

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met August 18, 2009. 4 products were added in the *Formulary*. 1 was deleted; 2 were designated nonformulary and not available. 2 interchanges were approved, 5 criteria for use were changed, and 2 drugs were reviewed and designated high-priority nonformulary drugs.

◆ ADDED

Cyclosporine Ophthalmic Solution (Restasis® by Allergan)

Lacosamide (Vimpat® by UCB Pharma)

Lamotrigine Extended-Release (Lamictal® XR by GlaxoSmithKline)

Lomustine (CeeNu® by Bristol Myers Squibb)*

*Must be ordered on Chemo Order Form

◆ DELETED

Buckberg Cardioplegia Solution (Compounded)†

†Nonformulary and not available

◆ NONFORMULARY AND NOT AVAILABLE

Efalizumab (Raptiva®)‡

‡Removed from the market

◆ INTERCHANGES

Acetylcysteine (Acetadote®)§

§IV to Oral conversion allowed

Amino Acid Injection (Trophamine®)¶

¶Used in all children less than 6 months of age (interchanged for Proso®)

(continued on next page)

POLICIES AND PROCEDURES

Pediatric PCA order form required

A new *Pediatric PCA [Patient-Controlled Analgesia] Order Form** is required if PCA is used on **any** pediatric patient. The purpose of this form is to promote the effective and safe use of patient-controlled analgesia in pediatric patients. This form was proposed and developed by the Department of Pediatrics. The P&T Committee made this form mandatory effective September 1, 2009.

The purpose of the new form is to promote the effective and safe use of patient-controlled analgesia in pediatric patients.

PCA cannot be used in children with a developmental age less than 5 years. This restriction is necessary to ensure that the child can operate the pump. In patients weighing greater than 50 kg, adult PCA orders can be considered. Currently, there is no mandatory *Adult PCA Order Form*;† however, there are orders that can be used. Whether the *Adult PCA Order Form* should be mandatory is currently being considered.

The *Pediatric PCA Order Form* provides dosage guidelines for opioid-naïve patients, but it has blanks that can be used to customize doses for opioid-experienced patients. Recommended dosages are provided for morphine (the primary agent), fentanyl, and hydromorphone, which are the only PCA agents currently available at Shands. PCA dose, lockout interval, continuous dose (basal), and one-hour dose limits must be specified. Instructions are provided on the form (eg, how to calculate the 1-hour dose limit).

A key component of the *PCA Order Form* is standard monitoring (eg, continuous pulse oximetry). Respiratory rate parameters are provided to guide the nurse about when to stop the PCA

and notify the prescriber of a potential problem. These parameters are based on the patient's age, since the appropriate values cannot be generalized in pediatric patients.

In addition to guidelines for the appropriate use of opioids, the *Pediatric PCA Order Form* also provides valuable information on the appropriate use of adjuvant medications (eg, adjuvant pain meds, drugs for itching, treatment of nausea and vomiting, and prevention and treatment of constipation).

The *Pediatric PCA Order Form* can be found on the portal by going to the UF Patient Care Form link under Clinical Links. Use the ICU tab under Pediatrics. Under PICU, you will see a link labeled [Order Set and Guidelines for Patient Controlled Analgesia \(PCA\)](#). Alternatively, you can use the search box in the upper right-hand corner of any portal page, or the search box on the UF Patient Care Forms page (ie, use the search term "Pediatric PCA" in the search box).

If you have additional questions about the *Pediatric PCA Order Form* or need additional assistance (ie, dosage recommendations for opioid experienced patients), contact one of our pediatric clinical pharmacists (Drs. Lisa Taylor or Brian Kelly).

LINKS

*https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Forms/UF/Tab6/81212_0.pdf

†https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Forms/UF/Tab18/67795_0.pdf

