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Boston University
UH Referral Criteria Established for Home Infusion Therapy Providers

Over the past 5 years, there has been an important shift in the delivery of care to patients from the hospital to alternative health care delivery sites that provide equal quality care at a lower cost. One successful lower cost substitute costly inpatient hospital care is the home infusion services industry. Through the use of new higher technology infusion pumps and devices as well as newer drugs that are suitable for long-term IV administration, patients are trained to self-administer IV infusions of medications at home, under the close monitoring and supervision of a specially trained nurse. It is estimated that this alternative health care provider has saved the US health care system more than $1 billion per year and most observers agree that only 40% of those patients who could receive home infusion care under current indications are now doing so. Furthermore, the number of medical indications for home infusion treatment is growing. Besides

Home Nutritional (TPN and enteral) support, antibiotic, chemotherapy and pain management - other therapies treated at home include iron overload therapy, immune globulin therapy, hydration therapy, line maintenance therapy, isotropic therapy, aerosolized pentamidine therapy, steroid therapy, hemotherapy, human growth hormone therapy, erythropoetin therapy, alpha-1 proteinase inhibitor therapy, colony stimulating factor therapy, and interferon therapy as well as a growing trend to treat HIV and Bone Marrow Transplant Patients in this setting.

Home infusion providers help UH by reducing length of stay and medication costs (important under DRGs). However, to take advantage of the cost savings, UH must insure the quality of care provided by these services. As this field grows, a number of providers of dubious quality have appeared. To assure high quality care for UH patients, a committee 3 years ago, selected acceptable and preferred

Formulary News:
Status of Formulary H2-receptor Antagonists Changes

Three years ago, the Pharmacy and Therapeutics made a decision to classify injectable cimetidine and ranitidine as therapeutic equivalents. Since then, injectable famotidine was released by the FDA and has been increasing in usage at UH, despite non-formulary status, to where it recently represented 50% of all injectable H2-receptor antagonist use. The Section on Gastroenterology was consulted about this issue. The Gastroenterology Section still believes that in most patients, there is little difference clinically between cimetidine, ranitidine and famotidine. However, it recognized that in specific patients different agents may be preferable. Hence, drug use criteria for the appropriate use of H2-receptor antagonists was submitted to the Pharmacy and Therapeutics Committee and approved at the June meeting for implementation on July 1st. As a result, cimetidine remains the formulary agent of choice. Famotidine and Ranitidine are the secondary agents of choice recommended for use according to the H2- Antagonist criteria. Oral and injectable Famotidine as well as oral Ranitidine are on the Formulary. Injectable ranitidine is non-formulary.

Drug Use Criteria for H2-Receptor Antagonists listed on page 5.

Index

Home Infusion Therapy Provider Criteria............. 1,2
Formulary News........................................ 1,6
Drug Review: Ondansetron............................ 3,4
Drug Use Criteria for H2-Receptor Antagonists..... 5
Director of Pharmacy Resigns....................... 6
P&T Committee Actions............................... 6

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Home Infusion Provider Criteria Approved (continued from previous page)

providers for UH patients. As the number of requests for inclusion on this list have appeared, it was felt necessary to define criteria for inclusion on the list of acceptable providers. Those criteria were submitted and approved, with modification, by the Pharmacy and Therapeutics Committee at its June meeting.

Acceptable providers meet all UH requirements for quality and service to be recommended for use as a home infusion therapy provider. If the patient's physician or insurance company wishes to refer the patient to a home therapy provider who is not classified as "acceptable" by UH standards, the nurse will inform the physician that the provider has been classified as "unacceptable" by UH standards. The physician is asked to reconsider his/her choice of home provider.

"Preferred" providers are "acceptable" providers who have a proven track record at UH for high quality service and care of UH patients. If the physician or insurance company does not have a preference for a home infusion therapy provider, the nurse will normally refer the patient to a "preferred provider".

Nothing above should indicate that the physician is required to make a referral to any source other than to his or her choosing. The criteria only provide a means for the physician to judge the quality of various providers.

CURRENT PREFERRED PROVIDERS include:
- Chartwell
- Critical Care America

CURRENT ACCEPTABLE PROVIDERS include:
- Caremark
- Deaconess Home Health
- Home Nutritional Service (HNS)

New Antibiotic Order Sheet and Form for Requesting Addition of a Drug to the Formulary Approved.

