PEPCID®
(FAMOTIDINE) TABLETS
PEPCID®
(FAMOTIDINE) FOR ORAL SUSPENSION
PEPCID RPD®
(FAMOTIDINE) ORALLY DISINTEGRATING TABLETS

CLINICAL PHARMACOLOGY In adults

Pharmacokinetics

PEPCID is incompletely absorbed. The bioavailability of oral doses is 40-45%. PEPCID Tablets, PEPCID for Oral Suspension and PEPCID RPD Orally Disintegrating Tablets are bioequivalent. Bioavailability may be slightly increased by food, or slightly decreased by antacids; however, these effects are of no clinical consequence. PEPCID undergoes minimal first-pass metabolism. After oral doses, peak plasma levels occur in 1-3 hours. Plasma levels after multiple doses are similar to those after single doses. Fifteen to 20% of PEPCID in plasma is protein bound. PEPCID has an elimination half-life of 2.5-3.5 hours. PEPCID is eliminated by renal (65-70%) and metabolic (30-35%) routes. Renal clearance is 250-450 mL/min, indicating some tubular excretion. Twenty-five to 30% of an oral dose and 65-70% of an intravenous dose are recovered in the urine as unchanged compound. The only metabolite identified in man is the S-oxide.

There is a close relationship between creatinine clearance values and the elimination half-life of PEPCID. In patients with severe renal insufficiency, i.e., creatinine clearance less than 10 mL/min, the elimination half-life of PEPCID may exceed 20 hours and adjustment of dose or dosing intervals in moderate and severe renal insufficiency may be necessary (see PRECAUTIONS, DOSAGE AND ADMINISTRATION).

In elderly patients, there are no clinically significant age-related changes in the pharmacokinetics of PEPCID. However, in elderly patients with decreased renal function, the clearance of the drug may be decreased (see PRECAUTIONS, *Geriatric Use*).

PRECAUTIONS

General

Symptomatic response to therapy with PEPCID does not preclude the presence of gastric malignancy.

Patients with Moderate or Severe Renal Insufficiency

Since CNS adverse effects have been reported in patients with moderate and severe renal insufficiency, longer intervals between doses or lower doses may need to be used in patients with moderate (creatinine clearance <50 mL/min) or severe (creatinine clearance <10 mL/min) renal insufficiency to adjust for the longer elimination half-life of famotidine (see CLINICAL PHARMACOLOGY IN ADULTS and DOSAGE AND ADMINISTRATION).

Geriatric Use

Of the 4,966 subjects in clinical studies who were treated with famotidine, 488 subjects (9.8%) were 65 and older, and 88 subjects (1.7%) were greater than 75 years of age. 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.

No dosage adjustment is required based on age (see CLINICAL PHARMACOLOGY IN ADULTS, *Pharmacokinetics*). This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. 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 adjustment in the case of moderate or severe renal impairment is necessary (see PRECAUTIONS, *Patients with Moderate or Severe Renal Insufficiency* and DOSAGE AND ADMINISTRATION, *Dosage Adjustment for Patients with Moderate or Severe Renal Insufficiency*

DOSAGE AND ADMINISTRATION

Dosage Adjustment for Patients with Moderate or Severe Renal Insufficiency

In adult patients with moderate (creatinine clearance <50mL/min) or severe (creatinine clearance <10mL/min) renal insufficiency, the elimination half-life of PEPCID is increased. For patients with severe renal insufficiency, it may exceed 20 hours, reaching approximately 24 hours in anuric patients. Since CNS adverse effects have been reported in patients with moderate and severe renal insufficiency, to avoid excess accumulation of the drug in patients with moderate or severe renal insufficiency, the dose of PEPCID may be reduced to half the dose or the dosing interval may be prolonged to 36-48 hours as indicated by the patient's clinical response.

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