# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Tagamet Syrup

Cimetidine 200 mg/5 ml Syrup

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Excipients with known effect:
5 ml of this medicine contains 12.8 mg sodium, 5 mg methyl hydroxybenzoate, 1 mg propyl hydroxybenzoate, 2.058 mg sucrose, 350 mg sorbitol, 500 mg propylene glycol, 0.05 mg Sunset Yellow and 118.1 mg ethanol (alcohol).

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

A clear, orange-coloured, peach-flavoured syrup.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Cimetidine is a histamine H2-receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output.

Cimetidine is indicated in the treatment of duodenal and benign gastric ulceration, including that associated with non-steroidal anti-inflammatory agents, recurrent and stomal ulceration, oesophageal reflux disease and other conditions where reduction of gastric acid by Cimetidine has been shown to be beneficial: persistent dyspeptic symptoms with or without ulceration, particularly meal-related upper abdominal pain, including such symptoms associated with non-steroidal anti-inflammatory agents; the prophylaxis of

gastrointestinal haemorrhage from stress ulceration in critically ill patients; before general anaesthesia in patients thought to be at risk of acid aspiration (Mendelson's) syndrome, particularly obstetric patients during labour; to reduce malabsorption and fluid loss in the short bowel syndrome; and in pancreatic insufficiency to reduce degradation of enzyme supplements. Cimetidine is also recommended in the management of the Zollinger-Ellison syndrome.

## 4.2 Posology and method of administration

The total daily dose by any route should not normally exceed 2.4 g. Dosage should be reduced in patients with impaired renal function (see section 4.4).

Posology

*Adults:*
For patients with duodenal or benign gastric ulceration, a single daily dose of 800mg at bedtime is recommended. Otherwise the usual dosage is 400mg twice a day with breakfast and at bedtime. Other effective regimens are 200mg three times a day with meals and 400mg at bedtime (1.0g/day) and, if inadequate, 400mg four times a day (1.6 g/day) also with meals and at bedtime.

Symptomatic relief is usually rapid. Treatment should be given initially for at least four weeks (six weeks in benign ulcer, eight weeks in ulcer associated with continued non-steroidal anti-inflammatory agents). Most ulcers will have healed by that stage, but those which have not will usually do so after a further course of treatment.

Treatment may be continued for longer periods in those patients who may benefit from reduction of gastric secretion and the dosage may be reduced as appropriate to 400mg at bedtime or 400mg in the morning and at bedtime.

In patients with benign peptic ulcer disease, relapse may be prevented by continued treatment, usually with 400mg at bedtime; 400mg in the morning and at bedtime has also been used.

In oesophageal reflux disease, 400mg four times a day, with meals and at bedtime, for four to eight weeks is recommended to heal oesophagitis and relieve associated symptoms.

In patients with very high gastric acid secretion (e.g. Zollinger-Ellison syndrome) it may be necessary to increase the dose to 400mg four times a day, or in occasional cases further.

Antacids can be made available to all patients until symptoms disappear.

In the prophylaxis of haemorrhage from stress ulceration in seriously ill patients, doses of 200-400mg can be given every four to six hours, by oral or nasogastric routes.

In patients thought to be at risk of acid aspiration syndrome an oral dose of 400mg can be given 90-120minutes before induction of general anaesthesia or, in obstetric practice prior to the start of labour. While such a risk persists, a dose of up to 400mg may be repeated at four-hourly intervals as required up to the usual daily maximum of 2.4g. Cimetidine Syrup should not be used. The usual precautions to avoid acid aspiration should be taken.

In the short bowel syndrome, e.g. following substantial resection for Crohn's disease, the usual dosage range (see above) can be used according to individual response.

To reduce degradation of pancreatic enzyme supplements, 800 – 1600mg a day may be given according to response in four divided doses, one to one and a half hours before meals.

*Elderly:* The normal adult dosage may be used unless renal function is markedly impaired (see section 4.4).

*Paediatric population:* Experience in children is less than that in adults. In children more than one year old, Cimetidine 25 – 30 mg/kg body weight per day in divided doses may be administered.

The use of Cimetidine in infants under one year old is not fully evaluated; 20 mg/kg body weight per day in divided doses has been used.