INSIDE THIS ISSUE

- ◆ Adding a drug in the *Formulary*
- ◆ Micromedex
- ◆ Warfarin dosing

◆ **CRITERIA-FOR-USE CHANGES**

Leflunomide (Arava®)**

**Removed from the Chemotherapy Policy

Panitumumab (Vectibix®)††

††Added in the Chemotherapy Policy

Pentobarbital (Generic)‡‡

‡‡Pediatric standard concentration changed to 8 mg/mL

Risperidone Long-Acting Injection (Risperdal® Consta®)§§

§§Formulary at Shands Vista with restrictions

Warfarin (Coumadin®)¶¶

¶¶Baseline INR less than 4 AND notification of service required before 1st dose

◆ **EVALUATED BUT NOT ADDED**

Cyclosporine Ophthalmic Solution, Compounded***

***High-Priority Nonformulary Drug

Fibrinogen Concentrate, Human (RiaSTAP®)***

***High-Priority Nonformulary Drug

Cyclosporine ophthalmic emulsion is a topical immunomodulator used to increase tear production in patients with keratoconjunctivitis sicca (ie, inflammation and dry eyes). Cyclosporine probably works by reducing lymphocyte aggregation around the lacrimal gland. At recommended doses, cyclosporine ophthalmic drops undergo very little or no systemic absorption and have a favorable safety profile. Current evidence-based guidelines recommend cyclosporine for moderate to severe dry eyes refractory to artificial tear use. The concomitant use of artificial tears is acceptable, but patients are advised to separate doses by at least 15 minutes.

Results from clinical trials show some instances where cyclosporine ophthalmic is equally or more beneficial than similar alternative therapies. However, comparative studies of cyclosporine eye drops are limited in number and quality due to the fact that there are no other agents approved for the treatment of dry eye associated with keratoconjunctivitis sicca and the lack of substantial data to prove its efficacy when used off-label.

Cyclosporine ophthalmic emulsion has been used off-label for corneal graft rejection prophylaxis, therapeutic keratoplasty for fungal keratitis, and dry eye due to various etiologies.

Several studies compared the use of cyclosporine with corticosteroid eye drops for the treatment and prevention of corneal graft rejection. Some researchers suggest that cyclosporine may provide additional benefit for transplant patients. However, most studies show no difference in outcomes between patients given steroids alone and those given steroids and cyclosporine. While labeling information for Restasis® suggests no additional benefit when administered with punctal plugs to treat dry eyes, some studies suggest that cyclosporine combined with punctal plugs provides more immediate results than cyclosporine alone.

Although commercially available cyclosporine ophthalmic solution was added in the *Formulary*, **compounded cyclosporine ophthalmic drops** were designated a high-priority nonformulary drug. This is a sterile product compounded from nonsterile ingredients. These products cannot be made at Shands at UF and must be obtained on a patient-specific basis from a compounding pharmacy. Per existing policy, an informed consent is necessary for the use of these products.

Lacosamide is a new antiepileptic drug labeled for adjunctive treatment of partial-onset seizures in patients with epilepsy aged 17 years and older. Lacosamide is available as oral and intravenous formulations with the injectable used when oral administration is temporarily not feasible. The exact mechanism of action of lacosamide is unknown. Lacosamide enhances slow inactivation of voltage-gated sodium channels and binds to collapsin-response mediator protein-2 (CRMP-2). Oral and intravenous lacosamide are bioequivalent at recommended doses. Food does not affect oral absorption.

Lacosamide has not been compared to other drugs used to treat epilepsy in controlled trials. In placebo-controlled trials, the median percent reductions in 28-day seizure frequency from baseline to maintenance for lacosamide 400 mg/day and lacosamide 600 mg/day compared to placebo were better than for the 200 mg/day dose. More patients receiving lacosamide 400 mg/day and lacosamide 600 mg/day achieved a 50% response rate compared to placebo, while lacosamide 200 mg/day did not reach significance for this endpoint.

The starting dose of lacosamide is 50 mg twice daily. The dose is titrated in increments of 100 mg/day at weekly intervals up to a maximum dose of 400 mg/day. Slower titrations may help avoid dose-dependent adverse effects. No dosage adjustments are required when switching between oral and

intravenous therapy. When discontinuing lacosamide, it should be tapered to reduce the risk of seizures in patients with epilepsy.

Dizziness, diplopia, headache, and nausea are the most common adverse reactions associated with the use of lacosamide. Dizziness, nausea, and diplopia appear dose related, occurring more often in patients receiving lacosamide 600 mg/day. Injection site reactions (0.5-2.5%) were reported with intravenous lacosamide. Similar to other drugs used to treat epilepsy, lacosamide increases the risk of suicidal ideation or behavior. No clinically significant drug interactions have been identified for lacosamide.

Lacosamide is a Schedule-V controlled substance because euphoria occurs in some patients. There is an FDA-approved Risk Evaluation and Mitigation Strategy (REMS) that requires a Medication Guide with each prescription, but this does not apply to the inpatient setting.