At the June meeting, the Pharmacy and Therapeutics Committee approved a new form for requesting addition of drugs to the UH Formulary. Questions regarding indications for use, toxicities and equivalency to formulary products were expanded, as well as the requirement for including 1-3 medical journal articles and appropriate criteria for drug use, were added to the form.

The Forms Committee recently approved a revised antibiotic order sheet. The new order sheet is designed to be easier to use and yet provide the information required by the JCAHO. The new order sheets will be available soon

The University Hospital
Requirements for “Acceptable” Status for Home Infusion Therapy Providers.

1. JCAHO accreditation as a home infusion therapy provider.
2. Will not provide direct financial compensation to UH personnel for patient referrals.
3. Must have a facility within the Commonwealth of Massachusetts and be able to serve patients throughout New England with additional facilities in the New England region.
4. Must have a full-time company-employed nursing staff primarily responsible for the caring of the patients. All nurses must be fully trained in infusion therapy.
5. Must have the ability to assess a new patient at UH within 2 hours in normal (usual and customary) situations.
6. Must be a 24 hour, full service (pharmacy/nursing/delivery/reimbursement) company providing a full range of infusion therapies including investigational drug protocols.

Requirements for “Preferred” Status for Home Infusion Therapy Providers.

1. Must have a minimum of 10 UH-referred patients treated by the company.
2. Have been an “acceptable” provider at UH over the past 12 months.
3. Provide value-added services to UH.
4. Must not have 2 or more complaints regarding the quality or level of service provided over the past 12 months or ten patients, whichever is greater.
5. Will accept all patients referred from UH, regardless of insurance status or ability to pay.

-2-
Drug Review:

Ondansetron (Zofran®)

By: Darryl S. Rich, Pharm.D., Department of Pharmacy Services, The University Hospital, Boston, MA

Description:
Ondansetron (Zofran® by Glaxo) is the first of a new class of highly effective antiemetic agents that are potent, highly selective, competitive antagonists of the 5-hydroxytryptamine-3 (5-HT3) serotonin receptors. Ondansetron is currently indicated by the FDA solely for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy. The drug is relatively free of side effects, mild headache being the most common. The drug lacks dopaminergic antagonist properties and extrapyramidal reactions have not been reported. This agent clearly offers significant advantages over many currently available antiemetic agents for this indication. However, its cost is substantially higher (100x) than any conventional antiemetic therapy and as a consequence, the Section on Medical Oncology submitted the following guidelines for the use of ondansetron, which were subsequently approved as "official" criteria for the appropriate use of ondansetron by the Pharmacy and Therapeutics Committee:

1. Patients receiving chemotherapy agents classified as “highly emetogenic” (>90%) for the first time (cisplatin, nitrogen mustard, dacarbazine, mecloretamine, streptozocin or high dose cytarabine).
2. Patients who have poor antiemetic control with prior non-ondansetron based antiemetic regimens.
3. Patients experiencing extrapyramidal symptoms (acute dystonia, akathisia) with prior non-ondansetron based antiemetic regimens.
4. Because ondansetron has not been proven effective in delayed emesis, no more than 3 doses of ondansetron should be given per chemotherapy treatment except in cases where patients receive multiple dose therapy. In situations other than listed above, the use of other conventional antiemetic therapy is indicated over ondansetron.

Mechanism of Action:
Ondansetron works by competitively antagonizing the central 5-HT3 receptors in the area postrema, blocking vagal afferent nerve stimulation of the vomiting center. The drug may also have some activity at the peripheral receptor sites in the upper GI tract. The drug lacks any dopaminergic antagonist properties.

Clinical Trials:
Ondansetron has been extensively studied in patients receiving cisplatin therapy, including extensive clinical trials by Dr. Paul Hesketh at UH. Ondansetron has been found to be significantly more effective in the prevention of nausea and vomiting than metoclopramide in patients receiving cisplatin therapy (73-77% vs. 35-51% respectively). In addition, patients who did experience vomiting with ondansetron did so considerably later than patients receiving metoclopramide (21hrs vs. 4.5hrs, respectively). Patients preferred the use of ondansetron (54-63%) over metoclopramide (26-30%). Ondansetron was also shown effective in the prevention of nausea and vomiting from the following combinations: ifosfamide, anthracycline, cyclophosphamide, and vincristine; epirubicin, mitoxanthrone, and methotrexate; doxorubicin and etoposide; and epirubicin, cyclophosphamide and 5-FU. In comparison with metoclopramide, ondansetron was also more effective in controlling nausea and vomiting following single exposure high-dose radiation therapy. Investigation in the use of ondansetron and other 5-HT3 antagonists is currently underway by the Section on Medical Oncology at the University Hospital and the Department of Anesthesiology in the treatment of post-operative nausea and vomiting.
**Pharmacokinetics:** Currently, ondansetron is only available parenterally, however, oral bioavailability of the product is 60% with peak levels in 1.5 hours. The half-life of ondansetron is 3-6 hours, however it appears that the elimination of the drug is non-linear. Accumulation at steady state has not been evident. Ondansetron is extensively metabolized, primarily by hydroxylation followed by glucuronide or sulfate conjugation with less than 5-10% of the parent drug excreted in the urine unchanged. Dose adjustment in renal failure is not necessary.

