PHYSICIANS CIRCULAR

Tablets

PEPCIDINE®†

(famotidine, USP)

PEPCIDINE (famotidine, USP) is a highly effective, long-acting histamine H_2-receptor antagonist. PEPCIDINE has a rapid onset of action and shows a high degree of specificity for the H_2 receptor. PEPCIDINE reduces the acid and pepsin content, as well as the volume, of basal and stimulated gastric secretion. In clinical studies, PEPCIDINE relieved the pain associated with peptic ulceration usually within the first week of treatment, and suppressed gastric acid secretion with once-a-day dosage at night.

PEPCIDINE is highly effective in the treatment of duodenal ulcer, benign gastric ulcer, and hypersecretory conditions such as the Zollinger-Ellison syndrome, as well as other conditions where reduction of gastric secretion is desirable.

In the treatment of gastroesophageal reflux disease (GERD), PEPCIDINE has been shown to relieve symptoms and promote healing of erosions or ulcerations of the esophageal mucosa. Furthermore, PEPCIDINE has been demonstrated to prevent the relapse of symptoms and erosions or ulcerations associated with GERD.

PEPCIDINE has also been shown to be highly effective for the prevention of relapse of duodenal and benign gastric ulceration.

INDICATIONS

- Duodenal ulcer
- Benign gastric ulcer
- Hypersecretory conditions such as Zollinger-Ellison syndrome
- Prevention of relapse of duodenal ulceration
- Prevention of relapse of benign gastric ulcer
- Symptomatic relief of gastroesophageal reflux disease
- Healing of esophageal erosion or ulceration associated with gastroesophageal reflux disease
- Prevention of relapse of symptoms and erosions or ulcerations associated with GERD

† Registered Trademark

DOSAGE AND ADMINISTRATION

TABLETS

DUODENAL ULCER

Initial Therapy:

The recommended dose of PEPCIDINE is one 40 mg tablet daily taken at night. Treatment should be given for 4 to 8 weeks, but the duration of treatment may be shortened if endoscopy reveals that the ulcer has healed. In most cases of duodenal ulcer, healing occurs within 4 weeks on this regimen. In those patients whose ulcers have not healed completely after 4 weeks, treatment should be continued for a further 4-week period.

Maintenance Therapy:

For the prevention of recurrence of duodenal ulceration, it is recommended that therapy with PEPCIDINE be continued with 20 mg tablet daily taken at night.

BENIGN GASTRIC ULCER

The recommended dose of PEPCIDINE is one 40 mg tablet daily taken at night. Treatment should be given for 4-8 weeks, but the duration of treatment may be shortened if endoscopy reveals that the ulcer has healed.

Maintenance Therapy:

For the prevention of recurrence of benign gastric ulcer, the recommended dosage is 20 mg tablet taken at night which may be given for up to one year.

ZOLLINGER-ELLISON SYNDROME

Patients without prior antisecretory therapy should be started on a dose of 20 mg every 6 hours. Dosage should be adjusted to individual patient needs and should continue for as long as clinically indicated. Doses up to 800 mg daily have been used for up to 1 year without the development of significant side effects or tachyphylaxis. Patients who have been receiving another H_2 antagonist may be switched directly to PEPCIDINE at a starting dose higher than that recommended for new cases; this starting dose will depend on the severity of the condition and the last dose of the H_2 antagonist previously used.

GASTROESOPHAGEAL REFLUX DISEASE

The recommended dosage for the symptomatic relief of gastroesophageal reflux disease is 20 mg of famotidine twice daily.

For the treatment of esophageal erosion or ulceration associated with GERD, the recommended dosage is 40 mg of famotidine twice daily.

Maintenance Therapy:

For the prevention of recurrence of symptoms and erosions or ulcerations associated with GERD, the recommended dosage is 20 mg of famotidine twice daily.

CONTRAINDICATIONS

Hypersensitivity to any component of these products. Cross sensitivity in this class of compounds has been observed. Therefore, PEPCIDINE should not be administered to patients with a history of hypersensitivity to other H_2-receptor antagonists.

PRECAUTIONS

GASTRIC NEOPLASM

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

RENAL DYSFUNCTION

Since PEPCIDINE 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).

USE IN PREGNANCY

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

NURSING MOTHERS

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

PEDIATRIC USE

Use of PEPCIDINE in pediatric patients is supported by evidence from adequate and well-controlled studies of PEPCIDINE in adults, and by the following studies in pediatric patients: In published studies in small numbers of pediatric patients 1-15 years of age, clearance of famotidine was similar to that seen in adults. In pediatric patients 11-15 years of age, oral doses of 0.5 mg/kg were associated with a mean area under the curve (AUC) similar to that seen in adults treated orally with 40 mg. Similarly, in pediatric patients 1-15 years of age, intravenous doses of 0.5 mg/kg were associated with a mean AUC similar to that seen in adults treated intravenously with 40 mg. Limited published studies also suggest that the relationship between serum concentration and acid suppression is similar in pediatric patients 1-15 years of age as compared with adults. These studies suggest a starting dose for pediatric patients who can swallow tablets as follows:

Peptic ulcer – For pediatric patients ≥40 kg, 20 mg p.o. at bedtime up to 40 mg/day (may be divided b.i.d.).

Gastroesophageal Reflux Disease - For pediatric patients ≥20 kg, 20 mg/day p.o. up to 40 mg b.i.d.

While published uncontrolled studies suggest effectiveness of famotidine in the treatment of gastroesophageal reflux disease and peptic ulcer, data in pediatric patients are insufficient to establish percent response with dose and duration of therapy. Therefore, treatment duration (initially based on adult duration recommendations) and dose should be individualized based on clinical response and/or pH determination (gastric or esophageal) and endoscopy. Published uncontrolled clinical studies in pediatric patients have employed doses up to 1 mg/kg/day for peptic ulcer and 2 mg/kg/day for GERD.

Based on the comparison of pharmacokinetic parameters for PEPCIDINE in adults and pediatric patients, dosage adjustment in pediatric patients with severe renal insufficiency should be considered.

Based on post-marketing reports, the adverse experience profile for pediatric patients seemed comparable to that in adults.

USE IN THE ELDERLY

When PEPCIDINE 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.

DRIVING AND OPERATING MACHINERY

PEPCIDINE may cause certain side effects such as dizziness, confusion, or hallucinations and, therefore, patients should know how they react to PEPCIDINE before they operate an automobile or machinery or engage in activities requiring mental alertness and coordination (see SIDE EFFECTS).

DRUG INTERACTIONS

No drug interactions of clinical importance have been identified. PEPCIDINE 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.

SIDE EFFECTS

PEPCIDINE has been demonstrated to be generally well-tolerated. Headache, dizziness, constipation and diarrhea have been reported rarely. Other side effects reported even less frequently included dry mouth, nausea and/or vomiting, abdominal discomfort or distention, anorexia, fatigue, rash, pruritus and urticaria, alopecia, liver enzyme abnormalities, hepatitis, cholestatic jaundice, anaphylaxis, angioedema, arthralgia, muscle cramps, taste disorder, reversible psychic disturbances including depression, anxiety disorders, agitation, confusion and hallucinations. Toxic epidermal necrolysis has been reported very rarely with H_2-receptor antagonists. In addition to the above side effects, A-V block has been reported very rarely with H_2-receptor antagonists administered intravenously.

OVERDOSAGE

There is no experience to date with overdosage.

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.

AVAILABILITY

PEPCIDINE (famotidine, USP) tablets are supplied in blister of 10's (1 x 10's strip). Each tablet contains 40mg Famotidine.