FAMOTIDINE TABLETS USP
20 mg and 40 mg

DESCRIPTION
The active ingredient in Famotidine Tablets USP is a histamine H₂-receptor antagonist. Famotidine is 1-[N-(4-Cl-3-quinazolinylmethyl)iminyl]cyclohexylamine hydrochloride and the molecular formula of famotidine is C₂₀H₂₁ClN₂O₂, and the molecular weight is 354.85. Its structural formula is:

![Famotidine Structural Formula]

It is a white to off-white crystalline compound that is freely soluble in glacial acetic acid, slightly soluble in methanol, very slightly soluble in water, and practically insoluble in ethanol.

Each tablet contains 20 mg or 40 mg of famotidine USP and the inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, starch, and red iron oxide.

CLINICAL PHARMACOLOGY IN ADULTS
GI Effects
Famotidine is a competitive inhibitor of histamine H₂-receptors. The primary clinically important pharmacologic activity of famotidine is inhibition of gastric secretion. Both the acid concentration and volume of gastric secretion are suppressed by famotidine, while changes in basal secretion are proportionate to volume output.

In normal volunteers and hypersecretory, biopsy-proven fingid and duodenal gastric secretions, all as induced by histamine or pentagastrin. After oral administration, the onset of the antipropulsive effect occurred within one hour; the maximum effect was dose-dependent, occurring within one to three hours. Mean inhibition of secretion by doses of 20 and 40 mg was 10 to 17 hours.

Single evening dose of 20 and 40 mg given orally and intravenous acid secretion in all patients: mean nocturnal gastric acid secretion was inhibited by 78% and 94%, respectively, on a period of at least 10 hours. The same doses given in the morning suppressed meal-stimulated and secretions in all subjects. The mean suppression was 76% and 94%, respectively, in 3 to 5 hours after administration. 0% and 30%, respectively, in 8 to 10 hours after administration. In some subjects who received the 30 mg dose, however, the antipropulsive effect was maintained for 12 to 16 hours. There was no cumulative effect with repeated doses. The nocturnal intragastric pH was raised by evening doses of 20 and 40 mg to mean values of 0.6 and 3.6, respectively. When famotidine was given after breakfast, the basal daytime intragastric pH at 3 and 8 hours after 20 or 40 mg of famotidine was similar to 5.5.

Famotidine had little or no effect on testing or postprandial serum gastrin levels. Gastric emptying and exocrine pancreatic functions were not affected by famotidine.

Other Effects
Systemic effects of famotidine in the CVS, cardiovascular, respiratory, or endocrine systems were not noted in clinical pharmacology studies. Also, no untoward effects were noted. (See ADVERSE REACTIONS) Serum hormone levels, including prolactin, cortisol, thyroxine (T₄), and triiodothyronine, were not altered after treatment with famotidine.

PHARMACOKINETICS
Famotidine is incompletely absorbed. The availability of oral doses is 40-60%. Famotidine tablets, famotidine oral suspension, and famotidine orally disintegrating tablets are bioequivalent. Bioavailability may be increased by food or slightly decreased by antacids; however, these effects are of no clinical consequence. Famotidine undergoes minimal first-pass metabolism. After oral doses, peak plasma levels occur in 1 to 2 hours. Plasma levels after multiple doses are similar to those after single doses. Normally, 50% of a dose is eliminated in the urine as unchanged drug, and 30% is metabolized. The major metabolite is 2-hydroxylated, and the metabolites are excreted in the urine and feces. The half-life of the drug is 2.5 to 3.5 hours. Famotidine is distributed to renal (65-75%) and metabolic (30-35%) phases. Renal clearance is 700-450 ml/min, indicating some renal excretion. Twenty-five to 35% of an oral dose and 50-70% of an intravenous dose are eliminated in the urine as unchanged drug. The only metabolite excreted in urine is the 2-hydroxy metabolite.