**Adverse Reactions:** The common side effects with ondansetron are mild headache, diarrhea and constipation. Elevation in total bilirubin and aminotransferase has been observed, but does not require discontinuation of therapy, normalization occurring after completion of therapy. In addition, similar changes have been reported with metoclopramide therapy. Other less common side effects include sedation, bradycardia, fatigue, fever, anorexia, dry mouth, bad taste in mouth, lightheadedness, restlessness, early satiety, stomach cramps, rash and stinging at injection site. Unlike metoclopramide and phenothiazines, ondansetron does not have the potential to cause extrapyramidal side effects or tardive dyskinesia.

**Pregnancy Category:** B

**Drug Interactions:** Ondansetron is metabolized by the P-450 cytochrome system, hence drugs that inhibit or induce this enzyme (benzodiazepines, cimetidine, etc.) may alter the half-life of ondansetron. Also, dexamethasone has been reported to increase the responsiveness of patients to ondansetron. This is currently being investigated at UH.

**Dosage and Administration:** The recommended IV dose of ondansetron is three 0.15mg/kg doses infused over 15 minutes given 30 minutes prior to chemotherapy, and then 4 and 8 hours after the first dose. Because of the mechanism of receptor site saturation and the lack of a correlation between serum level and response, exact dosing of ondansetron is not necessary and rounding off of doses (preferably to a 20mg dose) is recommended since it can reduce drug waste and significant cost to the patient. Doses in clinical trials have been three IV doses of 0.15-0.18mg/kg at 2-8hr intervals or an 8mg loading dose followed by a continuous infusion at 1mg/hr. The dose does not need adjustment in pediatrics (4-18 y.o.) or the elderly. A maximum dose of 0.36 mg/kg has been suggested.

The drug is stable for 48 hours at room temperature once reconstituted. The drug should be protected from light. The pharmacy will admix all doses of ondansetron.

**UH Acquisition Cost:** Ondansetron 20mg x 3 = $510.00
Metoclopramide 20mg TID x 5d = $10.20

**Status at UH:** Ondansetron has been added to the UH Formulary restricted to the approved drug use criteria listed above and for the sole use or approval of Medical Oncology Service. In addition, pharmacists will contact physicians whenever it is unclear if the appropriate usage criteria have not been met or when doses are not rounded. Ondansetron orders should be written on the chemotherapy order sheet, rather than the regular doctor's order sheet. Physicians who fail to use the proper order sheet to order ondansetron will be contacted by the pharmacy.
Drug Use Criteria for H2-Receptor Antagonists

Drug Selection

Cimetidine is the Primary H2-Receptor Antagonist of Choice. Both oral and injectable forms are available on the formulary.

Famotidine and Ranitidine are the Secondary H2-Receptor Antagonist of Choice. Oral and IV Famotidine as well as oral Ranitidine are available on the Formulary. Ranitidine IV is nonformulary. Both drugs are recommended for use as follows:

- Patients with thrombocytopenia (platelets <5,000), as documented in the patient’s chart.
- Elderly patients (Age >60) with decreased mental status (confusion), as documented in the patient’s chart.
- Patients with a history of a cimetidine-induced adverse drug reaction, as documented in the patient’s chart.
- Patient receiving concurrent theophylline, phenytoin, warfarin, quinidine, procainamide, or lidocaine therapy.

In Patients with Renal Impairment:

- Patients receiving cimetidine who have creatinine clearances <50ml/min shall receive no greater than 300mg Q12hrs.
- Patients receiving ranitidine who have creatinine clearances <50ml/min shall receive no greater than 150mg Q24hrs.
- Patients receiving famotidine who have creatinine clearances <10ml/min shall receive no greater than 20mg Q24hrs.

In cases of new medication orders, where the above guidelines are not met, the pharmacist must contact the physician and inform them of the guidelines. If the pharmacist is uncertain if the guidelines have been met, they should contact the physician to verify so. If the physician insists on the medication for use outside the above criteria, the pharmacist must document the interaction, for reporting to the P&T Committee.