Lacosamide is expensive and the oral dosage forms costs about a third of the cost of the IV dosage form. Off-labeled use could add significantly to pharmaceutical expenditures. Lacosamide was added in the *Formulary* for its labeled indication.

Lamictal® XR is an extended-release (ER) version of lamotrigine immediate-release (IR). Lamotrigine is an antiseizure drug that has been listed in the *Formulary* as the IR oral dosage form for many years.

The labeling for Lamictal® XR provides recommendations for converting from IR to ER, but recommends monitoring. "For patients being converted from immediate-release lamotrigine to LAMICTAL® XR, the initial dose of LAMICTAL® XR should match the total daily dose of the immediate-release lamotrigine. Patients should be closely monitored for seizure control after conversion to LAMICTAL® XR." Because of the controversial nature of interchanging seizure medications, the P&T Committee added Lamictal® XR in the *Formulary* as a new dosage form.

Lomustine capsules are oral alkylating agents that were deleted from the *Formulary* in May of this year. Since its deletion, several patients have been prescribed lomustine capsules. Since lomustine was deleted only because of lack of use, this increase in use stimulated the P&T Committee to re-add it in the *Formulary*.

Buckberg cardioplegia solution is a cardioplegia solution with glutamate and aspartate that is used to

(continued on next page)

Formulary update, from page 2
wean patients from cardiopulmonary bypass. It was added in the *Formulary* in January 2008. This mixture is not commercially available and requires compounding. The solution could not be compounded at Shands at UF, and had to be acquired from Central Admixture Pharmacy Services (CAPS).

Despite limited data to support this mixture, the P&T Committee approved its addition based on theory and the previous experience of the requesting surgeon. An agreement of terms and conditions was never reached with CAPS and this product was, therefore, never used. Therefore, Buckberg Cardioplegia Solution was deleted from the *Formulary* and designated nonformulary and not available.

Efalizumab was an anti-CD11a monoclonal antibody that caused immunosuppressive effects. It targeted T-cells to prevent their activation without destroying them. It had a labeled indication for the management of psoriasis. The FDA approved efalizumab on October 24, 2003.

Efalizumab was voluntarily withdrawn from the US market on April 8, 2009. The manufacturer took this action as a phased withdrawal because of the risks of developing progressive multifocal leukoencephalopathy (PML) on this drug. There is no known effective treatment for PML. Prescribers should continue to monitor patients who received efalizumab for neurological symptoms that might represent PML. Efalizumab has never been listed in the *Formulary*.

Acetylcysteine is an amino acid derivative used as a prophylactic measure to reduce the risk of radiocontrast-induced nephropathy. It (along with hydration) is usually given 12 hours before and up to 48 hours after contrast media is used for an X-ray or CT-scan. The evidence is mixed on the efficacy of this intervention, but in general, it is considered an appropriate practice. However, the cost of acetylcysteine injection stimulated an audit of this use. Most of the available evidence is for the oral dosage form.

Significant cost savings may be realized if the oral dosage form is used in appropriate cases instead of the injectable. Therefore, the P&T approved the automatic interchange from acetylcysteine injection to enteral acetylcysteine (ie, PO/PNG/PDHT) after the first dose. The injection may be required when the use of contrast is not planned, and quick administration is required. However, after the first dose, the oral dose is considered acceptable.

Trophamine® is a pediatric amino acid mixture used for parenteral nutrition in infants and children. Neonatologists requested that it be used routinely in “neonates” rather than Prosol® , which is the primary amino acid listed in the *Formulary*. This request is based on a lack of labeled indication for the use of Prosol® in neonates and benchmarking data that suggests that it is not used at other institutions. The off-labeled use is not a major concern, because most drugs used in neonates are used off-label. However, the amino acid mixture for Trophamine® has some theoretical advantages in neonates compared with Prosol® . For example, Trophamine® contains taurine, which may be conditionally essential in neonates and could help avoid parenteral nutrition-associated liver disease.

In order to establish a policy that could be operationalized, Trophamine® will be used automatically in all patients less than 6 months of age. Both Prosol® and Trophamine® are listed on the *Pediatric TPN Order Form*, and if Trophamine® is specified for patients older than 6 months, these orders will be honored.

