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Boston University
Policy & Procedure:
New Unit Dose Drug Distribution System Starts

It is with great excitement that the Department of Pharmacy announces the gradual phase-in of the unit dose drug distribution system for inpatients at The University Hospital. The implementation will take approximately 3 months to complete (see Table 1). The unit dose drug distribution system is currently considered the safest and best drug distribution system possible, being used in over 83% of all hospitals in the US. It is recommended by the Joint Commission on the Accreditation of Hospitals and the U.S. Government Accounting Office.

The main differences in the way drugs will be handled at The University Hospital as a result of the unit dose drug distribution system will include:

1) Greater packaging of drugs in single unit-of-use containers than is currently done.
2) Provision of patient drugs in a 24 hour supply in individually labelled patient medication bins. Currently a 48 hour supply is delivered.
3) Medications are placed directly in the medication bin when delivered to the nursing unit. Currently, medications are delivered in a bag to the nursing unit for nurses to put away.
4) Refills are provided through the daily exchange of prefilled patient medication bins between the pharmacy and nursing units.

The major benefits of the unit dose drug distribution system have been shown to include:

1) Better patient safety - individually labelled medication packages and medications specific to each patient in one specific patient medication bin reduces potential for medication errors.

(Continued on last page)

Policy & Procedure:
Which Departments Can Purchase Drugs?

Regulations of the Joint Commission on the Accreditation of Hospitals, Massachusetts Department of Public Health, Massachusetts Board of Pharmacy and Hospital Policy require that all drugs used in treatment of patients at The University Hospital be acquired, stored, and dispensed only through the Department of Pharmacy. The only exceptions to this policy are diagnostics, anesthetics, & radiopharmaceuticals. This includes all nonprescription and prescription drugs, as well as investigational drugs. The BUMC Institutional Review Board approves all drug protocols contingent upon the development of a satisfactory arrangement with the Department of Pharmacy to satisfy this policy.

This policy makes sense in accomplishing two important goals. First, the pharmacy can, through group purchasing obtain the best price for the institution, which if fractioned among different departments, would result in a higher cost for drugs. Second, and more importantly, centralizing acquisition, storage and distribution enables better control of drugs and makes diversion much more difficult.

The cooperation of all hospital departments in following this policy is appreciated.

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Current Information on Drugs:
Drug Review: Piroxicam
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Department of Pharmacy, The University Hospital, Boston MA.

Piroxicam (Feldene) is a nonsteroidal anti-inflammatory drug (NSAID) that was recently added to The University Hospital Formulary. It is a member of the oxicam family and possesses anti-inflammatory, analgesic and antipyretic activities. Its major advantage over other available NSAIDs is a long plasma half-life which allows once daily dosing. The classification of all NSAIDs and a list of the NSAIDs on the Formulary at The University Hospital are presented in Tables 1 and 2, respectively.

PHARMACOLOGY

The exact mechanism of action of piroxicam has not been determined. However, many of its actions appear to be related to prostaglandin synthesis inhibition. Piroxicam inhibits the activity of cyclooxygenase. This enzyme catalyzes formation of prostaglandin precursors from arachidonic acid. The lack of prostaglandin precursors results in decreased synthesis of prostaglandins which are necessary for the inflammatory response to occur.

Although the anti-inflammatory effect of piroxicam is related to its ability to inhibit prostaglandin synthesis, other mechanisms may play a significant role in its anti-inflammatory effect. These mechanisms have not been fully elucidated. In vitro studies have shown piroxicam inhibits superoxide formation. This mechanism may also contribute to its anti-inflammatory activity.

Piroxicam's analgesic effect may be due to inhibition of prostaglandin synthesis since prostaglandins appear to sensitize pain receptors to mechanical stimulation and chemical mediators.

It has been suggested that the suppression of prostaglandin synthesis is responsible for piroxicam's antipyretic effect.