Pharmacology
In elderly patients, there is no clinically significant age-related changes in the pharmacokinetics of famotidine. However, in elderly patients with decreased renal function, the dosing of the drug may be adjusted (see PRECAUTIONS, Geriatric Use).

Clinical Studies
Uncomplicated Ulcer
In a U.S. multicenter, double-blind study in outpatients with endoscopically confirmed duodenal ulcers, orally administered famotidine was compared to placebo. As shown in Table 1, 70% of patients treated with famotidine 40 mg b.i.d. were healed by week 4

<table>
<thead>
<tr>
<th>Week</th>
<th>Famotidine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>75%</td>
<td>42%</td>
</tr>
</tbody>
</table>

Table 1: Patients treated with famotidine 40 mg b.i.d. were healed by week 4

Patients treated with famotidine had healed versus 45% of patients treated with placebo. The incidence of ulcer healing with famotidine was significantly higher than with placebo at each time point based on comparison of endoscopically confirmed healed ulcers.

In this study, time to relief of daytime and nocturnal pain was significantly shorter for patients receiving famotidine than for patients receiving placebo. Patients receiving famotidine also took less time to return to normal diet than patients receiving placebo.

Long-Term Maintenance Treatment of Duodenal Ulcer
Famotidine, 20 mg b.i.d. for 4 weeks, was compared to placebo and maintenance therapy in two double-blind, multicenter studies of patients with endoscopically confirmed healed duodenal ulcers. In the U.S. study, the observed ulcer incidence in 12 months in patients treated with famotidine was 2.8% at 4 years in patients treated with placebo. Eighty patients treated with famotidine had a cumulative observed ulcer incidence of 2.4% compared to an observed ulcer incidence of 50% in the 83 patients receiving placebo (p<0.01). These results were confirmed in an international study where the cumulative observed ulcer incidence within 12 months in 141 patients treated with famotidine was 10.7%, compared to an incidence of 75% in the 265 patients treated with placebo (p<0.01).

Gastric Ulcer
In both a U.S. and an international multicenter, double-blind study in patients with endoscopically confirmed active benign gastric ulcer, orally administered famotidine, 40 mg b.i.d., was compared to placebo. All patients were permitted during the studies. The ulcer healing response was not significantly different between the famotidine and placebo groups. As shown in Table 2, ulcer healing response was significantly better than placebo in parts A and B in the U.S. study and in parts A and B in the international study, based on the number of patients that healed, confirmed by endoscopy.

Table 2: Patients with Endoscopically Confirmed Healed Gastric Ulcers

<table>
<thead>
<tr>
<th>U.S. Study</th>
<th>Famotidine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 mg b.i.d.</td>
<td>70%</td>
<td>42%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>International Study</th>
<th>Famotidine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 mg b.i.d.</td>
<td>70%</td>
<td>42%</td>
</tr>
</tbody>
</table>
4. Short-term treatment of gynecoproliferative vulvar disease (GERD): Famotidine Tablets USP are indicated for short-term treatment of patients with symptoms of GERD (see CLINICAL PHARMACOLOGY IN ADULTS, Clinical Studies).

5. Treatment of pathological hyperacidity conditions (e.g., Zollinger-Ellison Syndrome, multiple endocrine neoplasia) (see CLINICAL PHARMACOLOGY IN ADULTS, Clinical Studies).

CONTRAINDICATIONS
Hypersensitivity to any component of this product. Cautions particularly in states of compromised renal function have been observed. Therefore, Famotidine Tablets USP should not be administered to patients with a history of hypersensitivity to any of the major antigens.

PRECAUTIONS
General
Symptomatic response to therapy with famotidine does not preclude the presence of gastric malignancy.

Patients with Malignant or Severe Renal Insufficiency
Since CRI adverse events have been reported in patients with moderate and severe renal insufficiency, larger intervals between doses or lower doses may need to be used in patients with creatinine clearance <30 ml/min or serum creatinine clearance <15 ml/min. Renal insufficiency may be factored into the dose regimen. (see CLINICAL PHARMACOLOGY IN ADULTS, Dosage and Administration.)

