HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FAMOTIDINE INJECTION safely and effectively. See full prescribing information for FAMOTIDINE INJECTION.

FAMOTIDINE injection for intravenous use
Initial U.S. Approval: 1986

----------INDICATIONS AND USAGE----------

FAMOTIDINE Injection is a histamine-2 (H_2) receptor antagonist indicated:
In hospitalized adults, or as an alternative to oral famotidine in adults, for the treatment of:

- active duodenal ulcer (DU).
- active gastric ulcer (GU).
- symptomatic nonerosive gastroesophageal reflux disease (GERD).
- erosive esophagitis due to GERD, diagnosed by endoscopy.
- treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome, multiple endocrine neoplasias).
- reduction of the risk of DU recurrence.

In hospitalized pediatric patients 1 year of age and older, or as an alternative to oral famotidine in pediatric patients 1 year of age and older, for the treatment of:

- peptic ulcer disease.

----------DOSAGE AND ADMINISTRATION----------

Administration Information (2.1)

- Famotidine Injection is intended for use in adult and pediatric hospitalized patients, or as an alternative to oral famotidine.
- Discontinue as soon as the patient is able to tolerate oral treatment and switch to an appropriate oral medication.

Recommended Dosage (2.2)

- *Adults:* 20 mg every 12 hours.
  - For pathological hypersecretory conditions titrate the dosage to individual patient needs.
- *Pediatric Patients 1 year of age and older:* 0.25 mg/kg every 12 hours; titrate to a maximum of 0.5 mg/kg every 12 hours (up to maximum of 20 mg every 12 hours) based on clinical response and/or gastric pH determination and endoscopy.
- Administer as an intravenous injection over at least 2 minutes or an intravenous infusion over 15 minutes to 30 minutes.
- Refer to the prescribing information for oral famotidine products for the recommended duration of famotidine treatment.

Renal Impairment (2.3)

- See the full prescribing information for the recommended dosage for adult patients with moderate or severe renal impairment.

----------DOSAGE FORMS AND STRENGTHS----------

Injection:

- 20 mg/5 mL (4 mg/mL) single-dose vial
- 40 mg/10 mL (4 mg/mL) multi-dose vial
- 200 mg/50 mL (4 mg/mL) multi-dose vial

----------CONTRAINDICATIONS----------

History of serious hypersensitivity reactions (e.g., anaphylaxis) to famotidine or other H_2-receptor antagonists. (4)

----------WARNINGS AND PRECAUTIONS----------

- Central Nervous System (CNS) Adverse Reactions: Reported in elderly patients and patients with moderate and severe renal impairment; monitor elderly patients for CNS adverse reactions. (5.1, 8.5, 8.6)
- Concurrent GI Malignancy: Absence of GI symptoms does not preclude the presence of gastric malignancy; evaluate prior to initiating therapy. (5.2)
- Risk of Benzyl Alcohol Toxicity in Neonates: Famotidine Injection is not approved in neonates. Serious and fatal adverse reactions have been reported in low-birth weight and preterm neonates who received benzyl-alcohol-containing drugs intravenously. The minimum amount of benzyl alcohol at which these serious adverse reactions may occur is not known. (5.3)

----------ADVERSE REACTIONS----------

Most common adverse reactions (≥1%) are: headache, dizziness, constipation, and diarrhea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sagent Pharmaceuticals at 1-866-625-1618 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- Drugs Dependent on Gastric pH for Absorption: Systemic exposure of the concomitant drug may be significantly reduced leading to loss of efficacy. See the prescribing information for other drugs dependent on gastric pH for absorption. (7.1)
- Tizanidine (CYP1A2) Substrate: Potential for substantial increases in blood concentrations of tizanidine resulting in hypotension, bradycardia or excessive drowsiness; avoid concomitant use, if possible. (7.2)

----------USE IN SPECIFIC POPULATIONS----------

Renal Impairment: QT prolongation reported in patients with moderate and severe renal impairment. (2.3, 8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 07/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Famotidine Injection is indicated for use in hospitalized adults, or as an alternative to oral famotidine in adults, for the treatment of:

- active duodenal ulcer (DU).
- active gastric ulcer (GU).
- symptomatic nonerosive gastroesophageal reflux disease (GERD).
- erosive esophagitis due to GERD, diagnosed by endoscopy.
- treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome, multiple endocrine neoplasias).
- reduction of the risk of duodenal ulcer recurrence.