Method of administration:
For oral use

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

## 4.4 Special warnings and precautions for use

Dosage should be reduced in patients with impaired renal function according to creatinine clearance. The following dosages are suggested: creatinine clearance of 0 to 15ml per minute, 200mg twice a day; 15 to 30ml per minute, 200mg three times a day; 30 to 50ml per minute, 200mg four times a day; over

50ml per minute, normal dosage. Cimetidine is removed by haemodialysis, but not to any significant extent by peritoneal dialysis.

Clinical trials of over six years' continuous treatment and more than 15 years' widespread use have not revealed unexpected adverse reactions related to long-term therapy. The safety of prolonged use is not, however, fully established and care should be taken to observe periodically patients given prolonged treatment.

Cimetidine treatment can mask the symptoms and allow transient healing of gastric cancer. The potential delay in diagnosis should particularly be borne in mind in patients of middle age and over with new or recently changed dyspeptic symptoms.

Care should be taken that patients with a history of peptic ulcer, particularly the elderly, being treated with Cimetidine and a non-steroidal anti-inflammatory agent are observed regularly.

Due to possible interaction with coumarins, close monitoring of prothrombin time is recommended when cimetidine is concurrently used.
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Co-administration of therapeutic agents with a narrow therapeutic index, such as phenytoin or theophylline, may require dosage adjustment when starting or stopping concomitantly administered cimetidine (see section 4.5).

Excipients

This medicine contains methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reaction (possibly delayed).

This medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. Sucrose may be harmful to the teeth.

This medicine contains 350 mg sorbitol per 5 ml, equivalent to 70 mg per ml. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

This medicine contains Sunset Yellow which may cause allergic reactions.

This medicinal product contains 3 vol % ethanol (alcohol), i.e. up to 1.42 g per maximum daily dose (60 ml), equivalent to 36 ml beer, 15 ml wine per 60 ml. Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

This medicine contains 500 mg propylene glycol in each 5 ml which is equivalent to 100 mg/ml.

- Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old.
- While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.
- Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

This medicinal product contains 2.56 mg sodium per ml, equivalent to 0.13% of the WHO recommended maximum daily intake of 2 g sodium for an adult."

## 4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine can prolong the elimination of drugs metabolised by oxidation in the liver. Although pharmacological interactions with a number of drugs, e.g. diazepam, propranolol, have been demonstrated, only those with oral anticoagulants, phenytoin, theophylline and intravenous lidocaine appear, to date, to be of clinical significance. Close monitoring of patients on Cimetidine receiving oral anticoagulants or phenytoin is recommended and a reduction in the dosage of these drugs may be necessary.

In patients on drug treatment or with illnesses that could cause falls in blood cell count, the possibility that H2-receptor antagonism could potentiate this effect should be borne in mind.

Cimetidine has the potential to affect the absorption, metabolism or renal excretion of other drugs which is particularly important when drugs with a narrow therapeutic index are administered concurrently. The altered pharmacokinetics may necessitate dosage adjustment of the affected drug or discontinuation of treatment (see section 4.4).

Interactions may occur by several mechanisms including:

1) Inhibition of certain cytochrome P450 enzymes (including CYP1A2, CYP2C9, CYP2D6 and CYP3A3/A4, and CYP2C18); Inhibition of these enzymes may result in increased plasma levels of certain drugs including warfarin-type coumarin anticoagulants (e.g. warfarin), tricyclic antidepressants (e.g. amitriptyline), class I antiarrhythmics (e.g. lidocaine), calcium channel blockers (e.g. nifedipine, diltiazem), oral sulfonylureas (e.g. glipizide), phenytoin, theophylline and metoprolol.
2) Competition for renal tubular secretion; This may result in increased plasma levels of certain drugs including procainamide, metformin, ciclosporin and tacrolimus.

3) Alteration of gastric pH; The bioavailability of certain drugs may be affected. This can result in either an increase in absorption (e.g. atazanavir) or a decrease in absorption (e.g. some azole antifungals such as ketoconazole, itraconazole or posaconazole).
4) Unknown mechanisms: Cimetidine may potentiate the myelosuppressive effects (e.g. neutropenia, agranulocytosis) of chemotherapeutic agents such as carmustine, fluorouracil, epirubicin, or therapies such as radiation. Isolated cases of clinically relevant interactions have been documented with narcotic analgesics (e.g. morphine).