Drug Interactions
No drug interactions have been identified. Studies with famotidine in rats, in animal models, and in vitro have shown no significant interference with the disposition of compounds metabolized by the hepatic microsomal enzymes, e.g., coumarin, P450 systems. Compounds metabolized in vitro include chlordiazepoxide, phenytoin, diazepam, antipyrine, and amphetamine. Inducible forms of hepatic drug metabolism have been tested and no significant effects have been found.

Caution in ReCKS
Dyspepsia, Mallory-Weiss, Barrett's, and aspiration pneumonia have been reported.

Dyspepsia in rats and rabbits at oral doses of up to 2000 mg/kg has been reported. In dogs, a dose-dependent increase in gastric lesions was reported.

In 2 100 week study in rats and a 92 week study in mice given oral doses of up to 2000 mg/kg (approximately 2500 times the recommended human dose for active duodenal ulcer), there was no evidence of carcinogenic potential for famotidine.

Famotidine was negative in the microsomal mutagenic test (Ames test) using Salmonella typhimurium and Escherichia coli with or without metabolic activation of up to 10,000 mg/kg. In vivo studies in mice, with a microbacterial and a chromosomal aberration test, no evidence of a mutagenic effect was observed.

In studies with rats given oral doses of up to 2500 mg/kg or intravenous doses of up to 200 mg/kg, fertility and reproductive performance were not affected.

Pregnancy
Pregnancy Category B
Reproductive studies have been performed in rats and rabbits at oral doses of up to 2000 and 500 mg/kg, respectively, and in both species at oral doses up to 200 mg/kg, and have revealed no significant evidence of impaired fertility or harm to the fetus due to famotidine. No direct teratogenic effects have been observed, although abnormalities occurring only in maternal dosing may have occurred. Maternal toxicity was seen in some males at oral doses of 200 mg/kg (250 times the usual human dose) or higher. There are, however, no adequate and well-controlled studies in pregnant women. Therefore, animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers
Studies performed in lactating rats have shown that famotidine is excreted in breast milk. Transient gastrointestinal depression was observed in nursing rats suckling from mothers treated with famotidine. Tolerance to human milk, because of the potential for serious adverse reactions in nursing infants from famotidine, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Patients
Use in children 1-15 years of age is not recommended based on adequate and well-controlled studies of famotidine use in adults, and 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 1-15 years of age, oral doses of 0.3-0.5 mg/kg were associated with a mean area under the curve (AUC) that was similar to that seen in adults treated orally with 10 mg. Similar results were observed in 5-15 years of age, 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 overall suppression in pediatric patients 1-15 years of age may be comparable with adults. Those studies suggest that a starting dose for pediatric patients 1-15 years of age is as follows:

Pediatric patients: 0.5 mg/kg p.o. at bedtime or divided b.i.d. to 40 mg/day.

Gastroesophageal Reflux Disease: Description of approved and unapproved labeling or warnings and precautions.

Gastroesophageal reflux disease is a common, often chronic condition, and treatment may be lifelong. Famotidine Tablets USP are not a substitute for surgery or other anti-reflux therapies. Famotidine Tablets USP do not cure GERD or prevent esophageal complications such as Barrett's esophagus, eosinophilic esophagitis, or esophageal adenocarcinoma.

No pharmacokinetic or pharmacodynamic data are available on pediatric patients under 1 year of age.

Geriatric Use
Of the 1,474 subjects in clinical trials who were treated with famotidine, 488 subjects (33%) were 65 and older, and 88 subjects (7%) were 75 years of age or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. However, greater sensitivity of some older individuals cannot be ruled out.

