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New Formulary Drugs

Nitazoxanide (Alinia®)

This antimicrobial is FDA-approved for the treatment of pediatric patients with cryptosporidiosis and the treatment of pediatric and adult patients with giardiasis. Nitazoxanide offers a relatively short course of treatment (3 days) and is available both as liquid and tablet formulations. As treatment for giardiasis, it has not been shown to be more effective than metronidazole. Common side effects include abdominal pain, diarrhea/vomiting, and headache. Nitazoxanide is added to formulary with restriction for the treatment of *C. parvum* or upon ID approval.

this issue on the background of this therapy.

TPN process improvement

In order to reduce medication errors related to TPN, the following goals were presented as vision to standardize TPN process in preparation for implementation by May 2005:

- Decrease unneeded product variability
- Decrease unneeded orders by standardizing criteria for who receives TPN
- Standardize ordering process
- Reduce long process times (order to administration)
- Improve TPN administration and CVC management

Other Formulary Issues

CRRT protocol for patients with hepatic dysfunction

A special dialysis protocol for patients with hepatic dysfunction was presented and discussed. Cost of materials ~ \$800/day. See article in

Rituxan® (Rituximab) correction

Rituximab was approved in the July P&T meeting. In addition to PTLD and childhood arthritis, Rituximab will also be used for a variety of vasculitic diseases and the dose should be 4 weekly infusions of 750 mg/m².

Vancomycin and Gentamicin Levels

by Kristin Veal, PharmD

Gentamicin and Vancomycin serum levels are monitored in order to minimize toxicity and maintain therapeutic levels. Patients who are expected to receive these drugs for more than three days should have drug levels measured. Levels are checked with the 3rd to 5th dose following initiation of therapy or following a dose change. Patients should also have a baseline serum creatinine and BUN measured before starting treatment.

GENTAMICIN For patients receiving gentamicin, **both peak and trough** levels should be obtained. This is because high peak levels are associated with ototoxicity, and high trough levels are associated with renal toxicity. Peak gentamicin levels should range from 4-12mcg/ml, and trough levels should be <2 mcg/ml¹.

VANCOMYCIN Monitoring requires **trough levels** in order to ensure that therapeutic levels are obtained (5-10mcg/ml)¹. It is **not necessary to measure vancomycin peak levels**².

References:

1. CHRMC Formulary of medications 6th ed. 2003.
2. Jacob S. Vancomycin monitoring: are both peak and trough levels necessary? CHRMC medication update newsletter. Feb 2004.

Critical Drug Shortages

Alprostadiil – drop ship only

Alfentanil – sporadic supply; consider remifentanil

Codeine liquid – unavailable; consider tablet or acetaminophen with codeine

Gonadorelin injection – temporarily unavailable

Meropenem – drop ship only

Niferex liquid – manufacturer back order; consider ferrous sulfate elixir 8.8 mg Fe/ml

Pantoprazole injection – on allocation due to manufacturer’s recall

Respigam – discontinued by manufacturer, will not be available once limited pharmacy supply is used up; synagis as alternative

Senna Granules – unavailable from manufacturer; consider tablet or liquid

Watch List:

ADEKs liquid, thioguanine tablets, conjugated estrogen injection, diazepam injection, methadone liquid

Methylprednisolone injection, hydrocortisone injection – please try to use oral route when possible in order to preserve our injectable supply

Shortage Resolved:

Thiopental, rocuronium

Chest Irrigations for Mediastinitis

Pharmacy will start preparing all chest irrigations for the ICU, which include:

- 1) Povidone Iodine 10% (Betadine®) 50 ml in 1 liter NS
- 2) Cefazolin 1000 mg in 1 liter NS
- 3) NS 1 liter

These products will be used *strictly* for post-operative cardiac patients in the ICU. A CIS orderset will soon be available.

