

**Bon Secours Richmond  
Pharmacy & Therapeutics Committees  
Oral H<sub>2</sub> Antagonist  
3/2001**

**Recommendations: MEC approved**

Famotidine, the P&T preferred H<sub>2</sub> antagonist, is recommended for automatic substitution for ranitidine, cimetidine, nizatidine, other H<sub>2</sub> when ordered by the IV or oral route unless the physician has checked the dispense as written block or the patient is allergic to famotidine. A drug cost saving between \$ 43,211-\$72,222 per year is being realized currently by the use of famotidine IV in Richmond.

**Findings:**

- Famotidine is currently used for 98% of all IV doses and 89% of oral doses in Bon Secours Richmond.
- Famotidine is easier to prepare and administer, requiring less nursing and pharmacy time. Famotidine may be given IV push over 2 minutes through a saline lock. Cimetidine and ranitidine must be administered by small volume parenteral bag using additional IV tubing.
- Famotidine has the highest potency (20-60 times more potent than cimetidine and 7.5-15 times more potent than ranitidine on an equimolar basis) and longest duration of action, allowing twice daily IV dosing.
- Famotidine does not have antiandrogen effects seen with cimetidine.
- Famotidine does not inhibit cytochrome P-450 system or have drug interactions that are common with cimetidine and ranitidine.
- Famotidine does not increase serum creatinine by decreasing renal secretion, unlike cimetidine.
- Famotidine is the lowest cost IV H<sub>2</sub> antagonist to MRMC and is 50% the cost of ranitidine per day of therapy.
- Zantac syrup is very expensive costing 40 times an equivalent dose of a tablet.

**Dosage Conversion:**

Cimetidine	Famotidine
300 mg q6-8H	20 mg q12H
300 mg q12-24H	20 mg q24H
400 mg QHS	20 mg QHS
400 mg BID	10 mg BID or 20 mg QHS
400 mg QID	20 mg BID
800 mg QHS	40 mg QHS
800 mg BID	20 mg BID
Ranitidine	
50 mg q6-8H IV	20 mg q12H
50 mg q12-24H IV	20 mg q24H
150 mg QD	20 mg QD
150 mg BID	20 mg q12h
300 mg QHS	40 mg QHS
Nizatidine	
150 mg QD	20 mg QD
150 mg BID	20 mg BID
300 mg QHS	40 mg QHS

<b>FDA Approved and Commonly Recommended Doses</b>				
	<b>Rantidine</b>	<b>Nizatidine</b>	<b>Famotidine</b>	<b>Cimetidine</b>
<b>GERD</b>	150 mg BID	150 mg bid	20 mg bid	400 mg qid 800 mg bid
<b>Eros Esophagitis</b>	150 mg QID	150 mg bid	20-40 mg bid	400 mg qid 800 mg bid
<b>Maintenance</b>	150 mg BID		20 mg qd	
<b>Duodenal Ulcer</b>	150 mg bid 300 mg qhs	150 mg bid 300 mg qhs	20 mg bid 40 mg qhs	300 mg qid 400 mg bid 800 mg qhs
<b>Maintenance</b>	150 mg qhs	150 mg qhs	20 mg qhs	400 mg qhs
<b>Gastric Ulcer</b>	150 mg bid	150 mg bid 300 mg qhs	20 mg bid 40 mg qhs	300 mg qid 800 mg qhs
<b>Maintenance</b>	150 mg qhs			400 mg qhs

### Pharmacokinetics

The pharmacokinetics of the H<sub>2</sub> antagonist are similar including volume of distribution, % excreted unchanged (70%) after IV administration, protein binding (20-30%), half-life (1-3 hours), and bioavailability (40-60%) with the exception of nizatidine which is over 90% bioavailable when given orally. Famotidine has a longer duration of action, 10-12 hours, when compared to the other histamine H<sub>2</sub> antagonist.