PHARMACOKINETICS

Piroxicam is readily absorbed after oral administration with peak plasma concentration attained approximately two to three hours after ingestion. Food delays absorption but only marginally decreases the bioavailability of piroxicam.(1) The concomitant administration of antacids does not affect the absorption of piroxicam. Peak serum concentrations are achieved three to five hours after administration. Steady state plasma concentrations are reached following seven days of repeated dosing.

The apparent volume of distribution of piroxicam is approximately 0.12 to 0.14 L/kg.(1) Piroxicam penetrates the synovial fluid achieving levels of approximately 40% of plasma concentrations. It is highly protein bound to albumin with binding greater than 99% in humans.(2-3)

Piroxicam is extensively metabolized in the liver. An important metabolic pathway is hydroxylation of the pyridyl ring followed by conjugation with glucuronic acid.(4) It undergoes enterohepatic circulation and then is excreted in urine and feces. The urinary excretion of piroxicam is twice that of fecal excretion with approximately 10% excreted unchanged. The elimination half-life of piroxicam ranges from 14 to 158 hours. The average elimination half-life is 50 hours which permits once daily dosing.

CLINICAL EFFICACY

Rheumatoid Arthritis: A double blinded multicenter study compared piroxicam 20 mg daily to enteric coated acetylsalicyclic acid (EC-ASA) 3.9-5.2 g daily in 145 patients with rheumatoid arthritis. Prompt improvement in signs and symptoms was observed with a rapid decrease of morning stiffness within one week of therapy. Patients receiving piroxicam exhibited greater compliance than those receiving EC-ASA. The overall incidences of adverse effects with EC-ASA and piroxicam were similar. However, a higher frequency of tinnitus and decreased hearing was observed in the EC-ASA group. Although the overall incidence of GI related adverse reactions was similar for both agents, the frequency of heartburn was greater in the piroxicam group. Decreased hemoglobin and hematocrit concentrations were noted in a few patients in the piroxicam group. The levels stabilized and followup evaluations of these patients showed constant levels.

In a single blinded randomized study, piroxicam 20 mg daily was compared to sulindac 200 mg twice daily in 49 patients. The use of either agent lead
to significant improvement in duration of morning stiffness, total joint pain, total joint swelling and performance of daily activities. The overall incidence of adverse effects was similar in both groups. Three patients in each group required the discontinuation of the prescribed agent due to intolerable adverse effects. However, sulindac-treated patients experienced a greater number of moderate/severe adverse reactions than the piroxicam group. No change in hematologic, renal or hepatic function was observed.

A single blinded randomized trial compared piroxicam 20 mg to ibuprofen 2400 mg in 21 patients. Improvement was observed in virtually all viable parameters. However, when global assessments were analyzed, it showed that three of nine patients on ibuprofen had no change in their conditions while one patient worsened. Five of nine patients on ibuprofen showed slight or moderate improvement. Similarly, three of eleven patients on piroxicam had no change in their condition or became worse while eight patients demonstrated slight or moderate improvement. This difference in effectiveness was not statistically significant. Side effects reported were similar for both drugs with the most common side effects involving the GI system.

**Osteoarthritis**: A double blinded crossover study was conducted to assess the efficacy of piroxicam 20 mg daily to naproxen 500 mg twice daily in 19 patients. During the piroxicam treatment period, statistically significant improvement was achieved in six of nine clinical parameters as compared to five of nine clinical parameters for the naproxen treatment period. The clinical parameters included right grip strength, time to walk 50 feet, daily activity assessment and total joint pain. In addition, both physician and patient assessment of disease activity improved during piroxicam therapy. Naproxen therapy was associated with a significant decrease in total joint swelling. Adverse drug reactions were mild and involved the GI tract.

The long term efficacy and safety of piroxicam 20 mg daily was evaluated in 30 patients. The evaluation period ranged from three to seven years with the mean duration of six years. Twenty-eight of thirty patients were feeling well at the last visit. Total joint pain scores, total joint swelling and specific functional activity levels including ease of movement and ability to do specific tasks improved when the patient started piroxicam treatment. The initial improvement observed was sustained throughout the evaluation period. Adverse side reactions were relatively common but were mild or moderate. Most of these reactions involved the GI system and included abdominal discomfort.