New Lactobacillus Product

by Kristin Veal, PharmD

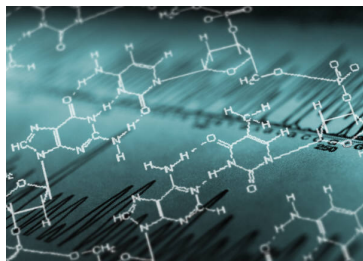
Probiotics are used in the prevention of antibiotic-associated diarrhea and the treatment of rotaviral diarrhea. Probiotics promote a balanced GI flora and maintain colonization resistance. Colonization resistance refers to the suppression of pathogenic bacterial growth by normal GI flora.

Lactinex® (L. acidophilus and L. bulgaricus) has been the probiotic product available at CHRMC. However, objective clinical data supporting the efficacy of this product are few, and available studies show mixed results¹. In contrast, studies have consistently demonstrated the efficacy of another Lactobacillus species, L rhamnosus GG (Culturelle®)^{1,2,3}. L rhamnosus GG may be more efficacious than L acidophilus because it is able to survive passage through the GI tract. It also adheres to the intestinal wall and can be found in stool up to 2 weeks following administration^{1,2}.

Culturelle® is now available at CHRMC, and will replace Lactinex®. The dosing for Culturelle® is 1 capsule twice daily (1/2 capsule in children less than 12 kilograms). The capsule can be opened and its contents sprinkled on food if necessary. The capsule is a gelatin capsule and contains casein and whey, so patients with true milk allergy (not lactose intolerance) should not use this product.

Reference:

1. Elmer GW. Probiotics: "living drugs". AJHP.2001; 58:1101-1108.
2. Vanderhoof JA et al. Lactobacillus GG in the prevention of antibiotic-associated diarrhea in children. J Pediatrics 1999; 135:564-568.
3. Arvola T et al. Prophylactic Lactobacillus GG reduces antibiotic-associated diarrhea in children with respiratory infections: a randomized study. Pediatrics 1999; 105:e64.



Tumor Lysis Syndrome

Etiology Patients with rapidly growing malignant tumors, those with a large tumor burden or tumors exquisitely responsive to cytoreduction (including ALL, AML, lymphomas such as Burkitt’s lymphoma) are at risk for developing tumor lysis syndrome (TLS). TLS results from the death of a large number of malignant cells, which in turn release their contents into the blood stream resulting in multiple metabolic disorders. These intracellular components include potassium, phosphate and nucleic acids from DNA.

Lymphoblasts contain especially high levels of phosphate, about four times the content of normal lymphocytes.⁽²⁾ Although TLS can occur before medical treatment due to high cell turnover rate, it usually appears 12-72 hours after the start of cytotoxic treatment.

Assessment TLS can lead to several metabolic disorders including:

- a) **Hyperkalemia** – may lead to muscle weakness, hypotension or cardiac arrhythmias.
- b) **Hyperphosphatemia** – large amounts of phosphorous are released from the destroyed cells, which may bind to serum calcium, precipitate into crystals and lead to renal impairment.
- c) **Hyperuricemia** –nucleic acids are metabolized to uric acid, which may precipitate in the collecting ducts of the renal tubules due to the acidic nature of the kidney.⁽²⁾ This leads to decreased renal function.
- d) **Hypocalcemia** – may occur due to the binding of elevated phosphate levels to circulating calcium. Monitor for muscle cramping, tingling or tetanus.
- e) **Renal impairment / failure** – may occur from uric acid and/or calcium–phosphate crystals within the renal tubules.

Prevention / supportive care To decrease the severity of TLS, there are several measures that can be taken:

- a) Increase IV hydration to 1.5-2x maintenance requirements to keep urine output at 2-3 ml/kg/hr. This will decrease the risk of precipitation and enhance elimination of uric acid.
- b) Hydrate with alkaline solution containing sodium bicarbonate to enhance solubility of uric acid and therefore decrease risk of crystal formation. The standard solution at CHRMC is D5 ¼ NS with 40 mEq sodium bicarbonate. Adjust the IV fluids to maintain urine pH ≥ 7.
- c) Monitor electrolyte levels: avoid potassium supplements until TLS is well controlled; supplement calcium only if patient has cardiac arrhythmias from hypocalcemia, as this may increase risk of calcium/phosphate precipitation in the face of hyperphosphatemia; consider administering phosphate or potassium binding agents as necessary.
- d) Monitor renal function tests and I&O carefully. Institute dialysis or CRRT if needed to treat renal failure, hyperkalemia, hyperphosphatemia, hyperuricemia or volume overload.