	half-life		bioavailability(%)
	normal	anuric	
Cimetidine	2	4.5	60-70
Ranitidine	2-3	7	50-60
Famotidine	2.5-3.5	20	40-45
Nizatidine	1-2	7	>90

### Dosage in Renal Dysfunction: percent of normal daily dosage

	< 10 ml/min	10-50 ml/min	> 50ml/min	≥ 80
Cimetidine	25%	50%	100%	100%
Famotidine	25%	25%	50%	100%
Nizatidine	25%	50%	75%	100%
Ranitidine	25%	50%	75%	100%

### Potency:

Famotidine is 20-60 times more potent than cimetidine and 7.5-15 times more potent than ranitidine on an equimolar basis. Therefore, famotidine is prescribed in lower doses.

### Gastric Emptying:

Cimetidine, ranitidine, and famotidine have no effect.

### Lower Esophageal sphincter Pressure:

Ranitidine, famotidine, and nizatidine have no effect.

**Drug Interactions:**

Cimetidine has been identified as a very potent inhibitor of the cytochrome mixed function oxidative enzymes. The inhibition is dependent on drug concentration and is reversible. The more potent H<sub>2</sub> antagonists are present in lower molar concentrations and thus cause less enzyme inhibition. Ranitidine has been reported to inhibit cytochrome P-450 in high doses. Ranitidine is reported to interact with procainamide, glipizide, theophylline, and warfarin. **Famotidine is present in the lowest molar concentration and is not reported to inhibit cytochrome P-450 system.**

**Drug Lab Interactions:**

Cimetidine causes a decrease in renal secretion of creatinine, elevating serum creatinine.

**Efficacy:**

All H<sub>2</sub> antagonist are safe and effective in the treatment of peptic ulcer disease, having approximately the same healing rates for duodenal ulcers and gastric ulcers.

**Adverse Effects:**

The histamine H<sub>2</sub> antagonists have similar adverse reaction profiles. Cimetidine has dose related antiandrogenic effects, while ranitidine and famotidine do not.

**Methods of IV Administration:**

Famotidine, ranitidine, and cimetidine may be administered by intermittent or continuous IV infusion. All are compatible with TPN. **Only famotidine may be administered by slow IV push over 2 minutes.** Ranitidine and cimetidine must be injected over  $\geq 5$  minutes by slow IV push to avoid cardiac effects.

## Continuous Infusion Dosage:

Cimetidine 900-2400 mg/day, start at 37.5 mg/hr

Famotidine 40-90 mg/day, start at 1.67 mg/hr

Ranitidine 150-400 mg/day, start at 6.25 mg/hr

## References:

1. Lauritsen K, Laursen LS, Rask-Madsen J. Clinical pharmacokinetics of drugs used in the treatment of gastrointestinal diseases (Part 1). Clin Pharmacokinetic 1990;19(1):11-31  
Berardi RR, Tankanow RM, Nostrant TT. Comparison of famotidine with cimetidine and ranitidine. Clin Pharm 1988;7:271-84
2. Fudge KA, Moore KA, Schneider DN, Sherrin TP, Wellman GS. Change in prescribing patterns of intravenous histamine<sub>2</sub>-receptor antagonists results in significant cost savings without adversely affecting patient care. Ann Pharmacother 1993;27:232-7
3. Felman M, Burton ME. Histamine<sub>2</sub>-receptor antagonists standard therapy for acid-peptic diseases. NEJM 1990;24:1672-80
4. Lipy RJ, Fennerty B, Fagan TC. Clinical review of histamine<sub>2</sub> receptor antagonists. Arch Inter Med 1990;150:745-51

**Pharmacy & Therapeutics Committee**  
**IV H<sub>2</sub> Antagonist**  
**11/98**

**Recommendations:**

Famotidine the P&T preferred IV H<sub>2</sub> antagonist is recommended for automatic substitution for ranitidine, cimetidine unless the physician has checked the dispense as written block or the patient is allergic to famotidine. A drug cost saving of approximately \$ 21,000 per year is realized by the use of famotidine