Oral vs. Injectable Therapy

For all H2-Receptor antagonists, the injectable therapy is recommended for use as follows:

- Patients with an active NPO order as documented in the patient’s chart, and the patient is not receiving any systemically acting oral medications.
- Patient has a diagnosis of severely impaired GI functioning (GI obstruction, complete bowel resection, acute pancreatitis, sprue, etc.). Simple constipation or diarrhea does not qualify.
- Patient is on a pre-operative or post-operative fast within 1 day before or after surgery.

Dosing

- The dose of cimetidine should not exceed 1200mg with increments of 300mg.
- The dose of ranitidine should not exceed 300mg per day PO with increment of 150mg.
- The dose of famotidine should not exceed 40mg per day, PO or IV, with increments of 20mg.

- The dosing interval of cimetidine shall not be more frequent than Q6h. (*see below)
- The dosing interval of ranitidine shall not be more frequent than Q8h.
- The dosing interval of famotidine shall not be more frequent than Q12h.

* When injectable cimetidine is ordered 300mg IV q6h, the pharmacist shall contact the physician and inform him/her that the GI service recommends that cimetidine be dosed 300mg IV q8h or 900mg/day by continuous infusion. The recommendation will then be documented as “accepted” or “rejected”.

In cases where cimetidine is prescribed and theophylline, phenytoin, quinidine, procainamide, lidocaine or warfarin is concurrently prescribed, the pharmacist must monitor the drug serum levels or serum prothrombin times, contacting the physician to change dosing appropriately, where necessary.

In cases where an oral H2-Receptor antagonist is prescribed and ketoconazole or fluconazole is concurrently prescribed, the pharmacist must inform the primary care nurse that the drugs must be scheduled for administration at least 2 hours apart.
The following definitions for "Monitored" and "Restricted" Drug Categories were approved:

**Monitored Drugs:**
Drugs must meet approved criteria for drug use or a pharmacist will contact the ordering physician to remind him or her of the criteria. If the physician still requests the drug, the drug will be dispensed and the interaction will be documented and reported to the P&T Committee.

**Restricted Drugs:**
Drugs must meet approved criteria for drug use or a pharmacist will contact the ordering physician to remind him or her of the criteria. If the physician still requests the drug, appropriate specialty service approval will be required.

**Pharmacy News:**

**Pharmacy Director Resigns**
Darryl S. Rich, Pharm.D., Director of Pharmacy at UH for the past 5 years, resigned July 1st to accept a position as National Director of Pharmacy for Critical Care America, Inc., a JCAHO-accredited home infusion therapy provider at their corporate headquarters in Westborough MA. Directors of Pharmacy from 54 branches across the US will report through 3 regional Directors of Pharmacy to Darryl. Daniel B. Dobson, M.S., Pharmacy Manager for Operations, will serve as the interim Director of Pharmacy until a new Director is appointed.

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**P&T Committee Actions**
**June 1991**

**Addition to the Formulary**
- Amoxicillin (various)
  - 250mg, 500mg capsule
- Amoxicillin/Clavulanic Acid (Augmentin®)
  - **Restricted to Infectious Disease Service Approval**
  - 250mg, 500mg tablet
- Ciprofloxacin IV (Cipro IV®)
  - **Restricted to Sensitive Multi-resistant Infections in Patients who are NPO or with Infectious Disease Service Approval**
  - 400mg/40ml vial
- Clozapine (Clozaril®)
  - **Restricted to Psychiatry Service Approval - special manufacturer requirements needed to start patients on therapy**
  - 25mg, 100mg tablets
- Famotidine IV (Pepcid®)
  - **Monitored Drug -to be used according to H2-Receptor Antagonist drug use criteria**
  - (see usage criteria on previous page)
  - 20mg/2ml vial
- Tobramycin (various)
  - 80mg/2ml vial

**Deletions from the Formulary**
- Ampicillin Oral (various) - replaced by Amoxicillin
  - 250mg, 500mg capsule
- Ticarcillin (Ticar®)
  - 3 gram vial
- Ticarcillin/Clavulanic Acid (Timentin®)
  - 3.1 gram vial

**Change in Formulary Status**
- Ranitidine Oral (Zantac) - Now in monitored category- to be used according to H2-Receptor Antagonist drug use criteria

**Denied Addition to the Formulary**
- Israpidine (Dynacirc®)