Dosage Adjustment in Renal Insufficiency (see CLINICAL PHARMACOLOGY IN ADULTS, Pharmacokinetics). This drug has been shown to be substantially extracted by the kidney, and the rate of drug elimination in the dog may be greater in patients with impaired renal function. Therefore, dosage recommendations should be made based on the degree of renal impairment. The dosage of famotidine may need to be reduced in patients with severe renal impairment or end-stage renal disease. A dosage adjustment in the case of moderate or severe renal impairment is necessary (see PRECAUTIONS). ADVERSE REACTIONS
The adverse reactions listed below have been reported during domestic and international clinical trials in approximately 2500 patients. In these controlled clinical trials in which famotidine tablets were compared to placebo, the incidence of adverse experiences in the group which received famotidine tablets, 40 mg at bedtime, was similar to that in the placebo group.

The following adverse reactions have been reported to occur in more than 2% of patients on therapy with famotidine in controlled clinical trials, and may be causally related to the drug: headache (4.7%), dizziness (3.4%), constipation (3.2%), and diarrhea (1.7%).

The following adverse reactions have been reported infrequently in clinical trials or since the drug was marketed. These are not necessarily causally related to the drug: gingival hyperplasia, dry mouth, dyspepsia, nausea, and 0.1%.
Table 7
Patients with Endoscopically Confirmed Gastric Ulcers

<table>
<thead>
<tr>
<th>Treatment</th>
<th>U.S. Study</th>
<th>International Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Famotidine</td>
<td>45 mg b.i.d.</td>
<td>40 mg b.i.d.</td>
</tr>
<tr>
<td>Placebo</td>
<td>45 mg b.i.d.</td>
<td>40 mg b.i.d.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week 4</th>
<th>45%</th>
<th>39%</th>
<th>41%</th>
<th>31%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6</td>
<td>46%</td>
<td>64%</td>
<td>65%</td>
<td>46%</td>
</tr>
<tr>
<td>Week 8</td>
<td>72%</td>
<td>64%</td>
<td>60%</td>
<td>54%</td>
</tr>
</tbody>
</table>

*Statistically significantly better than placebo (p < 0.01; p < 0.001 respectively).

Endoscopy or Recheck Risks (EORR)

Oral administration of famotidine was compared to placebo in a U.S. study that enrolled patients with symptoms of DU and without endoscopic evidence of erosion or ulceration of the esophagus. Famotidine 20 mg b.i.d. was statistically significantly superior to 40 mg b.i.d. and placebo in preventing a successful symptomatic outcome, defined as moderate or excellent improvement of symptoms (Table 3).

<table>
<thead>
<tr>
<th>% Successful Symptomatic Outcome</th>
<th>Famotidine 40 mg b.i.d. (N = 72)</th>
<th>Famotidine 20 mg b.i.d. (N = 72)</th>
<th>Placebo (N = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6</td>
<td>0%</td>
<td>3%</td>
<td>12%</td>
</tr>
<tr>
<td>Week 12</td>
<td>18%</td>
<td>44%</td>
<td>62%</td>
</tr>
</tbody>
</table>

Table 4
Endoscopic Healing - U.S. Study

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Famotidine 40 mg b.i.d. (N = 125)</th>
<th>Famotidine 20 mg b.i.d. (N = 125)</th>
<th>Placebo (N = 125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6</td>
<td>40%</td>
<td>32%</td>
<td>12%</td>
</tr>
<tr>
<td>Week 12</td>
<td>69%</td>
<td>54%</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Statistically significantly better than placebo (p < 0.001).

The study comparing famotidine 40 mg b.i.d. to placebo showed a significantly greater percentage of healing for famotidine 40 mg b.i.d. at weeks 6 and 12 (Table 4). There was, however, no significant difference among treatments in symptom relief.

Table 5
Endoscopic Healing - International Study

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Famotidine 40 mg b.i.d. (N = 115)</th>
<th>Famotidine 20 mg b.i.d. (N = 115)</th>
<th>Placebo (N = 115)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6</td>
<td>48%</td>
<td>52%</td>
<td>42%</td>
</tr>
<tr>
<td>Week 12</td>
<td>71%</td>
<td>68%</td>
<td>60%</td>
</tr>
</tbody>
</table>

*Statistically significantly better than placebo (p < 0.001).