**ADVERSE REACTIONS**

The most frequently reported adverse reactions involve the GI system and may affect 16% of patients. The most common reactions include heartburn, indigestion, nausea, vomiting and stomach pain. Other GI effects are constipation, anorexia and diarrhea. These adverse reactions require discontinuation of piroxicam in less than four percent of patients on chronic therapy.

Other adverse reactions are infrequent and include headache, skin rash, pruritis, drowsiness, dizziness and tinnitus. Anemia, leukopenia, decreased hematocrit and decreased hemoglobin have been reported. The bleeding time may be prolonged for up to two weeks following discontinuation of piroxicam due to suppression of platelet aggregation. Abnormal liver function tests include increases in serum alkaline phosphatase, serum lactic dehydrogenase and serum transaminase concentrations.

**DRUG INTERACTIONS**

Concurrent use of piroxicam and acetaminophen may increase the risk of adverse renal effects. Piroxicam can displace other highly protein bound drugs including the sulfonylureas. However, the second generation sulfonylurea (glipizide and glyburide) are nonionically bound and therefore are less likely to exhibit this interaction.

Prolonged bleeding may occur if the patient is receiving acetylsalicylic acid due to increased platelet aggregation. Concurrent use of dipyridamole, piperacillin, ticarcillin and valproic acid may increase the risk of bleeding due to additive inhibition of platelet aggregation, gastrointestinal ulceration and hemorrhage potential of piroxicam. Cefoperazone and plicamycin may cause hypoprothrombinemia as well as platelet aggregation, thus piroxicam may increase the risk of bleeding in patients receiving these agents.

**DOSAGE AND ADMINISTRATION**

Piroxicam is available as 10 mg and 20 mg capsules. It is administered as a single daily dose but may be given in divided doses. Normal dosing of piroxicam for symptomatic treatment of rheumatic arthritis or osteoarthritis is 20 mg. Some patients may require doses of 30 to 40 mg, however, the incidence of adverse reactions increases sharply as the dose is increased. Therapeutic efficacy is achieved seven to twelve days after initiation of therapy.
COST COMPARISON

A cost comparison between piroxicam and other formulary NSAIDs including average doses is presented in Table 3.

CONCLUSION

Piroxicam is a NSAID that was recently added to the Formulary. It possesses anti-inflammatory, analgesic and antipyretic actions. Its major advantages over currently available NSAIDS on Formulary include a higher potency and a long half-life which allows for once daily dosing. When the prescribed dose is greater than 20 mg daily, the cost and the frequency of adverse effects increase tremendously. In addition, piroxicam has a higher incidence of adverse reactions than other available NSAIDs. The gastrointestinal side effects most frequently reported are nausea, vomiting, indigestion, heartburn and stomach pain. Although the Pharmacy and Therapeutics Committee approved piroxicam's addition to the Formulary, some members felt that its use should be restricted to patients already receiving this agent because of its high cost and the fact that patient compliance is not a problem in the institutional setting.

