SUMMARY OF PRODUCT CHARACTERISTICS

1  NAME OF THE MEDICINAL PRODUCT
Famotidine 20 mg Film-coated Tablets

2  QUALITATIVE AND QUANTITATIVE COMPOSITION
One film-coated tablet contains 20 mg of famotidine.

*Excipients:*

One film-coated tablet contains 1.44 mg of lactose monohydrate.
For a 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

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 film-coated Famotidine 20 mg Film-coated Tablets 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 H₂-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 dosage of twice 20 mg famotidine is recommended.

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.

Mode 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 for 12 weeks.

4.3 Contraindications
Famotidine 20 mg Film-coated Tablets should not be taken in cases of hypersensitivity to famotidine or one of the other ingredients. If corresponding symptoms occur Famotidine 20 mg Film-coated Tablets should be withdrawn.

No sufficient experience has been gained on the safety and efficacy of famotidine in children. Therefore children should not be treated with Famotidine 20 mg Film-coated Tablets.

4.4 Special warnings and precautions for use
The symptomatic response to the treatment Famotidine 20 mg Film-coated Tablets does not exclude the possibility of malignancy of the ulceration. Malignancy in gastric ulcers should be excluded by suitable diagnostic measures before treatment with famotidine.

Famotidine 20 mg Film-coated Tablets is not suitable for the treatment of minor gastrointestinal symptoms.

Famotidine is mainly excreted via kidneys and partially metabolised in the liver. In patients with impaired kidney function, caution has to be exercised.

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.

Co-administration of H2-receptor antagonists such as famotidine with atazanavir/ritonavir in combination with tenofovir should be avoided (see section 4.5).

This medicinal product contains lactose and therefore should not be used by patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

4.5 Interactions with other medicinal products and other forms of interaction
No metabolism-related clinically important substance-specific interactions are known to date.
In case of concomitant application of substances whose absorption is influenced by the stomach’s acidity, an altered absorption may be taken into account. In case of ketoconazole or itraconazole it may be decreased. Ketoconazole should be taken 2 hours before application of famotidine.

Concomitant application of famotidine and 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 concomitant use of sucralfate decreases the absorption of famotidine. Therefore sucralfate should fundamentally be taken in a timely distance of 2 hours to the application of famotidine.

Application of probenecid can prolong the excretion of famotidine. Concomitant use of Famotidine 20 mg Film-coated Tablets should therefore be avoided.

**Atazanavir**
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 tenofovir is judged unavoidable, close clinical monitoring is recommended.

### 4.6 Pregnancy and lactation

Data on a limited number of exposed pregnancies indicate no adverse effects of famotidine on pregnancy or on the health of the fetus/newborn. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development (see section 5.3).

Famotidine should only be prescribed to pregnant women after a careful risk/benefit assessment has taken place. Famotidine passes into breast milk. Since it cannot be excluded that acid secretion in the infant is impaired by absorbed famotidine breast feeding should be avoided during treatment.

### 4.7 Effects on ability to drive and use machines

Famotidine has no or negligible influence on the ability to drive and use machines.

### 4.8 Undesirable effects
The following undesirable effects have been observed during treatment with famotidine with the following frequencies: common (>1%), uncommon (>0.1%, <1%), rare (>0.01%, <0.1%) very rare (<0.01%), including isolated reports.

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

**Psychiatric disorders**
**Very rare:** reversible psychological disturbances (e.g. hallucinations, disorientation, confusion, anxiety, agitation, depression)

**Nervous system disorders**
**Common:** headache, dizziness
**Very rare:** paraesthesia, drowsiness, sleeplessness, epileptic seizures (grand mal)

**Respiratory, thoracic and mediastinal disorders**
**Very rare:** feeling of tightness in the chest

**Gastrointestinal disorders**
**Common:** constipation, diarrhoea
**Uncommon:** dry mouth, nausea, vomiting, gastrointestinal complaints, flatulence, loss of appetite

**Hepato-biliary disorders**
**Rare:** intrahepatic cholestasis (visible sign: jaundice)

**Skin and subcutaneous tissue disorders**
**Uncommon:** rash, pruritus
**Rare:** urticaria
**Very rare:** severe skin reaction (toxic epidermal necrolysis), hair loss

**Musculoskeletal, connective tissue and bone disorders**
**Rare:** arthralgia
**Very rare:** muscle cramps

**Reproductive system and breast disorders**
**Very rare:** impotence, gynaecomastia reversible on discontinuing treatment

**General disorders and administration site conditions**
**Uncommon:** fatigue
**Rare:** hypersensitivity reactions (anaphylaxis, angioneurotic oedema, bronchospasm)
**Very rare:** reduced libido

**Investigations**
**Rare:** increase in laboratory values (transaminases, gamma-GT, alkaline phosphatase, bilirubin)

**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

There are no report of overdosing with famotidine.

If this should occur, efforts should be made to inhibit absorption and relieve symptoms.

The usual measures to remove unabsorbed material from gastro-intestinal tract should be employed together with clinical monitoring and supportive therapy.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC-classification: A02BA03, histamine H₂-receptor antagonist, guanylthiazole derivative

Famotidine is a competitive histamine H₂-receptor antagonist which leads to an inhibition of acid secretion mediated by H₂-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.

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.

Famotidine is quickly absorbed after oral administration.

Oral bioavailability is about 40%.

Peak plasma concentrations are achieved in approximately 1-3.5 hours after administration of famotidine. Peak plasma concentrations are approximately 0.04 –to 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 fluid/plasma ratio 4 hours after administering 40 mg of famotidine was a mean of 0.1.

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 insufficiency

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.

Liver function 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
hyprollose
colloidal anhydrous silica
magnesium stearate

*Film-coating*

Lactose monohydrate
hypermellose
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
Brampton road, Hampden Park, Eastbourne, East Sussex, BN 22 9 AG
UK

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
15/06/2015