Pathological Hypersecretory Conditions (e.g., Zollinger-Ellison Syndrome, Gastric Ectopic Aldosterone)

In studies of patients with pathological hypersecretory conditions such as Zollinger-Ellison Syndrome, with or without multiple endocrine abnormalities, famotidine significantly inhibited gastric secretion and controlled peptic ulcer symptoms. Oral administration of famotidine from 20 to 100 mg/day before meals and at bedtime resulted in acid secretion below 10 mEq/h. Initial doses were titrated to the individual patient need and subsequent adjustment were necessary with time in some patients. Famotidine would be expected at these high dose levels for prolonged periods (greater than 12 months) in eight patients. In the treatment of hypergastrinemia, increased plasma levels of gastrin were considered to be due to the drug.

CLINICAL PHARMACOLOGY IN PEDIATRIC PATIENTS

Pharmacokinetics

The pharmacokinetic data from this study of small numbers of pediatric patients given famotidine intravenously. AUC (area under the curve) was determined from a 1.0 mg/kg iv bolus injection in children aged 1-15 years and children with an intravenous dose in adults (extrapolation based on results obtained with a 20 mg iv adult dose).

Table 6
Pharmacokinetic Parameters of Intravenous Famotidine

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>AUC (mg·h/L)</th>
<th>Vss (L/kg)</th>
<th>CL (mg/h/L)</th>
<th>t1/2 (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-15 yrs</td>
<td>2.0 mg/kg</td>
<td>0.34</td>
<td>7.07</td>
<td>3.28</td>
</tr>
<tr>
<td>11-15 yrs</td>
<td>1.1 mg/kg</td>
<td>0.27</td>
<td>1.59</td>
<td>2.25</td>
</tr>
</tbody>
</table>

Adults (16+)

<table>
<thead>
<tr>
<th>AUC (mg·h/L)</th>
<th>Vss (L/kg)</th>
<th>CL (mg/h/L)</th>
<th>t1/2 (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 mg/kg</td>
<td>0.40</td>
<td>1.00</td>
<td>0.50</td>
</tr>
</tbody>
</table>

All values presented as mean ± 10 units indicated otherwise.

Mean value only.

Values of pharmacokinetic parameters for pediatric patients, ages 1-15 years, are comparable to those observed for adults.

Bioavailability studies of famotidine 20 mg iv bolus injection in children aged 1-15 years showed a mean oral bioavailability of 55% compared to adult values of 72% to 84%. Oral doses of 0.5 mg/kg achieved an AUC of 5600 ± 500 ng·h/mL in children.
Table 5

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Effect</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3 mg/kg, single</td>
<td>IV</td>
<td>gastric pH 0.5 for 2 hours</td>
<td>5</td>
</tr>
<tr>
<td>0.4 mg/L, single</td>
<td>IV</td>
<td>gastric pH 0.5 for 4 hours</td>
<td>18</td>
</tr>
<tr>
<td>0.5 mg/L, single</td>
<td>IV</td>
<td>a 0.2 pH unit increase above baseline in gastric pH for 4 hours</td>
<td>4</td>
</tr>
<tr>
<td>0.5 mg/L b.i.d.</td>
<td>IV</td>
<td>gastric pH 0.5 for 2 hours</td>
<td>4</td>
</tr>
<tr>
<td>0.5 mg/L b.i.d.</td>
<td>Oral</td>
<td>gastric pH 0.5 for 4 hours</td>
<td>4</td>
</tr>
</tbody>
</table>

Values reported in published literature.

Volunteer study population.

