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Pharmacy & Therapeutics Update: Drug Information for Health Care Professionals

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Pharmacy & Therapeutics

Update

Drug Information for Health Care Professionals

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Recombinant Activated Factor VIIa (NovoSeven®) Off-Label Use Guidelines

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Recombinant activated factor VII (NovoSeven®) [rFVIIa] is indicated for the treatment of bleeding in patients with hemophilia A or B who have developed antibody inhibitors to factor VIII or factor IX. rFVIIa has a number of characteristics that make it an appealing candidate for other bleeding disorders as well. First, because it is not enzymatically active by itself, rFVIIa does not appear to induce systemic activation of the coagulation system. This reduces the likelihood of potentially dangerous activation of clotting, as may occur with concentrates that contain activated coagulation factors. Second, its activity is not affected by circulating inhibitors such as antithrombin. Lastly, the absence of the usual transfusion-transmissible infections provides a safety advantage over plasma-derived coagulation-factor concentrates.

In the last 6 years, there have been numerous reports in the literature regarding the off-labeled uses of rFVIIa. These publications have been in the form of case reports, case series, and small randomized trials. Large, well-designed clinical trials are lacking. Despite this, there has been a steady increase in the use of rFVIIa both in hospitals nationwide as well as at MUSC.

Due to the lack of data, guidelines were developed for the use of rFVIIa in specific off-labeled uses. The overall objectives of the guidelines are to help guide appropriate use, minimize unwanted effects, improve the ordering process, enhance timely administration of rFVIIa, minimize drug-related errors, and educate health-care professionals.

The content of these guidelines is based on available evidence as well as clinical practice in adult patients only. Although there are several reported off-labeled uses, only guidelines for the four most common uses of rFVIIa have been developed, which include the following:

- Patients with closed-space bleeding
- Patients undergoing cardiothoracic (CT) surgery
- Patients undergoing liver transplantation
- Patients status post trauma

The closed-space bleeding guideline is comprised of 4 categories including acute intracranial hemorrhage (ICH), ICH secondary to oral anticoagulants, isolated traumatic head injury, and retroperitoneal bleed.

The criteria for use in CT surgery includes patients undergoing a CT procedure (eg, coronary artery bypass grafting, aortic or mitral valve replacement, ventricular assist device placement, thoracic aortic surgery, heart transplant) with coagulopathic bleeding or refractory blood loss.

In orthotopic liver transplant patients, rFVIIa has 2 indications, including rescue therapy for patients after significant clotting factor replacement has been attempted and prophylaxis therapy for patients who have an INR greater than 2 after induction of anesthesia has been administered.

Finally, in trauma, it is indicated for patients who have severe blunt or penetrating trauma with coagulopathic bleeding and for which further large transfusion requirements are anticipated.

These guidelines were reviewed and approved by physicians practicing at MUSC in their respective areas of expertise and by the Pharmacy and Therapeutic Committee.

The guidelines are available on the Formulary and Drug Information Resources Web page under Drug Information Resources and the Clinician Order Form page under Guidelines.

References available upon request.

MUSC-MC Formulary System Overview

The formulary system is a process whereby the professional staff, working through the Pharmacy and Therapeutics Committee, evaluates, appraises, and selects medications that are considered to be most useful in patient care. The formulary system is an important mechanism for optimizing patient outcomes while controlling expenditures.

The *MUSC-MC Formulary of Accepted Drugs* is a list of approved medications and dosage forms available for use throughout the Medical Center. The formulary is a tool that helps practitioners make rational drug therapy decisions. After careful review of current medical literature, the Pharmacy and Therapeutics Committee determines which agents are added to and deleted from the formulary.

The formulary is accessible at www.formluaryproductions.com/musc, and a link can be found on the MUSC Medical Center Intranet at www.musc.edu/medcenter/index.htm. The online formulary contains medications and respective formulations that are approved for use at the Medical Center, comments regarding restrictions, links to medication-specific preprinted order forms, and links to the Micromedex monograph, patient education leaflet, and PubMed citations for each medication. Other items pertinent to the formulary such as medication use guidelines, charts, and policies are also located on the online formulary under Drug Information Resources.

Any attending physician, fellow, resident, or intern may prescribe any unrestricted formulary medication listed in the *MUSC-MC Formulary of Accepted Drugs.* Nurse practitioners and physician assistants may prescribe formulary medications based on their scope of practice in accordance with South Carolina law and based on the individual collaborative practice agreement that each clinician has with their supervising physician.

The Pharmacy and Therapeutics Committee restricts the use of certain medications on the formulary. The purpose of placing a restriction on a formulary medication is to ensure patient safety and appropriate utilization. Medications may be restricted by physician status, physician specialty, specific patient care unit, specific disease state, or specific patient population. Physicians may prescribe formulary restricted medications so long as the condition of the formulary restriction is met. Nurse practitioners and physician assistants may prescribe formulary restricted medications within the scope of their practice in accordance with South Carolina law and based on the individual collaborative practice agreement that each clinician has with their supervising physician, so long as the condition of the formulary restriction is met.