**Findings:**

- Famotidine is currently used for 95% of all IV doses.
- Famotidine is easier to prepare and administer, requiring less nursing and pharmacy time. Famotidine may be given IV push over 2 minutes through a saline lock. Cimetidine and ranitidine must be administered by small volume parenteral bag using additional IV tubing.
- Famotidine has the highest potency (20-60 times more potent than cimetidine and 7.5-15 times more potent than ranitidine on a equimolar basis) and longest duration of action, allowing twice daily IV dosing.
- Famotidine does not have antiandrogen effects seen with cimetidine.
- Famotidine does not inhibit cytochrome P-450 system or have drug interactions that are common with cimetidine and ranitidine.
- Famotidine does not increase serum creatinine by decreasing renal secretion, unlike cimetidine.
- Famotidine is the lowest cost IV H<sub>2</sub> antagonist to MRMC and is 46.5% the cost of ranitidine per day of therapy.

**Dosage Conversion:**

Cimetidine	Famotidine
300 mg q6-8H	20 mg q12H
300 mg q12-24H	20 mg q24H
Ranitidine	
50 mg q6-8H	20 mg q12H
50 mg q12-24H	20 mg q24H

**Pharmacokinetics**

The pharmacokinetics of the H<sub>2</sub> antagonist are similar including volume of distribution, % excreted unchanged (70%) after IV administration, protein binding (20-30%), half-life (1-3 hours), and bioavailability (40-60%) with the exception of nizatidine which is over 90% bioavailable when given orally. **Famotidine has a longer duration of action, 10-12 hours, when compared to the other histamine H<sub>2</sub> antagonist.**

	half-life		bioavailability(%)
	normal	anuric	
Cimetidine	2	4.5	60-70
Ranitidine	2-3	7	50-60
Famotidine	2.5-3.5	20	40-45
Nizatidine	1-2	7	<b>&gt;90</b>

**Dosage in Renal Dysfunction:** percent of normal daily dosage

	< 10 ml/min	10-50 ml/min	> 50ml/min	≥ 80
Cimetidine	25%	50%	100%	100%
Famotidine	25%	25%	50%	100%
Nizatidine	25%	50%	75%	100%
Ranitidine	25%	50%	75%	100%

**Dosage Conversion:**

Cimetidine	Famotidine
300 mg q6-8H	20 mg q12H
300 mg q12-24H	20 mg q24H

Ranitidine	20 mg q12H
50 mg q6-8H	20 mg q24H
50 mg q12-24H	

**Potency:**

Famotidine is 20-60 times more potent than cimetidine and 7.5-15 times more potent than ranitidine on an equimolar basis. Therefore, famotidine is prescribed in lower doses.

**Gastric Emptying:**

Cimetidine, ranitidine, and famotidine have no effect.

**Lower Esophageal sphincter Pressure:**

Ranitidine, famotidine, and nizatidine have no effect.

**Drug Interactions:**

Cimetidine has been identified as a very potent inhibitor of the cytochrome mixed function oxidative enzymes. The inhibition is dependent on drug concentration and is reversible. The more potent H<sub>2</sub> antagonist are present in lower molar concentrations and thus cause less enzyme inhibition. Ranitidine has been reported to inhibit cytochrome P-450 in high doses. Ranitidine is reported to interact with procainamide, glipizide, theophylline, and warfarin. **Famotidine is present in the lowest molar concentration and is not reported to inhibit cytochrome P-450 system.**

**Drug Lab Interactions:**

Cimetidine causes a decrease in renal secretion of creatinine, elevating serum creatinine.

**Efficacy:**

All H<sub>2</sub> antagonist are safe and effective in the treatment of peptic ulcer disease, having approximately the same healing rates for duodenal ulcers and gastric ulcers.

**Adverse Effects:**

The histamine H<sub>2</sub> antagonist have similar adverse reaction profiles. Cimetidine has dose related antiandrogenic effects, while ranitidine and famotidine do not.