Pediatric Patients 1 Year of Age and Older

Famotidine Injection is indicated in hospitalized pediatric patients 1 year of age and older, or as an alternative to oral famotidine in pediatric patients 1 year of age and older, for the treatment of peptic ulcer disease.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Information

- Famotidine Injection is intended for use in adult and pediatric hospitalized patients, or as an alternative to oral famotidine.
- Discontinue Famotidine Injection as soon as the patient is able to tolerate oral treatment and switch to an appropriate oral medication.

2.2 Recommended Dosage in Adults and Pediatric Patients 1 Year of Age and Older

The recommended dosage of Famotidine Injection in adults and pediatric patients 1 year of age and older is shown in Tables 1 and 2, respectively.

Administer Famotidine Injection as an intravenous injection over at least 2 minutes or as an intravenous infusion over 15 minutes to 30 minutes *[see Dosage and Administration (2.4)]*.

Refer to the prescribing information for oral famotidine products for the recommended duration of famotidine treatment.

Table 1. Recommended Dosage[1] of Famotidine Injection in Adults

Indication	Recommended Dosage
Active Duodenal Ulcer	20 mg every 12 hours
Active Gastric Ulcer	
Symptomatic Nonerosive GERD	
Erosive Esophagitis Diagnosed by Endoscopy	
Reduction of the Risk of Duodenal Ulcer Recurrence	
Pathological Hypersecretory Conditions	Starting dosage is 20 mg every 12 hours; titrate the dosage to individual patient needs

[1] Refer to the prescribing information for oral famotidine products for the recommended duration of famotidine treatment.

Table 2. Recommended Dosage[1] of Famotidine Injection in Pediatric Patients 1 Year of Age and Older

Indication	Recommended Dosage
Peptic Ulcer Disease	• 0.25 mg/kg every 12 hours (maximum 20 mg every 12 hours) • Titrate to a maximum dosage of 0.5 mg/kg every 12 hours (maximum of 20 mg every 12 hours) based on clinical response and/or gastric pH determination and endoscopy.

[1] Refer to the prescribing information for oral famotidine products for the recommended duration of famotidine treatment.

2.3 Recommended Dosage in Patients with Renal Impairment

Adults

The recommended dosage for adult patients with moderate to severe renal impairment is shown in Table 3. Administer Famotidine Injection as an intravenous injection over at least 2 minutes or as an intravenous infusion over 15 minutes to 30 minutes *[see Dosage and Administration (2.4)]*.

Table 3. Recommended Dosage[1] of Famotidine Injection in Adults with Renal Impairment

Indication	Recommended Dosage	
	Creatinine Clearance 30 to 60 mL/minute	Creatinine Clearance less than 30 mL/minute
Active Duodenal Ulcer	20 mg once daily	10 mg once daily
Active Gastric Ulcer		
Symptomatic Nonerosive GERD		
Erosive Esophagitis Diagnosed by Endoscopy		
Reduction of the Risk of Duodenal Ulcer Recurrence		
Pathological Hypersecretory Conditions	Avoid use[2]	Avoid use[2]

[1] Refer to the prescribing information for oral famotidine products for the recommended duration of famotidine treatment.

[2] The dosage required to treat pathological hypersecretory conditions may exceed the maximum doses evaluated in patients with impaired renal function. The risk for increased adverse reactions in renally impaired patients treated with Famotidine Injection for pathological hypersecretory conditions is unknown.

Pediatric Patients

A safe and effective dosage has not been established in pediatric patients with renal impairment 1 year of age and older for the treatment of peptic ulcer disease *[see Use in Specific Populations (8.6)]*.

2.4 Preparation and Administration Instructions

Intravenous Injection over at least 2 Minutes

- Aseptically withdraw the required volume from the vial. **Do not dilute.**

Intravenous Infusion over 15 Minutes to 30 Minutes

1. Aseptically dilute the required dose of Famotidine Injection in 100 mL of one of the following solutions:
    - 5% Dextrose for Injection
    - 0.9% Sodium Chloride Injection

- 10% Dextrose for Injection
- Lactated Ringer's Injection

2. Gently invert the bag 4 to 5 times. Avoid shaking.
3. Before administration, inspect the bag for particulate matter and discoloration. Discard the bag if particulate and/or discoloration are observed.