Leflunomide is an immunomodulator used in the treatment of rheumatoid arthritis. It was incorrectly listed in the *Chemotherapy Policy*. Since it is not considered a chemotherapy agent, it was deleted from *Chemotherapy Policy* and does not need to be ordered on a *Chemotherapy Order Form*.

Panitumumab is a recombinant monoclonal immunoglobulin that binds to human epidermal growth factor (EGFR). It was originally approved by the FDA with a labeled indication for the treatment of EGFR-expressing colorectal cancer after disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing regimens. This approval was based on a single, open-label, randomized study that enrolled 463 patients with metastatic colorectal cancer. On July 17, 2009, the labeling was revised to narrow its indication for use. The revised labeled indication now limits its use to patients with specific gene mutations (KRAS mutation). This limitation is important considering it costs approximately \$8,000 to \$10,000 per month.

A review of the *Chemotherapy Policy* revealed that this agent was not currently restricted to orders written on a *Chemotherapy Order Form*, so it was added in this policy.

Pentobarbital is a short-acting intravenous barbiturate used to decrease intracranial pressure after head trauma. Trissel's *Handbook on Injectable Drugs* states that pentobarbital forms a visual precipitate in less than

24 hours if diluted with either normal saline or D5W at a concentration above 8 mg/mL. The previous pediatric standard concentration was 10 mg/mL (although this concentration had never been used). Therefore, the standard pediatric pentobarbital concentration was changed to 8 mg/mL.

Risperdal® Consta® was added in the *Formulary* on September 21, 2004, but restricted to use at Shands Vista. It was the first depot form of an atypical antipsychotic drug. Risperdal® Consta® has a labeled indication for the treatment of schizophrenia, and is used in patients in whom compliance is a concern.

The long-acting formulation of risperidone injection is an aqueous suspension of microspheres. Each microsphere is a small bead with a matrix of risperidone and a carbohydrate-based biodegradable copolymer, which is gradually hydrolyzed at the injection site releasing risperidone. Initially after an injection, very little risperidone is released. The release of risperidone begins 3 weeks after the first injection. This is why oral therapy with risperidone (or another antipsychotic) must be continued for 3 weeks after beginning Risperdal® Consta®.

The advantage of depot antipsychotics is assured compliance. Continuing therapy for a patient who has been hospitalized is a reasonable criterion for Risperdal® Consta® use at Shands at UF.

A recent audit at Shands Vista showed that it was not being used appropriately for about 25% of patients. In these cases, there was no coordination for continued use after its first administration. This adds to costs and does not provide any patient benefit.

Risperdal® Consta® is now limited to patients with a diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder. Patients must have a documented positive response to oral risperidone monotherapy and have tolerated risperidone for 48 hours prior to first Consta® injection. Patients must have a documented history of noncompliance. There must be a discharge plan in place that provides for continuation of Consta®. Finally, the plan will include hospitalization for 3 weeks following the first injection or that there will be a plan in place that insures continuation of oral risperidone for 3 weeks following the first injection. Following these criteria should prevent unnecessary use of this dosage form and reduce overall costs.

(continued on next page)

Requesting a drug for addition in the *Formulary*

The P&T Committee recently revised the policy governing requesting a drug for possible addition in the *Formulary*. Drugs are considered for addition in the *Formulary* when requested by an attending physician, but drugs are also considered proactively based on nonformulary use and safety concerns. High volume and costly drugs being used nonformulary will be reviewed by the P&T Committee to determine whether these agents should be readily available and/or whether any limitations need to be placed on these agents to assure safe and cost-effective use.

When drugs are reviewed by the P&T Committee, they can be added in the *Formulary* with no restrictions, added with restrictions, or designated nonformulary and not available. The nonformulary and not available category is used when there are more effective, safer, or more cost-effective options already listed in the *Formulary*.

Recently, there has been a trend where drugs are requested for re-evaluation shortly after the addition request was denied. Therefore, the P&T Committee established a policy that requires 12 months to pass before a drug will be reconsidered. Exceptions can be approved; however, the petitioner must write a summary highlighting new evidence or a new perspective that would justify a re-review. Only after the P&T Committee has approved this exception, will the re-review process begin.