**Cost Comparison RATIOS for IV Dosing:**

	<b>per Dose</b>	<b>per Day</b>	<b>Dosage</b>
Tagamet Injection 300 mg/50 ml NS	2.23	<b>8.93</b>	300 q6h
Zantac Injection Injection 50 mg/100ml 0.45% NS	3.6	<b>10.81</b>	50 q8h
Pepcid Injection 20 mg/2ml Push over 2 minutes	2.72	<b>5.44</b>	20 q12h

**Methods of IV Administration:**

Famotidine, ranitidine, and cimetidine may be administered by intermittent or continuous IV infusion. All are compatible with TPN. **Only famotidine may be administered by slow IV push over 2 minutes.** Ranitidine and cimetidine must be injected over ≥ 5 minutes by slow IV push to avoid cardiac effects.

Continuous Infusion Dosage:

Cimetidine 900-2400 mg/day, start at 37.5 mg/hr  
 Famotidine 40-90 mg/day, start at 1.67 mg/hr  
 Ranitidine 150-400 mg/day, start at 6.25 mg/hr

**Cost Analysis per year:**

Last year \$51,431 worth of Zantac injection was used for 5,522 patient days of therapy.

Famotidine would cost \$25,844.52 for 5,522 patient days of therapy to replace ranitidine.

Ranitidine 12 months Cost	\$51,431
Projected Famotidine 12 months Cost	<u>\$25,844.52</u>

**Projected Cost Saving by conversion to famotidine to LGH:**

\$25,586

**Projected Daily Charge Savings to the Patient:** \$37.6

**Assessment:**

Famotidine IV push over 2 minutes, when compared to the other histamine H<sub>2</sub> antagonist is equally effective, has a lower potential for drug interaction, is less expensive, is as safe, has the longest dosage interval, and requires less nursing time to administer. **Use of famotidine injection IV push as the preferred histamine H<sub>2</sub> antagonist would save the hospital approximately \$4.62 per patient day of therapy, an annualized savings of \$25,586 in drug acquisition cost. The patient would be charged \$37.6 less per day of therapy.**

Submitted By: Marshall Pierce, Pharm.D., Clinical Pharmacist

Ranitidine (Zantac)

Injection 50 mg/100ml 0.45% NS

Total Dose \$51,431 for 16,567 doses/year at \$3.10/dose

Ranitidine usage at LGH

$(16,560 + 2,952 + 10,383 + 2920 + 140 + 180 = 33,135$

doses/2 years or 16,567/year )

$\$58,235 + \$ 14,700.96 + \$ 21,631.25 + \$7,597.84 + 289.59 + 408.78 = 102,863.42/ 2 \text{ years or}$

\$51,431 per year

average cost of \$3.10 per dose

Famotidine (Pepcid)

Injection 10 mg/ml in 2 ml & 4 ml vials

cost 2.34/dose saving per year by conversion to famotidine \$25,586/year

Cost of equivalent no of doses of famotidine

$16,567 * 2/3 = 11,044.66$  doses of famotidine equivalent

at \$2.34/dose = \$25,844.52

Saving by using Famotidine

Cost saving =  $51,431 - 25,944.52 = 25,586 / \text{year}$

File: H2

**Richmond Memorial Hospital  
Pharmacy and Therapeutics Committee**

Dear Prescribing Physician,

The enclosed overview of IV Pepcid's advantages has been placed on the patient's chart so that prescribers of IV H<sub>2</sub> antagonists may reassess the potential advantages of IV Pepcid to the patient and Lewis-Gale Hospital.

If you have any comments, please call me at extension \_\_\_\_.  
Your consideration in this matter is appreciated.

Thank-you

Pharmacist

**Richmond Memorial Hospital  
Pharmacy and Therapeutics Committee  
Pepcid IV Push**

Dear Prescribing Physician,

The enclosed list of IV Pepcid's advantages has been placed on the patient's chart so that prescribers of IV H<sub>2</sub> antagonists may reassess the potential advantages of Pepcid IV push over 2 minutes to the patient and Richmond Memorial Hospital.

