

Drotrecogin Alfa Activated (Xigris) Protocol Orders

- **PRESCRIBERS:**

- Orders must be completely filled out and signed by the pulmonary intensivist or infectious disease consultant physician. No verbal orders will be accepted. No incomplete orders will be accepted.

- **PATIENT CHARACTERISTICS:**

- Adult patients 18 years of age or older who have severe sepsis and who have an especially high risk of dying from sepsis, as reflected by an **APACHE II score ≥ 25** based on their general health and the severity of their illness. Drotrecogin alfa must be administered within 48 hours once the patient has met the criteria outlined below in Section I and does not have any contraindications as listed in Section II.

I. CRITERIA FOR TREATMENT WITH DROTRECUGIN ALFA (ACTIVATED):

****MD must document criteria in columns provided as indicated.**

****Sections A, B, C, D, & E are required.**

A. Patient must be in ICU or admitted to ICU (waiting for an available bed.)

B. Infection: Patient must have suspected or proven infection.

Yes	No	Infection Type	Criteria
			Known or suspected infection (<i>Examples: positive blood culture, perforated viscus, white blood cells in normally sterile body fluid, pneumonia, etc.</i>)

C. SIRS: Patient must have 3 or more of the following 4 SIRS criteria. If the patient is on drugs that modify the heart rate, the patient must have 2 of the following 4 SIRS criteria.

Yes	No	Document Result	Criteria
		Tmax =	Fever $\geq 38^{\circ} \text{C}$ (100.4°F), or hypothermia $\leq 36^{\circ} \text{C}$ (96.8°F)
		HR =	Heart rate ≥ 90 beats/minute
		RR = PaCO ₂ =	Respiratory rate ≥ 20 breaths per minute, or a PaCO ₂ ≤ 32 mm Hg, or mechanical ventilation for an acute process
		WBC =	White blood cell (WBC) count $\geq 12,000/\text{mm}^3$, or $\leq 4,000/\text{mm}^3$, or $> 10\%$ immature neutrophils



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D. Acute Organ Dysfunction: Patient has at least 1 acute organ dysfunction (lasting no longer than 24 hours) due to sepsis.

Yes	No	Document Result	Criteria
		SBP =	<ul style="list-style-type: none"> CARDIOVASCULAR (any of the following) An arterial systolic blood pressure of ≤ 90 mm Hg for at least 1 hour despite adequate fluid resuscitation, OR
		MAP =	A mean arterial pressure (MAP) ≤ 70 mm Hg for at least 1 hour despite adequate fluid resuscitation, OR
			The need for vasopressors to maintain systolic blood pressure (SBP) ≥ 90 mm Hg or MAP ≥ 70 mm Hg despite adequate fluid resuscitation
		UO =	<ul style="list-style-type: none"> RENAL Urine output < 0.5 mL/kg/hr for one hour, despite adequate fluid resuscitation
		PaO ₂ /FiO ₂ =	<ul style="list-style-type: none"> RESPIRATORY PaO₂/FiO₂ ≤ 250 unless the lung is the only dysfunctional organ, then the PaO₂/FiO₂ must be ≤ 200
		Platelet Count =	<ul style="list-style-type: none"> HEMATOLOGY Platelet count of $< 80,000/\text{mm}^3$ or a 50% decrease in the platelet count from the highest value recorded over the last 3 days
		pH = Base deficit = Lactate level =	<ul style="list-style-type: none"> METABOLIC ACIDOSIS pH ≤ 7.30 or base deficit ≥ 5.0 mmol/L and a plasma lactate level $> 1.5x$ the upper limit of normal.

B. APACHE Score: Patient's APACHE Score must be ≥ 25 .

Yes	No	Document Result	Criteria
		Apache Score =	Apache score must be ≥ 25 . See: (http://www.sfar.org/scores2/scores2.html)

II. CONTRAINDICATIONS:

None of the following contraindications can be present:

Yes	No	Contraindication
		Moribund state in which death is perceived to be imminent
		Patients not expected to survive 28 days because of uncorrectable medical or surgical conditions such as poorly controlled malignancy or other end-stage disease.
		Active internal bleeding
		Recent (within 3 months) hemorrhagic stroke
		Recent (within 2 months) intracranial or intraspinal surgery, or severe head trauma
		Trauma patients with increased risk of life-threatening bleeding
		Patients with an epidural catheter
		Patients with history of intracranial neoplasm, mass lesions of the CNS, or evidence of cerebral herniation
		Known hypersensitivity to drotrecogin alfa or any component of the product



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Patient Allergies: _____

III. WARNINGS:

Bleeding is the most serious adverse effect associated with drotrecogin alfa therapy. Each patient being considered for therapy with drotrecogin alfa should be carefully evaluated and anticipated benefits weighed against potential risks associated with therapy.

Yes	No	Contraindication
		Concurrent therapeutic heparin (≥ 15 units/kg/hr)
		Platelet count $<30,000 \times 10^6/L$, even if the platelet count is increased after transfusion
		INR > 3.0
		History of a congenital bleeding diathesis or other known bleeding diathesis except for acute coagulopathy related to sepsis
		Recent (within 6 weeks) gastrointestinal bleeding
		Chronic severe hepatic disease (known or suspected portal hypertension, chronic jaundice, cirrhosis, or chronic ascites)
		Recent administration (within 3 days) of thrombolytic therapy (Note: Catheter clearance doses are not contraindications.)
		Recent use (within 7 days) of oral anticoagulants (e.g. warfarin or glycoprotein IIb/IIIa inhibitors)
		Recent administration (within 7 days) of aspirin > 650 mg per day or other platelet inhibitors, e.g. clopidogrel (Plavix), ticlopidine (Ticlid)
		Known hypercoagulable condition: <ul style="list-style-type: none"> • Resistance to activated protein C • Hereditary deficiency of protein C, protein S, or antithrombin III • Presence of anticardiolipin antibody, antiphospholipid antibody, lupus anticoagulant, or homocysteinemia • Or recently documented (within 3 months) or highly suspected DVT or PE
		Recent (within 3 months) ischemic stroke
		Intracranial arteriovenous malformation or aneurysm
		Any other condition in which in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location
		Patients who are pregnant or breastfeeding

- Drotrecogin alfa should be discontinued 2 hours prior to undergoing an invasive surgical procedure or procedures with an inherent risk of bleeding. Once adequate hemostasis has been achieved initiation of drotrecogin alfa may be reconsidered 12 hours after major invasive procedures or surgery or restarted immediately after uncomplicated less invasive procedures.



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- **LABORATORY MONITORING:**

- Daily PT, platelets, and HCT (MD to increase frequency as clinically indicated.)
- Discontinue drug and notify MD if platelets < 30,000; INR > 3.0; PTT > 100; or life-threatening bleed occurs.

- **IV/MEDICATIONS:**

- Drotrecogin alfa 24 mcg/kg/hr x 96 hours via continuous intravenous infusion
- Patient weight: _____ kg; Patient height: _____ in.

DATE/TIME

PHYSICIAN'S SIGNATURE



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