Formulary restrictions are noted in the online formulary and in the pharmacy order entry system un-

der each specific medication. Additionally, a cumulative list of restricted medications is available on the front page of the online formulary.

Authority to dispense most formulary medications is delegated to the pharmacist by the Director of Pharmacy Services. However, the Pharmacy and Therapeutics Committee requires that prior to dispensing high-cost formulary medications, a second-level administrative approval must be obtained. A high-cost formulary medication is defined as one in which the acquisition cost for the expected course of therapy exceeds $5,000. If the acquisition cost for the expected course is $5,000 or greater, the pharmacist processing the order will contact the Director of Pharmacy Services or the Chair of the Pharmacy and Therapeutics Committee to obtain second-level administrative approval prior to processing the order.

Attending-level members of the medical or dental faculty may request that a medication or dosage form be added to or deleted from the formulary. Formulary request forms may be obtained from the Drug Information Center at extension 2-3896 or by e-mail (druginfo@musc.edu). The completed form must be countersigned by the appropriate department chair or division chief.

A formulary monograph is then prepared by the Drug Information Center staff. Monographs are based on published medical literature and focus on the efficacy, safety, tolerability, and economic impact of the agent. The medication is then presented to the Pharmacy and Therapeutics Committee. Following the presentation and discussion, a vote is taken. Actions taken by the Pharmacy and Therapeutics Committee are generally given an effective date on or about the 15th day of the following month. Any action deemed necessary for patient safety becomes effective immediately.

Following each meeting, requesters are notified in writing of the Committee's actions. Changes to the formulary are published each month in *Pharmacy and Therapeutics Update.*

Clinical Pharmacy On-call Services

The Department of Pharmacy Services provides continuous 24-hour clinical pharmacy coverage. On weekdays, please consult the pharmacist covering your service. For nighttime, weekend, and holiday coverage, please page the clinical pharmacist on-call.

If you require clinical pharmacy services and are on a unit that does not have regular clinical pharmacy coverage, please page the clinical pharmacist on-call or call the Drug Information Center at extension 2-3896.

The clinical pharmacist on-call can design and monitor a patient's pharmacotherapy regimen, screen for drug-drug interactions, provide pharmacokinetic consults, follow up on adverse drug events, provide intensive patient counseling, and provide guidance for initiating or adjusting parenteral or enteral nutrition.

Clinical pharmacy on-call services are available for adult, pediatric, psychiatric, and inpatient family medicine services. To contact a clinical pharmacist on-call, go to http://simonweb.musc.edu and search "clinical" using the on-call search feature or call the paging operator at extension 2-2123.

Drug Information Services

The Drug Information Center provides evidence-based answers to the professional staff's medication-related questions.

In 2005, the Drug Information Center responded to more than 1,200 questions received from physicians, pharmacists, nurses, and other health care professionals.

The mission of the Center is to promote the best practices regarding medication usage. The principle activities of the Drug Information Center include the following:

- Providing responses to drug–related questions that support patient care and research activities
- Coordinating the Adverse Drug Event Reporting Program
- Coordinating the Medication Utilization Evaluation Program
- Preparing formulary monographs and class reviews to guide the Pharmacy and Therapeutics Committee in its formulary decisions

- Providing educational inservices
- Publishing *Pharmacy and Therapetuics Update: Drug Information for Health Care Professionals*
- Developing medication use policies
- Providing therapeutic alternatives in response to medication shortages

The Drug Information Center is open Monday through Friday, 9:00 AM to 5:30 PM. The telephone numbers to the Center are 792-3896 and 792-7625 or you can email your request to druginfo@musc.edu.

Required Elements for Inpatient and Clinic Medication Orders

For a medication order to be considered complete and valid, the Medical Executive Committee has mandated that the following criteria be met:

Regarding Orders for Adult Patients

- Prohibited abbreviations must not be used
- Date and time order must be written
- Weight in kilograms required for medications that are dosed based on weight (eg, chemotherapy)
- Medication name
  - generic name preferred, specify salt form (eg, potassium chloride, potassium phosphate), chemical names for electrolytes are acceptable, except for $MgSO_4$
- Dose
- Dosage units
  - metric units only, do not use ampules, tablets, bottles as the only dosage unit. If applicable, specify the concentration (eg, mg/mL)
- Diluent
  - specify if requiring diluent other than the standard (ie, 5% dextrose or 0.9% NaCl)
- Route of administration
- Frequency or interval
  - all orders for PRN medications must include an interval and an indication, do not use range orders with variable dosing frequencies (eg, q 4 - 6 hours)
- Signature/credentials
- Pager number of prescriber

Regarding Orders for Pediatric Patients
[≤ 17 years of age (except for obstetric patients)]