Storage of Diluted Product:
Use the diluted product immediately. Alternatively, refrigerate between 2° and 8°C (36° and 46°F) and use within 48 hours.

3 DOSAGE FORMS AND STRENGTHS

Injection: a clear, colorless, solution supplied ready-to-use as:

- 20 mg/5 mL (4 mg/mL) single-dose vial
- 40 mg/10 mL (4 mg/mL) multi-dose vial
- 200 mg/50 mL (4 mg/mL) multi-dose vial

4 CONTRAINDICATIONS

Famotidine Injection is contraindicated in patients with a history of serious hypersensitivity reactions (e.g., anaphylaxis) to famotidine or other H_2-receptor antagonists.

5 WARNINGS AND PRECAUTIONS

5.1 Central Nervous System Adverse Reactions

Central nervous system (CNS) adverse reactions, including confusion, delirium, hallucinations, disorientation, agitation, seizures, and lethargy, have been reported in elderly patients and patients with moderate and severe renal impairment treated with famotidine. Monitor elderly patients for CNS adverse reactions *[see Use in Specific Populations (8.5)]*. Dosage adjustments are recommended in adult patients with moderate and severe renal impairment due to higher famotidine systemic exposure compared to patients with normal renal function *[see Dosage and Administration (2.3), Use in Specific Populations (8.6), and Clinical Pharmacology (12.3)]*.

5.2 Concurrent Gastric Malignancy

In adults, symptomatic response to therapy with Famotidine Injection does not preclude the presence of gastric malignancy. Consider evaluation for gastric malignancy in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with Famotidine Injection.

5.3 Risk of Benzyl Alcohol Toxicity in Neonates

Famotidine Injection is not approved in neonates. Serious adverse reactions, including fatal reactions, of new onset or worsening metabolic acidosis that progressed to neurotoxicity, and in some cases gasping syndrome, have been reported in low-birth weight neonates (less than 2,500 grams) and preterm neonates (gestational age less than 34 weeks) who received benzyl alcohol (BA)-containing drugs intravenously. Gasping syndrome is a life-threatening condition in neonates caused by BA toxicity and is primarily characterized by multiorgan dysfunction secondary to metabolic acidosis, which leads to gasping respirations and death. The minimum amount of BA at which these serious

adverse reactions, including fatal reactions, may occur is not known (Famotidine Injection contains 3.6 mg of BA per mL) *[see Use in Specific Populations (8.4)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of Famotidine Injection has been established based on adequate and well-controlled studies of an oral famotidine product. The following is a summary of the adverse reactions reported in those studies.

Oral famotidine was studied in 7 U.S. and international placebo- and active-controlled trials in approximately 2,500 patients. A total of 1,442 patients were treated with oral famotidine, including 302 treated with 40 mg twice daily, 456 treated with 20 mg twice daily, 461 treated with 40 mg once daily, and 396 treated with 20 mg once daily. The population was 17 to 91 years old, fairly well distributed between sex and race; however, the predominant race was White.

Adverse reactions reported in ≥1% of patients treated with oral famotidine in clinical trials were: headache, dizziness, constipation, and diarrhea.

The following other adverse reactions were reported in less than 1% of patients treated with oral famotidine in clinical trials:

Body as a Whole: fever, asthenia, fatigue

Cardiovascular: palpitations

Gastrointestinal: cholestatic jaundice, elevated liver enzymes, vomiting, nausea, abdominal discomfort, anorexia, dry mouth

Hematologic: thrombocytopenia

Hypersensitivity: orbital edema, rash, conjunctival injection, bronchospasm

Musculoskeletal: musculoskeletal pain, arthralgia

Nervous System/Psychiatric: seizure, hallucinations, depression, anxiety, decreased libido, insomnia, somnolence

Respiratory: interstitial pneumonia

Skin: pruritus, dry skin, flushing

Special Senses: tinnitus, taste disorder

Other: impotence

Adverse reactions reported with oral famotidine may also occur with Famotidine Injection. In addition, transient irritation at the injection site was reported with intravenous famotidine.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of famotidine. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular: arrhythmia, AV block, prolonged QT interval