INDICATIONS AND USAGE

Famotidine Tablets USP are indicated in:
1. Short-term treatment of active duodenal ulcer: Most adult patients heal within 4 weeks; there is only a small likelihood of using Famotidine Tablets USP at full dosage for longer than 4 to 8 weeks. Studies have not assessed the activity of famotidine in uncomplicated active duodenal ulcer for periods of more than eight weeks.
2. Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of an active ulcer: Controlled studies in adults have not extended beyond one year.
3. Short-term treatment of active benign gastric ulcer: Most adult patients heal within 6 weeks. Studies have not assessed the safety or efficacy of famotidine in uncomplicated active benign gastric ulcer for periods of more than 8 weeks.
Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. Dosage adjustments in the case of moderate or severe renal insufficiency are necessary (see PRECAUTIONS). Patients with moderate or severe renal insufficiency and DISEASE AND ADMINISTRATION (Dosage Adjustment in Patients with Moderate or Severe Renal Insufficiency)

ADVERSE REACTIONS

The adverse reactions listed below have been reported during the clinical trials in approximately 2000 patients. In those controlled clinical trials in which lamotrigine tablets were compared to placebo, the incidence of adverse experiences in the group which received lamotrigine tablets, 40 mg at bedtime, was similar to that in the placebo group.

The following adverse reactions have been reported to occur in more than 2% of patients on therapy with lamotrigine in controlled clinical trials, and may be causally related to the drug: Rash (1.3%), Stevens-Johnson Syndrome (0.1%), and blepharoconjunctivitis (0.1%).

The following other adverse reactions have been reported in clinical trials or since the drug was marketed. The relationship to therapy with lamotrigine has been unclear in many cases. Within each category the adverse reactions are listed in order of increasing severity:

Body as a Whole: fever, asthenia, lupus
Cardiovascular: orthostatic, arrhythmia, AV block, hypotension
Respiratory: dyspnea, bronchitis, pneumonia, pneumothorax, hyperventilation, pharyngitis, rhinitis, epistaxis
Gastrointestinal: cramps, diarrhea, ileus, gastritis, nausea, anorexia, vomiting
Genitourinary: decreased or increased renal function, proteinuria, hematuria, renal failure, anuria
Central nervous system: headache, fatigue, dizziness, paresthesia, tremor, insomnia, ataxia
Musculoskeletal: myalgia, arthritis, tendinitis
Skin: rash, pruritus

OVERDOSAGE

There is no experience to date with deliberate overdose. Oral doses of up to 640 mg/day have been given to adult patients with pharmacological hyperactivity conditions with serious adverse effects. In the event of overdose, treatment should be symptomatic and supportive. Unabsorbed material should be removed from the gastrointestinal tract, the patient should be monitored, and supportive therapy should be employed.

The oral LD50 of lamotrigine in male and female rats and mice was greater than 2000 mg/kg and the minimum lethal dose was 100 mg/kg in mice and 10 mg/kg in rats. Lamotrigine did not produce any effects at high and doses in mice, rats, and dogs, but induced significant anorexia and growth depression in rats starting at 200 mg/kg/day orally. The intravenous LD50 of lamotrigine for mice and was greater than 3500 mg/kg, and the minimum lethal single i.v. dose in dogs was approximately 3000 mg/kg. Signs of acute intoxication in 1 treated dogs were emesis, salivation, pathy of muscles, uncoordinated movements or redness of mouth and ears, hypothermia, tachycardia and collapse.

DOSAGE AND ADMINISTRATION

Doxepin Oral
Acute Therapy
The recommended adult oral dosage for acute doxepin use is 40 mg once a day at bedtime. Most patients had within 4 weeks. There is no reason to use a doxepin LUP or doxepin dosage for longer than 6 to 8 weeks. A regimen of 20 mg b.i.d. is also effective.

Maintenance Therapy
The recommended adult oral dosage for active August use is 40 mg once a day at bedtime.

Acute Symptomatic Buffer Use
The recommended adult oral dosage for acute August use is 40 mg once a day at bedtime.

Cystoscopy or Reflux Disease (INTEROS)
The recommended oral dosage for treatment of patients with symptomatic GERD is 20 mg b.i.d. for 1 week. The recommended oral dosage for the treatment of adult patients with esophageal reflux disease who have dysphagia or aspiration, or who are undergoing an esophagogastroduodenoscopy, is 40 mg b.i.d. for 1 week (see CLINICAL PHARMACOLOGY IN ADULTS, Clinical Studies).