- Prohibited abbreviations must not be used
- Date and time order must be written
- Weight in kilograms or grams
- Medication name
  - generic name preferred, specify salt form (eg, potassium chloride, potassium phosphate), chemical names for electrolytes are acceptable, except for $MgSO_4$
- Dose
  - dose/kg/interval required for all patients weighing less than 40 kg (eg, mg/kg/dose or mg/kg/day), for combination medications, the dose/kg/interval should be specified for one of the medications in the combination, elemental preparations (eg, iron, zinc) should be ordered based on the desired dose of the element, not the salt
- Dosage units
  - metric units only, do not use ampules, tablets, bottles as the only dosage unit. If applicable, specify the concentration (eg, mg/mL)
- Diluent
  - specify if requiring diluent other than the standard (ie, 5% dextrose or 0.9% NaCl)
- Route of administration
- Frequency or interval
  - all orders for PRN medications must include an interval and an indication, do not use range orders with variable dosing frequencies (eg, q 4 - 6 hours)
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For more detailed information regarding medication orders, please refer to the medication orders policy C-78 located in the MUSC Medical Center Clinical Policy Manual. This manual may be accessed online at www.musc.edu/medcenter/policy/Med/clintoc.html.

Online Adverse Drug Reaction Reporting

Practitioners are urged to use the University HealthSystem Consortium Patient Safety Net to report potential ADRs. To access the reporting system click on the UHC PSN desktop icon located on all LYNX work stations and follow the menu-driven instructions. Please include all pertinent details

related to the occurrence including suspect medication(s), dose(s), clinical presentation, description of how the ADR was managed, and patient outcome.

Did You Know...

The Food and Drug Administration (FDA) has released a Public Health Advisory regarding important new safety information about taking 5-hydroxytryptamine receptor agonists (ie, triptans) concomitantly with selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs) [Table 1].

The combination may result in life-threatening serotonin syndrome, and is most likely to occur when starting or increasing the dose of a triptan, SSRI, or SNRI. Signs and symptoms of serotonin syndrome include restlessness, hallucinations, loss of coordination, tachycardia, rapid changes in blood pressure, hyperpyrexia, overactive reflexes, nausea, vomiting, and diarrhea. FDA has requested that the prescribing information for each of the medications be updated to warn of the possibility of serotonin syndrome when these medications are taken concomitantly.

Table 1. Medications that are Classified as a SSRI, SSNRI, or Triptans

SSRIs	SNRIs	Triptans
• Citalopram (Celexa®)*	• Duloxetine (Cymbalta®)*	• Almotriptan (Axert®)*
• Escitalopram (Lexapro®)	• Venlafaxine (Effexor®)	• Eletriptan (Relpax®)*
• Fluoxetine (Prozac®)		• Frovatriptan (Frova®)*
• Fluoxetine/olanzapine (Symbyax®)*		• Naratriptan (Amerge®)*
• Fluvoxamine (various)		• Rizatriptan (Maxalt®, Maxalt®-MLT)*
• Paroxetine (Paxil®)		• Sumatriptan (Imitrex®)
• Sertraline (Zoloft®)		• Zolmitriptan (Zomig®, Zomig®-ZMT)*

* Nonformulary Status

Formulary Update

The Pharmacy and Therapeutics Committee recently approved the following formulary changes:

Additions:
Effective July 1, 2006
NovoLog® Mix 70/30
100-units/10-mL vials

Effective July 17, 2006
Pregabalin (Lyrica®)
50-, 75-, 100-, and 150-mg capsules

Addition with restriction:
Effective July 17, 2006
Risperidone long-acting injection (Risperdal® Consta®)
25-, 37.5-, and 50-mg pre-filled syringes

Restriction Added:
Effective July 1, 2006
As part of the initiative to limit the use of regular insulin (Novolin® R), the subcutaneous administration of this product will be restricted to the Diabetes Management Service.
100-units/10-mL vials

Change in Restriction:
The use of factor VIIa recombinant (rFVIIa) for closed-space injury, cardiothoracic surgery, liver transplantation, and trauma will be restricted to attending physicians and fellows.

Line-extensions:
Effective July 17, 2006
Hyaluronidase (Vitrase®)
200-units/mL injection

Vitamin A (various)
10,000- and 15,000-unit tablets

Quetiapine fumarate (Seroquel®)
50- and 400-mg tablets

Deletions:
Effective July 1, 2006
Novolin® 70/30
100-units/10 mL vials

Effective July 17, 2006
Vitamin A (various)
25,000- and 50,000-unit capsules

Zalcitabine (Hivid®)
0.375- and 0.75-mg tablets

Stavudine (Zerit®)
15-, 20-, 30-, and 40-mg capsules; 1-mg/mL injection

Delavirdine mesylate (Rescriptor®)
100-mg tablets

Amprenavir (Agenerase®)
50-mg tablets; 15-mg/mL solution

Indinavir sulfate (Crixivan®)
200- and 400-mg capsules

Saquinavir mesylate (Invirase®)
200-mg capsules

Saquinavir (Fortovase®)
200-mg capsules