Gastrointestinal: cholestatic jaundice, hepatitis

Hematologic: agranulocytosis, pancytopenia, leukopenia

Hypersensitivity: anaphylaxis, angioedema, facial edema, urticaria

Musculoskeletal: rhabdomyolysis, muscle cramps

Nervous System/Psychiatric: confusion, agitation, paresthesia

Respiratory: interstitial pneumonia

Skin: toxic epidermal necrolysis/Stevens-Johnson syndrome

7 DRUG INTERACTIONS

7.1 Drugs Dependent on Gastric pH for Absorption

Famotidine can reduce the absorption of other drugs due to its effect on reducing intragastric acidity, leading to loss of efficacy of the concomitant drug. See the prescribing information for other drugs dependent on gastric pH for absorption.

7.2 Tizanidine (CYP1A2 Substrate)

Although not studied clinically, famotidine is considered a weak CYP1A2 inhibitor and may lead to substantial increases in blood concentrations of tizanidine, a CYP1A2 substrate. Avoid concomitant use with Famotidine Injection. If concomitant use is necessary, monitor for hypotension, bradycardia or excessive drowsiness. Refer to the full prescribing information for tizanidine.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data with H_2-receptor antagonists, including famotidine, in pregnant women over decades of use have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Reproductive studies have been performed in rats and rabbits at intravenous doses of up to 200 mg/kg/day, with no obvious adverse developmental effects *(see Data)*. Famotidine Injection contains benzyl alcohol as a preservative *[see How Supplied/Storage and Handling (16)]*. Because benzyl alcohol is rapidly metabolized by a pregnant female, benzyl alcohol exposure in the fetus is unlikely.

The background risk for major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Reproductive studies have been performed in rats and rabbits at oral doses of up to 2,000 and 500 mg/kg/day, respectively, and in both species at intravenous doses of up to 200 mg/kg/day and have revealed no significant evidence of impaired fertility or harm to the fetus due to famotidine.

8.2 Lactation

Risk Summary

There are limited data available on the presence of famotidine in human breast milk following oral administration. There were no effects on the breastfed infant. There are no data on famotidine effects on milk production. Famotidine Injection contains benzyl alcohol as a preservative. Because benzyl alcohol is rapidly metabolized by a lactating female, benzyl alcohol exposure in the breastfed neonate is unlikely.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Famotidine Injection and any potential adverse effects on the breastfed child from famotidine or from the underlying maternal condition.

8.4 Pediatric Use

Peptic Ulcer Disease

The safety and effectiveness of Famotidine Injection have been established in pediatric patients 1 year to less than 17 years of age for the treatment of peptic ulcer disease in hospitalized patients or as an alternative to oral famotidine. Use of Famotidine Injection in this age group is supported by evidence from adequate and well-controlled studies of oral famotidine in adults with additional pharmacokinetic and pharmacodynamic data in pediatric patients 1 year to less than 17 years of age *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.2, 12.3)]*.

A safe and effective dosage has not been established in pediatric patients 1 year to less than 17 years of age with renal impairment for the treatment of peptic ulcer disease.

The safety and effectiveness of Famotidine Injection for the treatment of peptic ulcer disease in pediatric patients less than 1 year of age have not been established.

Other Conditions

The safety and effectiveness of Famotidine Injection for the treatment of symptomatic nonerosive GERD, erosive esophagitis due to GERD, pathological hypersecretory conditions and reduction of the risk of DU recurrence have not been established in pediatric patients.

Risk of Benzyl Alcohol Toxicity in Neonates

Famotidine Injection is not approved for use in neonates. Serious adverse reactions, including fatal reactions, of new onset or worsening metabolic acidosis that progressed to neurotoxicity, and in some cases gasping syndrome, have been reported in low-birth weight neonates and preterm neonates who received benzyl alcohol (BA)-containing drugs intravenously. Gasping syndrome is a life-threatening condition in neonates caused by BA toxicity that is characterized by new onset or worsening metabolic acidosis with gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and kidney failure, hypotension, bradycardia, and gasping

respirations followed by death. In reported cases, BA in amounts of 99 to 234 mg/kg/day produced blood BA levels of 6.6 to 14.9 mg/dL, but the minimum amount of BA at which gasping syndrome may occur in neonates is not known (Famotidine Injection contains 3.6 mg of BA per mL) *[see Warnings and Precautions (5.3)]*.

