New Formulary Drugs

Gemtuzumab (Mylotarg®)
This is a recombinant, humanized anti-CD33 monoclonal antibody conjugated to calicheamicin. It provides highly specific “targeted” therapy and will be used mainly for both newly diagnosed and relapsed/refractory AML as part of phase III COG study in combination with other chemotherapy agents. Another use will be as monotherapy for relapsed AML after traditional chemotherapy or HSCT.

Sodium phenylacetate and sodium benzoate injection (Ammonul®)
Previously available only under an open label study, the committee decided to add this orphan drug to the formulary as adjunctive therapy for the treatment of acute hyperammonemia and associated encephalopathy in patients with urea cycle disorders. Sodium phenylacetate and sodium benzoate serve as alternatives to urea for the excretion of waste nitrogen.

Other Formulary Issue

Formulary change
Ursodiol 250 mg tablets will replace 300 mg capsules. This will align our ursodiol dose strength and form with the FHCRC and UWMC and allow better continuity of therapy for our SCCA patients.

Formulary deletion
Sandimmune brand of cyclosporine capsules and oral solution will be deleted from the formulary due to low usage and to increase medication usage safety.

Once daily tobramycin
The committee approved a guideline and process for the use of extended interval dosing for tobramycin. Results from clinical studies that compared every 8 hour versus every 24 hour dosing in CF patients showed that efficacy was equivalent and the safety profile was similar. The use of once daily tobramycin will be restricted to neonates and patients with Cystic Fibrosis. See article in this issue about the specifics of this new process.

WHAT ARE THESE NEW DISCHARGE MEDICATION FORMS ANYWAY?
BY Barb Marquardt, RPh

In April a team that included representatives from nursing, the pharmacy, medical staff and unit coordinators came together for a week-long Rapid Process Improvement Workshop. The workshop focused on the outpatient pharmacy flow with targets of improving the quality of orders received, shaping demand and improving the Outpatient pharmacy process.

One of the results of the workshop was to update the discharge medication forms. The new forms give the pharmacy additional information that helps decrease the need to call UCs, RNs and prescribers. The new forms go through a certification step completed by the UCs which also helps expedite the prescription filling process.

The outpatient pharmacy started with an average turn around time of 89 minutes which is now down to 55 minutes. Thanks to everyone for using the new forms!!!
Once Daily Tobramycin in Cystic Fibrosis
A New Policy

By Tom Nemeth, PharmD and Wade Benton, PharmD

The Pulmonary Department at Childrens Hospital and Regional Medical Center has established a new policy instituting Once Daily Tobramycin in Cystic Fibrosis.

Three times daily administration of aminoglycosides in combination with beta-lactam has long been the standard of practice for pulmonary exacerbations in patients with cystic fibrosis colonized with Pseudomonas aeruginosa. The recent publication of the TOPIC study, comparing once versus three time daily regimens of tobramycin treatment for pulmonary exacerbations in cystic fibrosis patients, showed no major difference in change of FEV1 (% predicted) between the two regimens. A recent meta-analysis published in Pediatrics showed no significant difference between once daily dosing and multiple daily dosing. Several other studies show similar results, but trend to favor once daily dosing.

The major clinical limitations to usage of aminoglycosides are nephrotoxicity and ototoxicity. Aminoglycoside-induced nephrotoxicity is associated with accumulation of these drugs in the proximal renal tubular epithelial cells. Their uptake into the proximal renal tubular epithelial cells appears to be saturated at relative low concentrations, which suggests that higher peaks do not associate with greater toxicity. A recent meta-analysis of extended interval aminoglycoside administration for children indicated that once daily dosing demonstrated trends toward lower rates of nephrotoxicity. The TOPIC study showed a change in serum creatinine concentrations in children that favored the once daily tobramycin group. Additionally the once daily group had a smaller rise in NAG (proximal tubular enzyme that is used as a marker of nephrotoxicity). Ototoxicity can occur in the form of cochlear or vestibular dysfunction. Typical pattern of aminoglycoside-induced high frequency hearing loss results from progressive loss of function from the outer hair cells to the inner hair cells. Experimental models have shown that the half-life of aminoglycosides in the inner ear can be measured for months. The Pediatric meta-analysis on once daily aminoglycosides showed no difference in ototoxicity rates between once daily dosing and multiple daily dosing. The TOPIC study showed no deterioration in hearing in audiograms on days 1 and 14 of treatment in either arm.

Monitoring of peak concentrations with once daily aminoglycosides is not performed. Additionally, monitoring trough concentrations is not practical due to the levels being too low to be detected by traditional assay technology (0.05 mg/L). Therefore, monitoring of 24-hour Area Under the Curve is a logical method for monitoring aminoglycoside therapy.
Here are some guidelines to the new once daily dosing for tobramycin only. Amikacin will still have standard thrice daily dosing.

- **Starting dose is their previous Q8H dosing given as one big dose daily or 10 mg/kg/dose daily**
- **We will draw levels at 2 hours and 6 hours after the infusion**
- **Do not need to wait after the 3rd dose to get levels, can do it right away**
- **Repeat levels can be done using just a 2 hour level like before**
- **AUC range we are shooting for is 86-101, higher AUC’s are ok if the patient has a low trough of below 0.3**
- **Still need to document infusion time properly**
- **Don’t care how close to 2 or 6 hours the lab draw is, just that the time is recorded accurately**
- **Notes will be left in CIS just as before**

The potential advantages of once daily dosing of aminoglycosides includes probable lower rates of toxicities, straightforward dosage calculations, high peak serum levels, decreased staff time (pharmacy and nursing), fewer assays, and lower costs.

Based on the evaluation of current literature, the Pulmonary Department and P & T Committee recommend that once daily dosing of intravenous tobramycin in cystic fibrosis be instituted.