Medication Therapy Medications can be used to decrease uric acid levels, thereby decreasing risk of uric acid crystal formation and subsequent renal impairment. Comparison of Uric Acid Lowering Agents:

	Allopurinol	Rasburicase (ELITEK™)
Mechanism of Action	xanthine oxidase inhibitor which decreases production of uric acid	recombinant urate-oxidase enzyme which enhances the metabolism of uric acid to an inactive compound
Plasma uric acid levels 4 hours after first dose ⁽¹⁾	12% reduction (N=25)	86% reduction (N=27)
Route	PO	IV
Adverse Drug Reactions	- rash 10-15%*, may be severe with prolonged usage - nausea, vomiting 1.5%	- headache 26% - abdominal pain, diarrhea, constipation 20% - rash 13% - anaphylaxis <1% -other ADRs (often associated with current disease state or chemotherapy) nausea (27%), vomiting (50%), fever (46%), mucositis (15%)
Drug acquisition cost at CHRMC for a 50 kg-pt	200 mg PO TID x5 days = \$0.12/dose x15 doses = \$1.80/course	0.15-0.2 mg/kg ~ 10 mg IV x1 dose (minimum) = \$2066.24
Guidelines for usage at CHRMC	none	- Cancer known to likely cause TLS - Uric acid level >6 mg/dl - SCr >2 x baseline

* The incidence of rash increases with concurrent administration of ampicillin or amoxicillin

References:

- 1) Goldman SC, Holcenberg JS, Finklestein JZ et al. A randomized comparison between rasburicase and allopurinol in children with lymphoma or leukemia at high risk for tumor lysis. *Blood* 2001; 98:22998-3003.
- 2) "Principles and Practice of Pediatric Oncology" fourth edition, pages 1195-8.
- 3) Micromedex Healthcare Series database, volume 121.
- 4) "Tumor Lysis Syndrome" CHRMC SCCA guideline of care.
- 5) Allopurinol package insert, Watson Laboratories 2002.
- 6) ELITEK™ package insert, Sanofi-Synthelabo Inc 2002.

Conversion of Intranasal/Oral to Intravenous

DESMOPRESSIN

by Gretchen Linggi, PharmD.

Desmopressin acetate, an analog of vasopressin, can be used for a variety of indications such as diabetes insipidus, primary nocturnal enuresis and to control bleeding (Hemophilia A or Von Willebrand's disease). The dosing for desmopressin is dependent upon the indication and route of administration. It is preferred to have the patients use either the intranasal or oral formulation whenever possible. In emergency situations, 10% of the intranasal dose can be administered intravenously.¹ The manufacturer of the intravenous desmopressin does not have any recommendations for the conversion from oral desmopressin to the intravenous formulation. However, given the bioavailability and dosing of the IV formulation, the IV dose is estimated to be about 0.5-1% of the oral desmopressin dose, divided twice daily.

Vasopressin is preferred for patients who are unable to control their fluid intake, as it has a shorter duration of action in comparison to desmopressin. The only downside to the use of vasopressin is that infusion of this agent must occur in the intensive care unit.

Intravenous administration of desmopressin should be over 15 to 30 minutes and diluted with saline to a maximum concentration of 0.5 mcg/mL.² If you have any questions regarding the conversion of intravenous desmopressin, please feel free to contact the pharmacy.

References:

1. MICROMEDEX® Healthcare Series, Thomson MICROMEDEX, Greenwood Village, Colorado (September 2004).
2. Children's Hospital and Regional Medical Center: Formulary of Medications: 6th Edition, 2001-2003.

Outpatient Rx Corner



Outpatient pharmacy is located on Train 3, next to the inpatient pharmacy. Hours are 9AM- 8PM Mondays through Fridays and 8AM-4:30PM on Saturdays and Sundays. Prescriptions after hours will be dispensed by the inpatient pharmacy. Messages can be left on 206-987-2138 for refills.

