

**DROTRECIGIN ALPHA (ACTIVATED)
in Adults with Severe Sepsis
(RECOMBINANT HUMAN ACTIVATED PROTEIN C)
PREPRINTED ORDER**

DRAFT

KEY: R - REQUISITIONED P - PROCESSED (KARDEX) P & T 00/00

NON-MEDICATION ORDERS	R	P	MEDICATION ORDERS	P
<ol style="list-style-type: none"> 1. Patient meets all inclusion criteria and none of the exclusion criteria. (See criteria on Page 1) 2. Complete all invasive procedures (including line placement) prior to initiating drotrecogin infusion. 3. Baseline CBC, INR, aPTT prior to infusion, if not done in previous 24h. 4. CBC, INR daily while on drotrecogin. 5. Assess and document all venous/arterial puncture sites, urine, stool, gastric secretions, emesis for bleeding q 6h while on drotrecogin. 6. Avoid venous or arterial punctures during drotrecogin infusion if possible. 7. Check vitals and neurologic status q 6h during drotrecogin infusion and p.r.n. 8. Notify attending physician if: <ul style="list-style-type: none"> • platelets < 30 x 10⁹/L • INR > 3.0 • neurological deterioration • signs of bleeding (hold drotrecogin infusion and notify pharmacy) 			<p>Patient's actual or estimated body weight _____kg*</p> <p><i>*Note: For patients >135 kg, maximal weight of 135 kg will be used to calculate dose requirements.</i></p> <ol style="list-style-type: none"> 1. Administer drotrecogin 24mcg/kg/hr I.V. continuous infusion for a total of 96 hours via dedicated peripheral or central line. Each 12 hour infusion bag to contain _____ mg drotrecogin in _____ mL 0.9% NaCl as per chart on reverse. Run at _____ mL/h x 96h. Infusion to be prepared by Pharmacy. 2. Discontinue LMWH, NSAIDS, ASA, antiplatelet drugs or I.M. injections while on drotrecogin. If on unfractionated heparin, the maximum dose should not exceed 15,000 units/24 hours. <input type="checkbox"/> heparin _____ <input type="checkbox"/> no heparin 3. Hold drotrecogin 2 hours prior to invasive procedures and resume 2 hours after procedure or 12 hours after major surgery. Document infusion interruptions in patient chart. <div style="border: 1px solid black; padding: 10px; margin-top: 20px; text-align: center;"> <p>STAFF INTENSIVIST APPROVAL REQUIRED</p> <p>Approved by Staff Intensivist: _____ (PRINT NAME)</p> </div>	

PRESCRIBER'S PRINTED NAME / SIGNATURE:			DATE (YYYY/MM/DD):	TIME:	
PROCESSOR INITIALS:	DATE (YYYY/MM/DD):	TIME:	RN INITIALS:	DATE (YYYY/MM/DD):	TIME:

The APACHE II Severity of Disease Classification Systems

Physiologic Variable	High Abnormal Range				Low Abnormal Range				
	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature – rectal (°C)	≥41°	39 to 40.9°		38.5 to 38.9°	36 to 38.4°	34 to 35.9°	32 to 33.9°	30 to 31.9°	≤29.9°
Mean Arterial Pressure – mm Hg	≥160	130 to 159	110 to 129		70 to 109		50 to 69		≤49
Heart Rate (ventricular response)	≥180	140 to 179	110 to 139		70 to 109		55 to 69	40 to 54	≤39
Respiratory Rate (non-ventilated or ventilated)	≥50	35 to 49		25 to 34	12 to 24	10 to 11	6 to 9		≤5
Oxygenation: A-aDO ₂ or PaO ₂ (mm Hg)			200 to 399		<200				
a. FI _O ₂ ≥0.5 record A-aDO ₂	≥500	350 to 499			PaO ₂ >70	PaO ₂ 61 to 70		PaO ₂ 55 to 60	PaO ₂ <55
b. FI _O ₂ <0.5 record PaO ₂									
Arterial pH (preferred)	≥7.7	7.6 to 7.69		7.5 to 7.59	7.33 to 7.49		7.25 to 7.32	7.15 to 7.24	<7.15
Serum HCO ₃ (venous mEq/l)	≥52	41 to 51.9		32 to 40.9	22 to 31.9		18 to 21.9	15 to 17.9	<15
(not preferred, but may use if no ABGs)									
Serum Sodium (mEq/l)	≥180	160 to 179	155 to 159	150 to 154	130 to 149		120 to 129	111 to 119	≤110
Serum Potassium (mEq/l)	≥7	6 to 6.9		5.5 to 5.9	3.5 to 5.4	3 to 3.4	2.5 to 2.9		<2.5
Serum Creatinine (mg/dl)	≥305	170 to 304	130 to 169		54 to 129		<54		
Double point score for acute renal failure									
Hematocrit (%)	≥60		50 to 59.9	46 to 49.9	30 to 45.9		20 to 29.9		<20
White Blood Cell Count (total/mm ³) (in 1000s)	≥40		20 to 39.9	15 to 19.9	3 to 14.9		1 to 2.9		<1
Glasgow Coma Score (GCS)									
Score = 15 minus actual GCS									