8.5 Geriatric Use

Of the 1,442 patients treated with oral famotidine in clinical studies, approximately 10% were 65 and older. In these studies, no overall differences in safety or effectiveness were observed between elderly and younger patients. In elderly patients, there are no clinically significant age-related changes in the pharmacokinetics of famotidine *[see Clinical Pharmacology (12.3)]*.

In postmarketing experience, CNS adverse reactions have been reported in elderly patients with and without renal impairment receiving famotidine. Monitor elderly patients for CNS adverse reactions *[see Warnings and Precautions (5.1)]*. Famotidine is known to be substantially excreted by the kidney, and the risk of adverse reactions to Famotidine Injection may be greater in elderly patients, particularly those with impaired renal function *[see Dosage and Administration (2.3) and Use in Specific Populations (8.6)]*.

8.6 Renal Impairment

CNS adverse reactions and prolonged QT intervals have been reported in patients with moderate and severe renal impairment *[see Warnings and Precautions (5.1)]*. The clearance of famotidine is reduced in adults with moderate and severe renal impairment compared to adults with normal renal function *[see Clinical Pharmacology (12.3)]*. The recommended dosage in adults with moderate or severe renal impairment (creatinine clearance <60 mL/minutes) is less than the recommended dosage in adults with normal renal function *[see Dosage and Administration (2.3)]*. The recommended dosage in adults with mild renal impairment (creatinine clearance ≥60 mL/minute) is the same as the recommended dosage in adults with normal renal function.

Data are not available to establish a safe and effective dosage in pediatric patients 1 year to less than 17 years of age with renal impairment for the treatment of peptic ulcer disease.

10 OVERDOSAGE

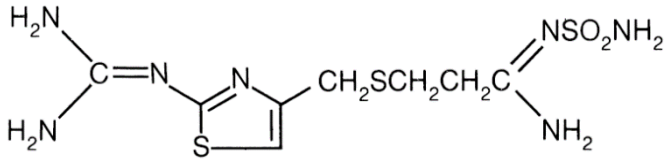
Adverse reactions reported in cases of overdosage are similar to the adverse reactions reported with use of the recommended dosage *[see Adverse Reactions (6)]*. In the event of overdosage, treatment should be symptomatic and supportive. In the event of overdosage, monitor the patient, and employ supportive therapy. Due to low binding to plasma proteins, famotidine is eliminated by hemodialysis. There is limited experience on the usefulness of hemodialysis as a treatment for famotidine overdosage.

Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

The active ingredient in Famotidine Injection is a histamine H_2-receptor antagonist.

Famotidine, USP is N'-(aminosulfonyl)-3-[[[2-[(diaminomethylene)amino]-4 thiazolyl]methyl]thio]propanimidamide. The empirical formula of famotidine is $C_8H_{15}N_7O_2S_3$ and its molecular weight is 337.45. Its structural formula is:



Famotidine, USP is a white to pale yellow crystalline compound that is freely soluble in glacial acetic acid, slightly soluble in methanol, very slightly soluble in water, and practically insoluble in ethanol.

Famotidine Injection is supplied as a premixed, ready-to-use, sterile solution for intravenous injection. Each mL contains 4 mg of famotidine and the following inactive ingredients: L-aspartic acid 1.6 mg, mannitol 8 mg, sodium chloride 7 mg, and Water for Injection q.s. 1 mL. The multiple-dose vials of 10 mL and 50 mL also contain benzyl alcohol 0.36% (3.6 mg per mL) added as a preservative. The pH ranges for all three concentrations range from 5.7 to 6.4 and may have been adjusted with sodium hydroxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Famotidine is a competitive inhibitor of histamine H_2-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 pepsin secretion are proportional to volume output.

12.2 Pharmacodynamics

Adults

Famotidine inhibited basal and nocturnal gastric secretion, as well as secretion stimulated by food and pentagastrin. After intravenous administration, the maximum effect was achieved within 30 minutes. Single intravenous doses of 20 mg inhibited nocturnal secretion for a period of 10 to 12 hours.