Miralax® (polyethylene glycol 3350 powder) and Diflucan®(fluconazole) are now available in generic form. Miralax® is stocked in a 255 gram container (14 doses of 17 grams) under the name Glycolax™. It is covered by most insurances with the exception of straight DSHS. It requires that the patient must have tried and failed a less costly alternative and be used for treatment of occasional constipation. Fluconazole generic tablet is round and can be more accurately cut in half. The liquid preparation is good for only 14 days after mixing. If at all possible use the tablet form so that patients can receive a 30-day supply and can avoid an additional trip to the pharmacy. – *Rose Velikanje, RPh*

Albumin-Enhanced CVVH

by Susan Jacob, PharmD

Liver failure is a serious and life-threatening syndrome. Liver transplantation often becomes the sole effective therapy for acute liver failure, where mortality rates can run as high as 60-80% without transplantation. Severe shortage of compatible donor organs has prompted the development of special liver assist modalities that can provide temporary liver support until suitable donor organs are available for patients.

In acute liver failure, extensive loss of functional hepatocytes leads to disruption of important synthetic, metabolic pathways, as well as the detoxification process. In the absence of proper detoxification function, accumulation of water-soluble toxins (ammonia, phenols, and mercaptans) and albumin-bound hepatic toxins (bilirubin, aromatic amino acids, bile acids, endogenous benzodiazepines, free fatty acids, and false neurotransmitters) occur and are possibly responsible for late-stage compromises such as hepatic encephalopathy, hemodynamic instability, pulmonary and renal failure. Since conventional dialysis and renal replacement therapies only remove water-soluble toxins, several systems of albumin dialysis have been developed that assist in the removal of albumin-bound toxins. The concept of albumin dialysis involves perfusing a patient's blood through a circuit containing a dialysis filter, and an albumin dialysate flows on the opposite side of this semi-permeable membrane. The circulating toxins diffuse across the membrane and bind to albumin in the dialysate, and are eventually removed from the circuit.

Molecular Adsorbent Recirculating System (MARS) - this is a closed system of albumin dialysis introduced by Mitzner, Spange and colleagues and is available commercially. The albumin dialysate is partially regenerated and reused after passing through a series of filters. This system also requires additional equipment such as a MARS monitor and a recirculation pump. More than 400 patients have been placed on this liver dialysis system since 1993 across Europe, USA and Asia. On the other hand, **Single-Pass Albumin Dialysis (SPAD)** is a simpler version of albumin dialysis. It utilizes a standard CRRT circuit and machines. The albumin dialysate is disposed after each pass through the circuit, and therefore any concern for loss of efficiency with using regenerated dialysate solution would be minimized. SPAD has been used effectively for liver detoxification, and recent in vitro studies indicate similar clearance parameters for MARS and SPAD. SPAD can be expensive due to the significant amount of albumin needed to make fresh dialysate solution. However, when compared to the more specialized and complicated MARS, SPAD costs about the same or may be even less.

In September 2004, the P&T at CHRMC approved SPAD for the support of critically ill patients with liver failure.

References:

1. Awad et al. Results of a phase I trial evaluating a liver support device utilizing albumin dialysis. *Surgery* 2001;130:354-62.
2. Askenazi et al. Management of severe carbamazepine overdose using albumin-enhanced CVVH. *Pediatrics* 2004;113:406-409.
3. Kreyman et al. Albumin-dialysis: effective removal of copper in a patient with fulminant Wilson disease. *Journal of Hepatology* 1999;31:1080-1085.
4. Mitzner et al. Extracorporeal detoxification using the MARS for critically ill patients with liver failure. *J Am Soc Nephrol* 2001;12:S75-S82.
5. Protocol for liver dialysis: CHRMC, Seattle, WA.
6. Sauer et al. In vitro comparison of the MARS and SPUD. *Hepatology* 2004;39:1408-1414.
7. Stange, Mitzner et al. MARS: Clinical results of a new membrane-based blood purification system for bioartificial liver support. *Artificial Organs* 23(4): 319-330.



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