## Advantages of Pepcid IV Push Over 2 Minutes

1. Unsurpassed safety and efficacy.
2. Pepcid is easier to prepare and administer, requiring less nursing and pharmacy time. Pepcid may be given IV push through a prn adapter. Tagamet and Zantac must be administered by small volume parenteral bag using additional IV tubing.
3. Pepcid has the highest potency (20-60 times more potent than Tagamet and 7.5-15 times more potent than Zantac on a equimolar basis) and longest duration of action, allowing twice daily IV dosing.
4. Pepcid does not have antiandrogen effects seen with Tagamet.
5. Pepcid does not inhibit cytochrome P-450 system or have drug interactions that are common with Tagamet and Zantac.
6. Pepcid does not increase serum creatinine by decreasing renal secretion, unlike Tagamet.
7. Pepcid is the lowest cost IV H<sub>2</sub> antagonist to RMH and is 50% the cost of Zantac per day of therapy. It also has the lowest patient charge.

## Pepcid IV Push Twice a Day Over 2 Minutes

If you have any comments, please call your pharmacist at extension \_\_\_\_\_. Your consideration in this matter is appreciated.

Thank-you,

Pharmacist

### Richmond Memorial Hospital Pharmacy and Therapeutics Committee IV H<sub>2</sub> Antagonists

#### Assessment:

Pepcid (famotidine) IV push over 2 minutes, when compared to the other histamine H<sub>2</sub> antagonist is equally effective, has a lower potential for drug interaction, is less expensive, is as safe, has the longest dosage interval, and requires less pharmacy and nursing time to prepare and administer. Use of Pepcid IV push as the preferred histamine H<sub>2</sub> antagonist provides cost savings to RMH and the patient.

#### Recommendations:

Pepcid (famotidine) IV push over 2 minutes is recommended as the as the preferred IV H<sub>2</sub> antagonist. The availability of other intravenous H<sub>2</sub> antagonist, Tagamet (cimetadine) and Zantac (ranitidine), will be unchanged.

The oral route for H<sub>2</sub> antagonists is recommended, unless the oral route is unusable as the patient is NPO, unable to take oral medicines, receiving a clear liquid diet, or unable to receive feedings or medicines by tube.

### Background Material

#### Pharmacokinetics

The pharmacokinetics of the H<sub>2</sub> antagonist are similar including volume of distribution, % excreted unchanged (70%) after IV administration, protein binding (20-30%), half-life (1-3 hours), and bioavailability (40-60%) with the exception of nizatidine which is over 90% bioavailable when given orally. **Pepcid has a longer duration of action, 10-12 hours, when compared to the other histamine H<sub>2</sub> antagonist.**

		half-life	bioavailability(%)
	normal	anuric	
Cimetidine	2	4.5	60-70
Ranitidine	2-3	7	50-60
Famotidine	2.5-3.5	20	40-45
Nizatidine	1-2	7	>90

**Dosage in Renal Dysfunction:** percent of normal daily dosage

	< 10 ml/min	10-50 ml/min	> 50ml/min	≥ 80
Cimetidine	25%	50%	100%	100%
Famotidine	25%	25%	50%	100%
Nizatidine	25%	50%	75%	100%
Ranitidine	25%	50%	75%	100%

**Dosage Conversion:**

Cimetidine	Famotidine
300 mg q6-8H	20 mg q12H
300 mg q12-24H	20 mg q24H
Ranitidine	
50 mg q6-8H	20 mg q12H
50 mg q12-24H	20 mg q24H

**Potency:**

Famotidine is 20-60 times more potent than cimetidine and 7.5-15 times more potent than ranitidine on a equimolar basis. Therefore, famotidine is prescribed in lower doses.

**Gastric Emptying:**

Cimetidine, ranitidine, and famotidine have no effect.