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

In clinical pharmacology studies, systemic effects of famotidine in the central nervous system (CNS), cardiovascular, respiratory or endocrine systems were not noted. Also, no antiandrogenic effects were noted. Serum hormone levels, including prolactin, cortisol, thyroxine (T_4), and testosterone, were not altered after treatment with famotidine.

Pediatric Patients

Pharmacodynamics of famotidine were evaluated in five pediatric patients 2 to 13 years of age using the sigmoid E_{max} model. These data suggest that the relationship between serum concentration of famotidine and gastric acid suppression is similar to that observed in one study of adults (Table 4).

Table 4: Pharmacodynamics of Famotidine Using the Sigmoid E_{max} Model

	EC_{50}(ng/mL) [a]
Pediatric Patients	26 ± 13
Data from one study	
a) Healthy adult subjects	26.5 ± 10.3
b) Adult patients with upper GI bleeding	18.7 ± 10.8

[a] Using the sigmoid E_{max} model, serum concentration of famotidine associated with 50% maximum gastric acid reduction. Values are presented as means ± SD

Five published studies (Table 5) examined the effect of famotidine on gastric pH and duration of acid suppression in pediatric patients. While each study had a different design, acid suppression data over time are summarized as follows:

Table 5: Effect of Intravenous Famotidine on Gastric pH and Duration of Acid Suppression in Pediatric Patients 1 to 15 Years of Age

Dosage Regimen	Number of Patients	Effect on Gastric Acid[a]	Patient Age Range
0.3 mg/kg, single-dose	6	gastric pH >3.5 for 8.7 ± 4.7[b] hours	2 to 7 years
0.5 mg/kg, single-dose	9	a >2 pH unit increase above baseline ingastric pH for >8 hours	2 to 13 years
0.5 mg/kg twice daily	4	gastric pH >5 for 13.5 ± 1.8[b] hours	6 to 15 years

[a] Values reported in published literature
[b] Means ± SD
[c] Mean (95% confidence interval)

12.3 Pharmacokinetics

Plasma levels after multiple doses are similar to those after single doses.

Distribution

Fifteen to 20% of famotidine in plasma is protein bound.

Elimination

Metabolism

Famotidine undergoes minimal first-pass metabolism. Sixty-five to 70% of an intravenous dose are recovered in the urine as unchanged compound. The only metabolite identified in humans is the S-oxide.

Excretion

Famotidine has an elimination half-life of 2.5 to 3.5 hours. Famotidine is eliminated by renal (65 to 70%) and metabolic (30 to 35%) routes. Renal clearance is 250 to 450 mL/minutes, indicating some tubular excretion.

Specific Populations

Pediatric Patients

Table 6 presents pharmacokinetic data for famotidine administered intravenously. Areas under the curve (AUCs) are normalized to a 0.5 mg/kg intravenous dose for pediatric patients 1 to 15 years of age and compared with an extrapolated 40 mg intravenous dose in adults. Extrapolation is based on results obtained with a 20 mg intravenous adult dose). The pharmacokinetic parameters for pediatric patients, aged 1 year to 15 years, are comparable to those obtained for adults.

Table 6: Pharmacokinetic Parameters[a] of Intravenous Famotidine In Pediatric Patients 1 Year to 15 Years of Age and Adults

Age (N=number of patients)	Area Under the Curve (AUC) (ng-hr/mL)	Total Clearance (Cl) (L/hr/kg)	Volume of Distribution (V_d) (L/kg)	Elimination Half-Life ($T_{1/2}$) (hours)
1 to 11 years (N=20)	1089 ± 834	0.54 ± 0.34	2.07 ± 1.49	3.38 ± 2.6
11 to 15 years (N=6)	1140 ± 320	0.48 ± 0.14	1.5 ± 0.4	2.3 ± 0.4
Adults (N=16)	1726[b]	0.39 ± 0.14	1.3 ± 0.2	2.83 ± 0.99

[a] Values are presented as means ± SD unless indicated otherwise
[b] Mean value only
[c] Single center study
[d] Multicenter study

Geriatric Patients

In elderly patients, there are no clinically significant age-related changes in the pharmacokinetics of famotidine. However, in elderly patients with decreased renal function, the clearance of the drug may be decreased *[see Use in Specific Populations (8.5)]*.