- A. Total Acute Physiology Score (sum of 12 above points)
- B. Age points (years) ≤44 = 0, 45 to 54 = 2, 55 to 64 = 3, 65 to 74 = 5, ≥75 = 6
- C. Chronic Health Points (see below)

Total APACHE II Score (add together the points from A+B+C)

Chronic Health Points: If the patient has a history of severe organ system insufficiency or is immunocompromised as defined below, assign points as follows:

- 5 points for nonoperative or emergency postoperative patients
- 2 points for elective postoperative patients

Definitions: organ insufficiency or immunocompromised state must have been evident **prior** to this hospital admission and conform to the following criteria: **Liver** – biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma. **Cardiovascular** – New York Heart Association Class IV. **Respiratory** – Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction (i.e., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mmHg), or respirator dependency. **Renal** – receiving chronic dialysis.

Immunocompromised – the patient has received therapy that suppresses resistance to infection (e.g., immunosuppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, e.g., leukemia, lymphoma, AIDS).

Interpretation of Score:

0 to 4 = ~4% death rate	10 to 14 = ~15% death rate	20 to 24 = ~40% death rate	30 to 34 = ~75% death rate
5 to 9 = ~8% death rate	15 to 19 = ~25% death rate	25 to 29 = ~55% death rate	Over 34 = ~85% death rate

§ Adapted from Crit Care Med 1985;13:818-829

**DROTRECOGIN ALPHA (ACTIVATED)
in Adults with Severe Sepsis
(RECOMBINANT HUMAN ACTIVATED PROTEIN C)**

INCLUSION CRITERIA - Must Answer "YES" to all 3 Criteria

1. SUSPECTED OR PROVEN SERIOUS INFECTION

Must have at least 1 of the following (check all that apply):

- | | |
|---|--|
| <input type="checkbox"/> Documented infection | <input type="checkbox"/> White cells in a normally sterile body fluid |
| <input type="checkbox"/> Perforated viscus | <input type="checkbox"/> Radiologic evidence of pneumonia with purulent sputum |
| <input type="checkbox"/> Syndrome associated with a high likelihood of infection (e.g. ascending cholangitis). Please specify: _____ | |

2. SIGNS OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

Must have at least 3 of the following (check all that apply):

- | | |
|--|---|
| <input type="checkbox"/> Core temperature $\geq 38^{\circ}\text{C}$ or $\leq 36^{\circ}\text{C}$ | <input type="checkbox"/> Heart rate ≥ 90 beats/min |
| <input type="checkbox"/> Respiratory rate ≥ 20 breaths/min or $\text{PaCO}_2 \leq 32\text{mm Hg}$ or the use of mechanical ventilation for an acute respiratory process | <input type="checkbox"/> White blood cell count $\geq 12 \times 10^9/\text{L}$ or $\leq 4 \times 10^9/\text{L}$ or a differential showing $> 10\%$ immature neutrophils |

3. ONGOING EVIDENCE OF SEPSIS-INDUCED MULTIPLE ORGAN DYSFUNCTION (NOT > 48 HOURS) OR APACHE II SCORE ≥ 25 WITH AT LEAST ONE SEPSIS-INDUCED ORGAN FAILURE

Must meet at least TWO of the following criteria (check all that apply):

- Cardiovascular:** The use of vasopressors or $\text{SBP} \leq 90\text{mm Hg}$ or $\text{MAP} \leq 70\text{mm Hg}$ for at least 1 hour, despite adequate fluid resuscitation
 - Renal:** Urine output $< 0.5\text{mL/kg/hr}$ for one hour, despite adequate fluid resuscitation
 - Respiratory:** Mechanical ventilation (invasive or non-invasive) with $\text{PaO}_2 / \text{FiO}_2 \leq 250$
 - Hematologic:** Platelet count $< 80 \times 10^9/\text{L}$ in the last 3 days or platelet count decreased by 50% in the last 3 days
 - Arterial Lactic Acidosis:** Plasma lactate $> 3.3 \text{mmol/L}$
- OR
- One of the above sepsis-induced organ failures AND APACHE II Score ≥ 25**

