 40 mg of famotidine was a mean of 0.1.

Biotransformation
Oral bioavailability is about 40%.

Elimination
Famotidine is excreted into maternal milk. 6 hours after oral application a milk/plasma ratio of 1.78 was reached. The elimination half-life in plasma is 2.6 to 4 hours.

Up to 30 - 35% of the active ingredient is metabolised in the liver; a sulfoxide-metabolite is formed.

24 hours after oral administration 25 - 30% of the active ingredient is excreted via the urine unchanged; after intravenous administration, 65-70% is excreted unchanged in urine. Renal clearance is 250 - 450 ml/min which indicates tubular excretion. A slight amount can be eliminated as sulfoxide.

Renal impairment
As renal function declines, renal and total clearance of famotidine decrease without there being an increase in non-renal elimination. The elimination half-life after intravenous injection of a single dose of 20 mg or 10 mg of famotidine is increased to 4.5 - 9 hours in moderate renal insufficiency (creatinine clearance 60-30 ml/min), to 10 - 12 hours in severe renal insufficiency (creatinine clearance < 30 ml/min) and to 18 - 27 hours in patients with terminal insufficiency or anuria.

The amount of unchanged famotidine excreted with the urine is reduced to 60% in patients with moderate renal insufficiency. In cases of severe renal insufficiency it is only 25%.

Depending on the dialysis procedure (haemofiltration, 5-hour haemodialysis or continuous haemofiltration), dialysis patients have an elimination half-life of 7 - 14 hours after intravenous administration of 20 mg of famotidine after oral administration of 20 mg of famotidine it is 22.5 hours.

Hepatic impairment
The pharmacokinetics of famotidine are unchanged in liver function impairment.

Kinetics among elderly patients:
Pharmacokinetic studies on elderly patients showed no signs of any clinically significant age-related changes; however age-related impairment of renal function should be considered when determining the dosage.

5.3 Preclinical safety data
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Tablet core

Pregelatinised starch
maize starch
microcrystalline cellulose
hyprolose
colloidal anhydrous silica
magnesium stearate

Film-coating

Lactose monohydrate
hypromellose
macrogol 4000
red and yellow iron oxide (E172)
titanium dioxide (E171)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVdC-aluminium-blisters with 7, 14, 20, 21, 28, 30, 50, 56, 60, 100, 200 film-coated tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited
Ridings Point, Whistler Drive,
Castleford, WF10 5HX,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/0344

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/04/2010

10 DATE OF REVISION OF THE TEXT

03/10/2023