Patients with Renal Impairment

In adult patients with severe renal impairment (creatinine clearance less than 30 mL/min), the systemic exposure (AUC) of famotidine increased at least 5-fold. In adult patients with moderate renal impairment (creatinine clearance between 30 to 60 mL/minute), the AUC of famotidine increased at least 2-fold *[see Dosage and Administration (2.3) and Use in Specific Populations (8.6)]*.

Drug Interaction Studies

Human Organic Anion Transporter (OAT) 1 and 3

In vitro studies indicate that famotidine is a substrate for OAT1 and OAT3. Following coadministration of probenecid (1500 mg), an inhibitor of OAT1 and OAT3, with a single oral 20 mg dose of famotidine in eight healthy subjects, the serum $AUC_{0\text{-}10h}$ of famotidine increased from 424 to 768 ng•hr/mL and the maximum serum concentration (C_{max}) increased from 73 to 113 ng/mL. Renal clearance, urinary excretion rate and amount of famotidine excreted unchanged in urine were decreased. The clinical relevance of this interaction is unknown.

Multidrug and Toxin Extrusion Protein 1 (MATE-1)
An in vitro study showed that famotidine is an inhibitor of MATE-1. However, no clinically significant interaction with metformin, a substrate for MATE-1, was observed.

CYP1A2
Famotidine is a weak CYP1A2 inhibitor *[see Drug Interaction (7.2)]*

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of intravenously administered famotidine has not been determined. In a 106-week study in rats and a 92-week study in mice given oral doses of up to 2,000 mg/kg/day there was no evidence of carcinogenic potential for famotidine.

Famotidine was negative in the bacterial mutagen test (Ames test) using *Salmonella typhimurium* and *Escherichia coli* with or without rat liver enzyme activation at concentrations up to 10,000 mcg/plate. In *in vivo* studies in mice, with a micronucleus test and a chromosomal aberration test, no evidence of a mutagenic effect was observed.

In studies with rats given oral doses of up to 2,000 mg/kg/day or intravenous doses of up to 200 mg/kg/day, fertility and reproductive performance were not affected.

16 HOW SUPPLIED/STORAGE AND HANDLING

Famotidine Injection is a clear, colorless, sterile solution supplied premixed and ready-to-use as follows:

	Famotidine Injection (Preservative-free)	
NDC	**(4 mg per mL)**	**Package Factor**
25021-755-05	20 mg per 5 mL Single-Dose Vial	25 vials per carton

	Famotidine Injection (Preservative)	
NDC	**(4 mg per mL)**	**Package Factor**
25021-756-10	40 mg per 10 mL Multi-Dose Vial	10 vials per carton
25021-756-50	200 mg per 50 mL Multi-Dose Vial	1 vial per carton

Storage Conditions
Store at room temperature between 20° to 25°C (68° to 77°F); excursions permitted between 15° and 30°C (59° and 86°F). [See USP Controlled Room Temperature.]

If not used immediately, store diluted solutions of Famotidine Injection between 2° and 8°C (36° and 46°F) for up to 48 hours *[see Dosage and Administration (2.4)]*.

Do not freeze.
Protect from light. Retain in carton until time of use.

The container closure is not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION

Central Nervous System (CNS) Adverse Reactions

Advise elderly patients and those with moderate and severe renal impairment of the risk of CNS adverse reactions, including confusion, delirium, hallucinations, disorientation, agitation, seizures, and lethargy *[see Warnings and Precautions (5.1)]*. Report symptoms immediately to a healthcare provider.

QT Interval Prolongation

Advise patients with moderate and severe renal impairment of the risk of QT interval prolongation *[see Use in Specific Populations (8.6)]*. Report new cardiac symptoms, such as palpitations, fainting and dizziness or lightheadedness, immediately to a healthcare provider.

Risk of Benzyl Alcohol Toxicity in Neonates

Inform caregivers that serious adverse reactions, including fatal reactions, have been reported in neonates who received drugs containing benzyl alcohol intravenously. Inform the healthcare provider if neurologic, hematologic or cardiac adverse reactions occur *[see Warnings and Precautions (5.3)]*.

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