

Drotrecogin Alfa (Activated Protein C) for Severe Sepsis

Patient factors determining administration of drotrecogin alfa:

1. The patient must be in or admitted to a critical care setting prior to and during the drug's administration
2. The patient or family must be consenting to undergo all necessary life support measures
3. The patient must have a favorable prognosis of survival (life expectancy of > 6 months) aside from this sepsis episode
4. Having at least **3 Systemic Inflammatory Response Syndrome (SIRS)** criteria (Check all that apply):
 - Temp > 38°C OR Temp < 36°C
 - HR \geq 90bpm
 - RR \geq 20 breaths/min OR PaCO₂ \leq 32mmHg OR mechanical ventilation
 - WBC \geq 12,000/mm³ OR WBC \leq 4,000/mm³ OR >10% bands
5. Patient must have **two or more** of the following acute (< 48 hours) organ failures.
 - Cardiovascular**
 - i. **An arterial systolic blood pressure of \leq 90mmHg or a mean arterial pressure (MAP) of \leq 70mmHg for at least one hour despite adequate fluid resuscitation, adequate intravascular volume status, or the use of vasopressors**
 - Renal**
 - i. Urine output < 0.5ml/kg/hr for \geq 4 continuous hours, despite adequate fluid resuscitation (unless patient is on chronic hemodialysis)
 - Respiratory**
 - i. PaO₂/FiO₂ \leq 250 OR
 - ii. If the patient has pneumonia, a PaO₂/FiO₂ < 200
 - Hematology**
 - i. Platelet count < 80,000/mm³ OR
 - ii. 50% decrease in the platelet count from the highest value recorded over the past 3 days
 - Hepatic**
 - i. Serum bilirubin > 2mg/dL x 2 days OR
 - ii. Elevated liver enzymes > 2x the upper limit of normal
 - Metabolic Acidosis**
 - i. pH \leq 7.3 OR
 - ii. Base deficit \geq 5mEq/L in conjunction with a plasma lactic acid level > 1.5 times the upper limit of normal
6. Proven or suspected infection (Check all that apply)
 - Gram negative isolate
 - Gram positive isolate
 - Multiple organisms cultured
 - Viral
 - Fungal
 - No pathogen isolated

Dose: 24mcg/kg/hr for 96 hours (4 days)

Contraindications

- Active internal bleeding
- Recent (within 3 months) hemorrhagic stroke
- Recent (within 2 months) intracranial, intraspinal surgery, or severe head trauma
- Trauma patients with increased risk of life-threatening bleeding
- Presence of an epidural catheter
- Patients with intracranial neoplasm OR mass lesion OR evidence of cerebral herniation
- Patients with a known hypersensitivity to drotrecogin alfa (or any component of the product)

Warnings: (Bleeding is the most common side effect associated with Drotrecogin alfa and the potential benefits should outweigh the potential risks associated with therapy)

- Concomitant use of heparin (≥ 15 units/kg/hr), low-molecular weight heparin, warfarin, or any other anticoagulant therapy as FULL-DOSE anticoagulation therapy
- Patients with known or interventional chest or abdominal trauma are at an increased risk for bleeding (i.e. chest tubes or surgeries)³
- Platelet count $< 30,000/\text{mm}^3$
- Patients with INR > 3
- Recent administration (within 3 days) of thromolytic therapy
- Recent (within 6 weeks) GI bleed
- Recent administration (within 7 days) of oral anticoagulants OR Glycoprotein IIb/IIIa inhibitors
- Recent administration (within 7 days) of aspirin $> 650\text{mg/day}$ OR any other platelet inhibitors
- Recent (within 3 months) ischemic stroke
- Presence of intracranial arteriovenous malformation or aneurysm
- Known bleeding diathesis except for acute coagulopathy due to sepsis (e.g. hemophilia)
- Chronic severe hepatic disease (e.g. cirrhosis with portal hypertension)
- Any condition in which bleeding constitutes a significant risk OR makes it difficult to treat a bleeding episode because of its location
- **Discontinue drotrecogin alfa 2 hours pre-op and 12 hours post-op**
- **Hold drotrecogin alfa 1 hour before and 1 hour after line changes**

Pregnancy Category **C**

Pediatrics data is currently in study

Patients $> 135\text{kg}$ have not been studied