Table 1. Classification of Nonsteroidal Anti-Inflammatory Agents

<table>
<thead>
<tr>
<th>Propionic Acid Derivatives</th>
<th>Indene Derivatives</th>
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</thead>
<tbody>
<tr>
<td>Fenoprofen (Nalfon)</td>
<td>Indomethacin (Indocin)</td>
</tr>
<tr>
<td>Ibuprofen (Motrin)</td>
<td>Sulindac (Clinoril)</td>
</tr>
<tr>
<td>Ketoprofen (Orudis)</td>
<td>Tolmetin (Tolectin)</td>
</tr>
<tr>
<td>Naproxen (Naprosyn)</td>
<td>Naproxen Na+ (Anaprox)</td>
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<table>
<thead>
<tr>
<th>Fenamate</th>
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<tbody>
<tr>
<td>Meclofenamate (Meclomen)</td>
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<tr>
<td>Mefenamic Acid (Ponstel)</td>
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<tr>
<td>Piroxicam (Feldene)</td>
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</tbody>
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<thead>
<tr>
<th>Oxicams</th>
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</thead>
<tbody>
<tr>
<td>Meclofenamate (Meclomen)</td>
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<tr>
<td>Mefenamic Acid (Ponstel)</td>
</tr>
<tr>
<td>Piroxicam (Feldene)</td>
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</tbody>
</table>

Table 2. Formulary Status of Nonsteroidal Anti-Inflammatory Agents at The University Hospital

<table>
<thead>
<tr>
<th>Formulary Agents</th>
<th>Non-Formulary Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen (Motrin)</td>
<td>Fenoprofen (Nalfon)</td>
</tr>
<tr>
<td>Indomethacin (Indocin)</td>
<td>Ketoprofen (Orudis)</td>
</tr>
<tr>
<td>Naproxen (Naprosyn)</td>
<td>Meclofenamate (Meclomen)</td>
</tr>
<tr>
<td>Piroxicam (Feldene)</td>
<td>Mefenamic Acid (Ponstel)</td>
</tr>
<tr>
<td>Sulindac (Clinoril)</td>
<td>Naproxen Na+ (Anaprox)</td>
</tr>
<tr>
<td></td>
<td>Suprofen (Suprol)</td>
</tr>
<tr>
<td></td>
<td>Tolmetin (Tolectin)</td>
</tr>
</tbody>
</table>

Additional references are available upon request.

References


Cardiac Drugs on The University Hospital Formulary

The following page contains a listing of all cardiac drugs on The University Hospital Formulary. This category of drugs was recently reviewed by the Pharmacy and Therapeutics Committee of the Medical Staff. The list summarizes all the final deliberations of the Committee. Please keep the list for future reference.
## Cardiovascular Drugs on The University Hospital Formulary

### Beta-Adrenergic Blockers
- Atenolol (Tenormin)
- Metoprolol (Lopressor)
- Pindolol (Visken)
- Timolol (Blocadren)
- Labetolol (Normodyne/Trandate)*IV RESTRICTED*
- Nadolol (Corgard)
- Propranolol (Inderal)

### Antihypertensives
- Captopril (Capoten)
- Diazoxide (Hyperstat)
- Hydralazine (Apresoline)
- Minoxidil (Loniten)
- Phentolamine (Regitine)
- Reserpine
- Clonidine (Catapres)
- Enalapril (Vasotec)
- Methylldopa (Aldomet)
- Phenoxybenzamine (Dibenzyline)
- Prazosin (Minipress)
- Trimethaphan (Arfonad)

### Antiarrhythmics
- Amiodarone (Cordarone)*RESTRICTED*
- Disopyramide (Norpace)
- Lidocaine (Xylocaine)
- Phenytoin (Dilantin)
- Quinidine Sulfate
- Tocainide (Tonocard)
- Bretylium (Bretylol)
- Flecainide (Tambocor)*RESTRICTED*
- Mexilitene (Mexitil)*RESTRICTED*
- Procainamide (Pronestyl)
- Quinidine Gluconate (Quinaglute)

### Vasodilators
- Isosorbide Dinitrate (Isordil)
- Papaverine (Pavabid)-IV only
- Nitroglycerin
- Sodium Nitroprusside (Nipride)

### Vasopressors
- Dopamine (Intropin)
- Isoproterenol (Isuprel)
- Norepinephrine (Levophed)
- Epinephrine (Adrenalin)

### Diuretics
- Acetohexamide (Diamox)
- Bumetanide (Bumex)
- Furosemide (Lasix)
- Metolazone (Zaroxolyn)
- Spironolactone+HCTZ (Aldactazide)
- Amiloride (Midamor)
- Chlorothiazide (Diuril)-IV only
- Hydrochlorothiazide or HCTZ (Esidrex)
- Spironolactone (Aldactone)
- Triamterene +HCTZ (Dyazide)