**Lower Esophageal sphincter Pressure:**

Ranitidine, famotidine, and nizatidine have no effect.

**Drug Interactions:**

Cimetidine has been identified as a very potent inhibitor of the cytochrome mixed function oxidative enzymes. The inhibition is dependent on drug concentration and is reversible. The more potent H<sub>2</sub> antagonist are present in lower molar concentrations and thus cause less enzyme inhibition. Ranitidine has been reported to inhibit cytochrome P-450 in high doses. Ranitidine is reported to interact with procainamide, glipizide, theophylline, and warfarin. **Famotidine is present in the lowest molar concentration and is not reported to inhibit cytochrome P-450 system.**

**Drug Lab Interactions:**

Cimetidine causes a decrease in renal secretion of creatinine, elevating serum creatinine.

**Efficacy:**

All H<sub>2</sub> antagonist are safe and effective in the treatment of peptic ulcer disease, having approximately the same healing rates for duodenal ulcers and gastric ulcers.

**Adverse Effects:**

The histamine H<sub>2</sub> antagonist have similar adverse reaction profiles. Cimetidine has dose related antiandrogenic effects, while ranitidine and famotidine do not.

**Methods of IV Administration:**

Famotidine, ranitidine, and cimetidine may be administered by intermittent or continuous IV infusion. All are compatible with TPN. **Only famotidine may be administered by slow IV push over 2 minutes.** Ranitidine and cimetidine must be injected over  $\geq 5$  minutes by slow IV push to avoid cardiac effects.

Continuous Infusion Dosage:

Cimetidine 900-2400 mg/day, start at 37.5 mg/hr

Famotidine 40-90 mg/day, start at 1.67 mg/hr

Ranitidine 150-400 mg/day, start at 6.25 mg/hr

**Relative Cost Ratios of Antiulcer Medications at RMH****Injectable H<sub>2</sub> Antagonist**

Pepcid 20 mg/50 ml q12h IV 5.3

Pepcid 20 mg/2ml q12h IV **2.5**  
IV push over 2 minutes

Zantac 50 mg/50ml q8h IV 5

**Oral H<sub>2</sub> Antagonist**

Axid Capsules 150 mg q12h 1.4

Axid Capsule 300 mg qhs 1.3

Pepcid Susp. 20 mg q12h 3

Pepcid Tablets 20 mg q12h 1.1

Pepcid Tablet 40 mg qhs 1

Zantac Syrup 150 mg q12h 4.5

Zantac Effer. Gran 150 q12h **1.4**

Zantac Tablets 150 mg q12h 1.1

Zantac Tablet 300 mg po qhs 1

**Other Oral Agents**

Carafate Tablet 1 gm q6h 1.2

Carafate Susp. 1 gm q6h 1.1

Prilosec Cap. 20 mg qd 1.7

Prilosec Cap. 40 mg qd 3.3

Submitted By: Marshall Pierce, Pharm.D., Clinical Pharmacist

## References:

1. Lauritsen K, Laursen LS, Rask-Madsen J. Clinical pharmacokinetics of drugs used in the treatment of gastrointestinal diseases (Part 1). Clin Pharmacokinetic 1990;19(1):11-31
2. Berardi RR, Tankanow RM, Nostrant TT. Comparison of famotidine with cimetidine and ranitidine. Clin Pharm 1988;7:271-84
3. Fudge KA, Moore KA, Schneider DN, Sherrin TP, Wellman GS. Change in prescribing patterns of intravenous histamine<sub>2</sub>-receptor antagonists results in significant cost savings without adversely affecting patient care. Ann Pharmacother 1993;27:232-7
4. Felman M, Burton ME. Histamine<sub>2</sub>-receptor antagonists standard therapy for acid-peptic diseases. NEJM 1990;24:1672-80
5. Lipsy RJ, Fennerty B, Fagan TC. Clinical review of histamine<sub>2</sub> receptor antagonists. Arch Inter Med 1990;150:745-51