Please use website to calculate (www.sfar.org/scores2/apache22.html), or use attached form to calculate manually

Score: _____ Calculated by: _____ Time: _____

EXCLUSION CRITERIA - All must be checked as "NO"

	YES	NO
<input type="checkbox"/> Patient death expected within 28 days due to underlying uncorrectable medical condition		
<input type="checkbox"/> Moribund state in which death is perceived to be imminent		
<input type="checkbox"/> Sepsis-induced organ failure > 48 hours		
<input type="checkbox"/> Evidence or concern for active internal bleeding		
<input type="checkbox"/> Recent (< 3 months) hemorrhagic stroke		
<input type="checkbox"/> Recent (< 2 months) intracranial or intraspinal surgery		
<input type="checkbox"/> Presence of an epidural catheter		
<input type="checkbox"/> Recent (< 2 months) severe head trauma		
<input type="checkbox"/> Evidence of CNS mass lesion or cerebral herniation		
<input type="checkbox"/> Recent trauma, considered to be at increased risk of life-threatening bleeding		

WARNINGS - Consider eligibility on an individual basis based on benefit-to-risk assessment

- Platelet count $< 30 \times 10^9/\text{L}$, even if the platelet count is increased after transfusions
- Recent administration (within 7 days) of thrombolytics, oral anticoagulants or glycoprotein IIb-IIIa inhibitors
- Recent administration (within 7 days) of ASA or other platelet inhibitors (i.e. clopidogrel, ticlopidine, dipyridamole, NSAIDs)
- Recent therapeutic doses of heparins (i.e. unfractionated heparin within 8 hours or low molecular weight heparin within 12 hours)
- Elevated INR
- Recent (within 6 weeks) gastrointestinal bleeding
- Recent (within 3 months) ischemic stroke
- Intracranial arteriovenous malformation or aneurysm
- Known bleeding diathesis

DOSING CHART
12 Hour Infusion Bags - to provide 24 mcg/kg/hr

Pt. Weight (Kg)	Drug Amt. (mg)	NS Bag Size (mL)	Rate (mL/hr)	Pt. Weight (Kg)	Drug Amt. (mg)	NS Bag Size (mL)	Rate (mL/hr)	Pt. Weight (Kg)	Drug Amt. (mg)	NS Bag Size (mL)	Rate (mL/hr)
40	15	100	6.4	73	25	250	17.5	106	30	250	21.2
41	15	100	6.6	74	25	250	17.8	107	30	250	21.4
42	15	100	6.7	75	25	250	18	108	35	250	18.5
43	15	100	6.9	76	25	250	18.2	109	35	250	18.7
44	15	100	7	77	25	250	18.5	110	35	250	18.9
45	15	100	7.2	78	25	250	18.7	111	35	250	19
46	15	100	7.4	79	25	250	19	112	35	250	19.2
47	15	100	7.5	80	25	250	19.2	113	35	250	19.4
48	15	100	7.7	81	25	250	19.4	114	35	250	19.5
49	15	100	7.8	82	25	250	19.7	115	35	250	19.7
50	15	100	8	83	25	250	19.9	116	35	250	19.9
51	15	100	8.2	84	25	250	20.2	117	35	250	20.1
52	15	100	8.3	85	25	250	20.4	118	35	250	20.2
53	15	100	8.5	86	25	250	20.6	119	35	250	20.4
54	15	100	8.6	87	25	250	20.9	120	35	250	20.6
55	15	100	8.8	88	25	250	21.1	121	35	250	20.7
56	20	100	6.7	89	25	250	21.4	122	35	250	20.9
57	20	100	6.8	90	30	250	18	123	35	250	21.1
58	20	100	7	91	30	250	18.2	124	35	250	21.3
59	20	100	7.1	92	30	250	18.4	125	40	250	18.8
60	20	100	7.2	93	30	250	18.6	126	40	250	18.9
61	20	100	7.3	94	30	250	18.8	127	40	250	19.1
62	20	100	7.4	95	30	250	19	128	40	250	19.2
63	20	100	7.6	96	30	250	19.2	129	40	250	19.4
64	20	100	7.7	97	30	250	19.4	130	40	250	19.5
65	20	100	7.8	98	30	250	19.6	131	40	250	19.7
66	20	100	7.9	99	30	250	19.8	132	40	250	19.8
67	20	100	8	100	30	250	20	133	40	250	20
68	20	100	8.2	101	30	250	20.2	134	40	250	20.1
69	20	100	8.3	102	30	250	20.4	135	40	250	20.3
70	20	100	8.4	103	30	250	20.6	>135	use 135 Kg dose		
71	20	100	8.5	104	30	250	20.8				
72	20	100	8.6	105	30	250	21				