## 4.6 Fertility, Pregnancy and lactation

Although tests in animals and clinical evidence have not revealed any hazards from the administration of Cimetidine during pregnancy or lactation, both animal and human studies have shown that it does cross the placental barrier and is excreted in milk. As with most drugs, the use of Cimetidine should be avoided during pregnancy and lactation unless considered essential by the physician.

## 4.7 Effects on ability to drive and use machines

Not relevant.

## 4.8 Undesirable effects

Adverse experiences with cimetidine are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), 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).

**Blood and lymphatic system disorders**
Uncommon: Leukopenia
Rare: Thrombocytopenia, aplastic anaemia
Very rare: Pancytopenia, agranulocytosis

**Immune system disorders**
Very rare: Anaphylaxis. Anaphylaxis is usually cleared on withdrawal of the drug.

**Psychiatric disorders**

Uncommon: Depression, confusional states, hallucinations. Confusional states, reversible within a few days of withdrawing cimetidine, have been reported, usually in elderly or ill patients.

**Nervous system disorders**
Common: Headache, dizziness

**Cardiac disorders**
Uncommon: Tachycardia
Rare: Sinus bradycardia
Very rare: Heart block

**Gastrointestinal disorders**
Common: Diarrhoea
Very rare: Pancreatitis. Pancreatitis cleared on withdrawal of the drug.

**Hepatobiliary disorders**
Uncommon: Hepatitis
Rare: Increased serum transaminase levels. Hepatitis and increased serum transaminase levels cleared on withdrawal of the drug.

**Skin and subcutaneous tissue disorders**
Common: Skin rashes
Very rare: Reversible alopecia and hypersensitivity vasculitis. Hypersensitivity vasculitis usually cleared on withdrawal of the drug.

**Musculoskeletal and connective tissue disorders**
Common: Myalgia
Very rare: Arthralgia

**Renal and urinary disorders**
Uncommon: Increases in plasma creatinine
Rare: Interstitial nephritis. Interstitial nephritis cleared on withdrawal of the drug. Small increases in plasma creatinine have been reported, unassociated with changes in glomerular filtration rate. The increases do not progress with continued therapy and disappear at the end of therapy.

**Reproductive system and breast disorders**
Uncommon: Gynaecomastia and reversible impotence. Gynaecomastia is usually reversible upon discontinuation of cimetidine therapy. Reversible impotence has been reported particularly in patients receiving high doses (e.g. in Zollinger-Ellison Syndrome). However, at regular dosage, the incidence is similar to that in the general population.
Very rare: Galactorrhoea

**General disorders and administration site conditions**
Common: Tiredness
Very rare: Fever. Fever cleared on withdrawal of the drug.

**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

Acute overdosage of up to 20g has been reported several times with no significant ill-effects. Induction of vomiting and/or gastric lavage may be employed together with symptomatic and supportive therapy.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: H2-receptor antagonists, ATC code: A02BA01

Cimetidine is a histamine H2-receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output.

### 5.2 Pharmacokinetic properties

Cimetidine is well absorbed after oral administration, metabolised in the liver and excreted mainly through the kidney with a half-life of about two hours. The effects on acid secretion are of longer duration.

### 5.3 Preclinical safety data

Not applicable

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Saccharin sodium
Hydrochloric acid (E507)
Ethanol
Methyl parahydroxybenzoate (E 218)
Propyl parahydroxybenzoate (E 216)
Propylene glycol
Sodium chloride
Disodium hydrogen phosphate (E 339)
Sorbitol (E 420)
Sucrose
Sunset Yellow (E110)
Peach flavour
Mafco Magnasweet 180
Ethylene oxide
Propylene oxide polymer
Purified water

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

3 years.

## 6.4 Special precautions for storage

Amber glass or white opaque HDPE bottles with screw cap containing 600 ml.

## 6.5 Nature and contents of container

Amber glass or white opaque HDPE bottles with screw cap containing 600 ml.

### 6.6 Special precautions for disposal

No special requirements.

## 7 MARKETING AUTHORISATION HOLDER

Rosemont Pharmaceuticals Ltd,
Yorkdale Industrial Park, Braithwaite Street,
Leeds, LS11 9XE, UK.

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 00427/0290

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

25 June 2004

## 10 DATE OF REVISION OF THE TEXT

23/02/2022