Dosage for Pediatric Patients
See PRECAUTIONS. Pediatric Patients
The studies described in PRECAUTIONS. Pediatric Patients suggest the following starting doses in pediatric patients 1-18 years of age:

Peak: 0.5-1.5 mg/dl per patient per day b.i.d. up to 40 mg/day.

Adult: 8-16 mg/dl per patient per day b.i.d. up to 40 mg/day.

While published and unpublished studies suggest effectiveness of lamotrigine in the treatment of generalized epilepsy seizures and epilepsy, data in pediatric patients are insufficient to establish a long-term efficacy of lamotrigine. Therefore, in patients with prolonged uncontrolled seizures and/or refractory status epilepticus, lamotrigine should be used cautiously and with close monitoring. Published controlled clinical studies in pediatric patients have employed dosages to 5 mg/day for epilepsy and 15 mg/day for patients with moderate to severe renal insufficiency.

Serum Electrolytes
Fentanyl oral suspension may be substituted for lamotrigine tablets in any of the above indications.

Oral Disintegrating Tablet
Fentanyl orally disintegrating tablets may be substituted for fentanyl tablets in any of the above indications in the same recommended dosages.

Contraindications
Fentanyl tablets are contraindicated in patients with known allergy to fentanyl or its components

WARNINGS

Dose adjustment in patients with moderate or severe renal insufficiency

In adult patients with moderate (creatinine clearance 30-60 ml/min) or severe (creatinine clearance <30 ml/min) renal insufficiency, the elimination half-life of fentanyl is increased. For patients with severe renal insufficiency, it may exceed 20 hours, reaching approximately 24 hours in anuric patients. Dose should be adjusted to individual patient needs and should continue as long as clinically indicated. Doses up to 50 mg 5 times a day have been administered to some adult patients with severe Zollinger-Ellison Syndrome.

Dose of a single dose should be increased in patients with moderate to severe renal insufficiency. The dose of fentanyl should be increased in patients with severe renal insufficiency should be considered.
Benign Gastric Ulcer
Acute Therapy
The recommended adult oral dosage for active benign gastric ulcer is 40 mg once a day at bedtime.

Gastrinomas (Zollinger-Ellison Syndrome)
The recommended oral dosage for treatment of adult patients with symptoms of a Zollinger-Ellison Syndrome is 20 mg b.i.d. for up to 6 weeks. The recommended oral dosage for the treatment of adult patients with acid-secreting tumors is 10 mg every 8 hours. The recommended oral dosage for the treatment of adult patients with gastrinomas is 40 mg every 8 hours. The recommended oral dosage for the treatment of adult patients with gastrinomas is 20 mg every 8 hours.

Doseage for Pediatric Patients
See PRECAUTIONS, Pediatric Patients. The adult dose of Famotidine tablets USP is 1 mg/kg b.i.d. for children aged 3 months to 11 years of age.

Oral Suspension
Famotidine oral suspension may be substituted for famotidine tablets in any of the above instructions.

 Seriously Disturbing Tablets
Famotidine orally disintegrating tablets may be substituted for famotidine tablets in any of the above instructions. The dosage in adults and children does not exceed 1 mg/kg every 8 hours. In patients with severe renal insufficiency, the dosage should be reduced to 1 mg/kg every 24 hours.

Dosage Adjustment for Patients with Moderate to Severe Renal Insufficiency
In adult patients with moderate renal insufficiency (creatinine clearance 20 to 60 mL/min) and severe renal insufficiency, the dosage may be adjusted. The dosage in patients with severe renal insufficiency should be reduced to 1 mg/kg every 24 hours.

Storage
Store at controlled room temperature 15°-30°C (59°-86°F) (see USP). Protect from moisture. Dispense in a tight, light-resistant container (see USP).

TORPHARM
FAMOTIDINE TABLETS USP
20 mg and 40 mg
Manufactured by:
TORPHARM
Tolworth, London
Canada M9W 6Y3
Rev.: March 2001
13075