All drugs that are considered for addition in the *Formulary* must have an evidence-based monograph prepared that summarizes the current literature. This report may take as long as a month to prepare. After the monograph is prepared, the request is first considered by the Formulary Subcommittee or the Anti-Infective Subcommittee. The recommendations of these subcommittees are considered at the next scheduled P&T Committee meeting. Depending on the time of the year, the entire process could take 2 to 3 months.

All requesters must complete a *Request for Formulary Addition Form** and a *Disclosure Form*.† Requesters, or alternate faculty members, are expected to attend the P&T Committee when the drug will be considered to provide any background needed by the Committee to make the appropriate decisions.

Addition information on this process can be found on the Shands Portal.‡

LINKS

*https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Pharmacy/UF/P-T-Committee/Adding-Drug/docs/3E43A3CC18EBD076E0439FB21E78D076

†https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Pharmacy/UF/P-T-Committee/Adding-Drug/docs/disclosure.pdf

‡https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Pharmacy/UF/P-T-Committee/Adding-Drug

Formulary update, from page 3

Warfarin is the oral anticoagulant used for the prevention and treatment of venous thrombosis. The National Patient Safety Goals for anticoagulant use states, "For patients being started on warfarin, a baseline International Normalized Ratio (INR) is available...."

The Shands at UF policy, which required an automatic baseline PT/INR on patients started on warfarin and no warfarin administration unless there is a documented INR is less than 4, was revised to require that the prescribing service will be notified before the administration of warfarin. Even if the value is less than 4, the prescribing service may change their orders if they prefer a lower cutoff (eg, 3.5).

Human fibrinogen concentrate became available for purchase

in May 2009. This product, made from pooled plasma, has a labeled indication for the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. According to the FDA, fibrinogen deficiency affects only about 150 to 300 people in the US and is usually diagnosed at birth when newborns bleed from their umbilical cord sites.

Due to what appears to be a very limited niche, this product was not considered for addition in the *Formulary*. In the event that the product is needed for its labeled indication, it will be ordered emergently and received within 12 hours as a "high-priority" nonformulary drug. Adult and pediatric hematologists supported this decision.

Micromedex becomes the Portal's drug reference

Effective September 1, 2009, the Point of Care interface for the *Micromedex Healthcare Series* replaced *Clinical Pharmacology* as Shands at UF's primary electronic drug information reference. When logged into the Shands Portal, the [Drug Reference](#) link will now take you to Micromedex for general drug information.

This reference will provide background information about a specific drug (eg, pharmacology, uses, dosages, etc). There are links on the left side of the page for [Drug Interactions](#), [IV Compatibility](#), and [Drug Identification](#) using the imprint on tablets and capsules. Across the top of the page are links to search for [Drug](#) information, [Disease](#) information, [Lab](#) information, [Alternative Medicine](#) information, [Patient Education](#), and [Calculators](#). The patient education information provided is *CareNotes*, which is a Micromedex product selected by Nursing a year ago for patient discharge information. Selecting Micromedex as our primary electronic drug information reference allows disease and laboratory information to be integrated with patient educational materials for their discharge medications.

Although representatives will be on site to conduct training, there is an online training center that provides instructions on how to maximize the value of this new reference.* Online training sessions can be live or you can view a recorded session.

Changing references is always difficult, but the integration with *CareNotes* and the coordination so that all Shands hospitals and UF Clinics now have access to the same reference supported this decision.

LINKS

*<http://www.micromedex.com/support/training/HCSkit/>

New warfarin guidelines

The Joint Commission seeks to improve patient safety through the creation of standards, including National Patient Safety Goals (NPSGs).¹ NPSGs promote safety by identifying problematic areas but differ from other Joint Commission standards in that they are more detailed and structured. As with other standards, NPSGs influence all areas of practice and are divided into *Elements of Performance* to guide facilities in meeting the standards and maintaining accreditation.

Accreditation is required for Medicare reimbursement, and failure to meet NPSGs, as well as other standards set forth by the Joint Commission, can result in citations that can ultimately delay or prevent accreditation. Goals are updated yearly and one of the new goals for 2009 was anticoagulation therapy management. The purpose of NPSG 03.05.01 is to reduce the likelihood of patient harm associated with the use of anticoagulant therapy as this therapy often involves complex dosing, follow-up monitoring, and inconsistent compliance.