### Calcium Antagonists
- Diltiazem (Cardizem)
- Verapamil (Calan/Isoptin)
- Nifedipine (Procardia)

### Other Cardiac Drugs:
- Digoxin
- Amrinone
Policy & Procedure: New Unit Dose Drug Distribution System Starts (Continued from page 1)

2) Reduced drug wastage-
lower supply of drugs on the floor and removal of expired medications from the bins reduces wastage and increases credit for drugs to patients.

3) Better drug control.

The major noticeable changes with the implementation of the system will be:
1) Use of hallways and elevators at 2:30PM for exchange of the patient medication bin between the Pharmacy and Nursing Units.
2) Smaller supply of drugs at the Nursing Unit.
3) Ease at finding patient medications when needed.

The cooperation of all hospital employees in the implementation of this new system is appreciated.

<table>
<thead>
<tr>
<th>Table 1. Implementation Schedule</th>
<th>Dates</th>
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<tbody>
<tr>
<td>E8, CCU, SDU</td>
<td>Dec 8-28</td>
</tr>
<tr>
<td>E7, MICU</td>
<td>Dec 29-Jan 11</td>
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<tr>
<td>F5, F4</td>
<td>Jan 12</td>
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<tr>
<td>F3</td>
<td>Jan 19</td>
</tr>
<tr>
<td>F2</td>
<td>Jan 26</td>
</tr>
<tr>
<td>B7, B6, PCU</td>
<td>Feb 2</td>
</tr>
<tr>
<td>C4</td>
<td>Feb 9</td>
</tr>
<tr>
<td>C3, C5</td>
<td>Feb 16</td>
</tr>
<tr>
<td>B3</td>
<td>Feb 23</td>
</tr>
</tbody>
</table>

In order for the unit dose distribution system to work properly, it was necessary for all scheduled medications be given at the same time throughout the institution, rather than at different time depending on the nursing unit as was previously done. A standardized medication administration schedule was thus approved by the Pharmacy-Unit Secretary-Nursing Committee, to coincide with the implementation of Unit Dose. It is vital that all nursing units follow these standard times for scheduled medications. Copies will be distributed to all nursing units.

Pharmacy & Therapeutics Committee Decisions
November 1986 Meeting

Additions to the Formulary:
alpha-Interferon 1-a (Intron) - Restricted to Oncology or Hematology Service approval.

Approved Deletions from the Formulary:
Acetohexamide (Dymelor)
Ethacrynic Acid (Edecrin)
Guanethidine (Ismelin)
Isoxsuprine (Vasodilan)
Metaraminol (Aramine)
Methylthiziazide (Enduron)
Nylidrin (Arlidin)
Pentaerythritol tetradinitrate (Peritrate)
Triamterene (Dyrenium)

The following will be retained in their IV form only:
Chlorthiazide (Diuril)
Papaverine (Pavabid)

Proposed Deletions from the Formulary
The Committee requests comments about the proposed deletion of the following drugs from The University Hospital Formulary:

Dicyclomine HCL (Bentyl),
Aluminum Phosphate Liquid (Phosphajel),
Medlizine HCL (Antivert),
Thiethylperazine maleate (Torecan),
Trimethobenzamine HCl (Tigan)

Removed from Therapeutic Equivalent Status
Cefazolin will no longer be considered therapeutically equivalent to cephalothin and cephrapin. Cephalothin and cephrapin will still be considered therapeutic equivalents with cephalothin presently remaining the drug stocked at UH.

Policies Approved
In addition to specialty service approval, Category III (Restricted) Drugs will require completion of a Utilization Form like Category II (Monitored) Drugs.

There will be no meeting of the Pharmacy and Therapeutics Committee in December.