Shands at UF has recently made available guidelines to assist in warfarin initiation and maintenance therapy. The guidelines are available on the Department of Pharmacy homepage. To reach the homepage from the Portal, select Services then All Services and Pharmacy at UF from the middle column. From there, select Anticoagulation Management Program and finally Warfarin Dosing Guidelines under Protocol.

The guidelines provide assistance in selecting an appropriate goal INR, initial dose, and monitoring plan, as well as warfarin reversal guidelines. The table from the guidelines (*reproduced below and continued on page 6*) prompts adjustments based on the number of days the patient has been on warfarin and the target INR. For example, the standard dosage on Day 1 is 5 mg. On Day 2, if the measured INR was 1.5 and the target INR is 2 to 3, 5 mg should be continued. If the INR was 1.7 on Day 3, the dosage would remain 5 mg. If on Day 4, the INR is still 1.7, the dosage would be increased to 7 mg

(ie, a 2 mg per day increase). If the INR is now 2 on Day 5, no dosage change is needed (ie, continue 7 mg). If however, the INR increased to 3.1 on Day 9, the dosage would be decreased to 6 mg (ie, decreased by 1 mg per day).

The warfarin dose will be given when ordered on Day 1. All subsequent doses will be given at 1800 (6 PM), which gives the prescriber time to evaluate that day's INR and make appropriate adjustments before the next dose is given. If the INR is too high (which is defined by the target INR and day of treatment), guidelines for warfarin reversal are provided in the table on page 6. Please note that vitamin K is generally not indicated unless the patient has an INR above 9 (or there is significant bleeding).

Please take a moment to familiarize yourself with the location and content of these guidelines.

By Robyn Keen, PharmD

REFERENCES

1. The Joint Commission. *National Patient Safety Goals*. Available at <http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/>; accessed August 21, 2009.

WARFARIN DOSING PROTOCOL

DAY	TARGETED INR			DOSING	
	(1.8 – 2.5)	(2 – 3)	(2.5 – 3.5)	STANDARD	LOW
1				5 mg	2.5 mg
2, 3	below 1.4	below 1.6	below 1.8	5 mg	2.5 mg
	1.4 – 1.5	1.6 – 1.8	1.8 – 2	5 mg	2.5 mg
	1.6 – 1.8	1.9 – 2	2.1 – 2.5	4 mg	2 mg
	1.9 – 2.5	2.1 – 3	2.6 – 3.5	2.5 mg	1 mg
	above 2.5	above 3	above 3.5	See Reversal Guidelines on page 6	See Reversal Guidelines on page 6
4 and on	below 1.2	below 1.6	below 1.8	Increase previous day's dose by 4 mg*	Increase previous day's dose by 2 mg*
	1.3 – 1.7	1.6 – 1.9	1.8 – 2.4	Increase previous day's dose by 2 mg	Increase previous day's dose by 1 mg
	1.8 – 2.5	2 – 3	2.5 – 3.5	Repeat last dose given	Repeat last dose given
	2.6 – 2.9	3.1 – 3.9	3.6 – 4.5	Decrease previous day's dose by 1 mg	Decrease previous day's dose by 1 mg
	above 2.9	above 3.9	above 4.5	See Reversal Guidelines on page 6	See Reversal Guidelines on page 6

* After any dose change, wait 2 days instead of one for the next dose change. (Example: INR = 1.1 on day 4, then increase dose by 2 mg then wait to make any further changes until day 6).

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**EDITOR,
DRUGS & THERAPY BULLETIN**

Randy C. Hatton, PharmD

**DIRECTOR,
PHARMACY SERVICES**

Alan Knudsen, MS, RPh

**CHAIRMAN,
PHARMACY & THERAPEUTICS
COMMITTEE**

Ricardo Gonzalez-Rothi, MD

EDITING, DESIGN, & PRODUCTION

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WARFARIN REVERSAL GUIDELINES

INR	ACTION
Less than 5 and no significant bleeding	Hold Warfarin and resume at lower dose when INR is within the appropriate range. Vitamin K not indicated.
Greater than or equal to 5 and less than 9 and no significant bleeding	Hold Warfarin 1 or 2 doses and resume at lower dose when INR is within the appropriate range.
Greater than 9 without significant bleeding	Hold Warfarin doses. Give Vitamin K 2.5 – 5 mg PO (expected reduction in 24 – 48hr). Vitamin K can be repeated. Resume warfarin at lower dose.
Any elevated INR with serious bleeding	Call Physician Stat.