Northern Ireland Intensive Care Society

PRESCRIBING CRITERIA CHECKLIST FOR DROTRECOGIN ALFA (ACTIVATED)
Use this checklist alongside NIICS guidelines for use.
Consider administration to adult patients with severe sepsis and > 1 organ failure*

1. Contraindications (from UK Summary of Product Characteristics)	
Any of the following: ❑ Active internal bleeding. ❑ Patients with intracranial pathology; mass lesion or evidence of cerebral herniation. ❑ Concurrent heparin therapy ≥ 15 international units/kg/hr ❑ Known bleeding diathesis *except* for acute coagulopathy related to sepsis. ❑ Chronic, severe hepatic disease. ❑ Platelet count <30 x 10^9/l, even if platelet count is increased after transfusions.** ❑ Less than 12 hours since any surgery that required general or spinal anaesthesia ❑ Any post-operative patient with evidence of active bleeding. ❑ History of severe head trauma requiring hospitalization, intracranial or intraspinal surgery, or haemorrhagic stroke within the previous 3 months. ❑ History of intracerebral arteriovenous malformation or cerebral aneurysm. ❑ Planned insertion of an epidural catheter or < 6 hours since removal of same.*** ❑ Gastro-intestinal bleeding within the last 6 weeks that has required medical intervention unless definitive surgery has been performed. ❑ Trauma patients at increased risk of bleeding. ❑ Known hypersensitivity to drotrecogin alfa (activated) or any component of the product. ❑ Decision not to pursue aggressive medical care.	(1 or more?**) ❑ Yes **Patient is NOT eligible for drotrecogin** ❑ No **Proceed to Section 2.**
2. Other Exclusions	
❑ Recent administration (within 3 days) of thrombolytic therapy (except for treatment of thrombosed catheters) ❑ Recent (within 3 months) ischaemic stroke	(1 or more?) ❑ Yes **Patient is NOT eligible for drotrecogin** ❑ No **Proceed to Section 3.**
3. Strongly suspected or proven infection	
Patient has known or suspected infection defined as: ❑ Positive culture ❑ White cells in a normally sterile body fluid ❑ Perforated viscus ❑ Radiological and clinical evidence of pneumonia ❑ Other syndrome with high probability of infection (e.g., ascending cholangitis)	(1 or more?) ❑ Yes ❑ No **If no, patient is NOT eligible for drotrecogin**
4. Best standard of care	
Patient is receiving continuous monitoring and intensive care	❑ Yes ❑ No **If no, patient is NOT eligible for drotrecogin**

* NB Organ failure definition differs from that of Knaus (see Section 5)
** On its own, a platelet count < 30 x 10^9/L need not be an *absolute* contra-indication if the consultant intensivist considers that it is a result of Disseminated Intravascular Coagulation . Clinicians who prescribe it in this setting need to recognise that they are stepping outside the terms of the product license.
***prescription in the *presence* of an epidural catheter is outside the product licence.

Continued Overleaf

5. Multiple Organ System Dysfunction (Must have at least 2)	
Dysfunction defined as: ❑ CARDIOVASCULAR: Arterial systolic BP ≤ 90mmHg or a mean arterial pressure (MAP) ≤70mmHg for at least 1 hour despite adequate fluid resuscitation or adequate intravascular volume status **OR** The need for vasopressors to maintain systolic blood pressure (SBP) ≥ 90 mmHg or MAP ≥ 70 mmHg ❑ RENAL: Urine output < 0.5 ml/kg/hr for > 1 hour, despite adequate fluid resuscitation (excl. CRF). ❑ RESPIRATORY: PaO_2/FIO_2 ≤ 33 kPa ❑ HEMATOLOGIC: Platelet count < 80 x 10^9/l or decreased by 50% from highest value in the previous 72 hours **AND** Other evidence of DIC ❑ METABOLIC: PH ≤ 7.30 or base deficit ≥ 5 mmol/l with plasma lactate > 2.4mmol/l	(**2** or more?) ❑ Yes ❑ No **If no, patient is NOT eligible to receive drotrecogin**
6. Acuity	
Less than 72 hours after the onset of the first sepsis induced organ dysfunction **OR** Less than 48 hours after a new deterioration in existing multiple organ dysfunction consistent with a new septic insult. There is no value (and possible harm) in delaying treatment to towards the end of these time windows. Trends in vasopressor requirement may influence need for treatment, but can usually be determined within a few hours.	❑ Yes ❑ No **If no, patient is NOT eligible for drotrecogin**

Any of the following should prompt caution regarding administration of Drotrecogin alfa (activated):

- Age < 18 (Marketing approval is for use in adults)
- INR >3.0 or prothrombin time >36 seconds
- Patients receiving treatments which decrease clotting activity. Use of Aspirin/glycoprotein IIb/IIIa inhibitor within 7 days are suitable examples
- Recent administration (within 12 hours) of greater than 10,000 U of antithrombin III
- Patients who are pregnant or breastfeeding
- HIV+ with < 50 x 10^6 /l $CD4^+$ cells.
- Bone marrow, lung, liver, pancreas or small bowel transplant recipient.
- Chronic renal failure requiring haemodialysis or peritoneal dialysis
- Planned or anticipated surgery during the drug infusion period (infusion will need to be stopped at least 2 hours prior to surgery)

❑ **Patient deemed SUITABLE for administration of Drotrecogin alfa (activated)**

Patient Name: ……..…… **Hospital Nº:** ……...……...

Completed by: …….…… **Date/time:** ….:… **on** …/…/…

Intensive Care Consultant approving: ….……..…… **Date/time:** ….:… **on** …/…/…

NIICS Guidelines for use of Drotrecogin alfa (activated) (aPC)

These guidelines are only to be used in conjunction with Prescribing Criteria Checklist and are not a substitute for clinical judgement, nor should they be seen as a standard of care.

Storage.
Observe storage and compatibility restrictions

Reconstitution.
Choose appropriate vial sizes (20mg or 5mg) to minimise wastage/unnecessary expense.
During reconstitution of the drug minimise agitation to avoid degradation. If in doubt, consult Pharmacy.

Dose.
24 mcg/kg body weight/hour for total duration of 96 hours.

Side-effects.
The major concerns with the appropriate use of this drug relate to serious bleeding. The increased incidence of bleeding is anticipated to be largely confined to the time when the infusion is running.

Invasive procedures
Stop infusion at least 2 hours before invasive procedures (e.g. Central venous lines, arterial lines, or chest drains) or surgery. Following uncomplicated minor procedures, drotrecogin alfa (activated) can be commenced/recommenced immediately. Complicated/more invasive procedures may require a delay of up to 12 hours afterwards. Procedures in which direct compression of the potential bleeding point is difficult, eg large bore subclavian access, body cavity surgery, should prompt a longer delay than those where potential bleeding would be relatively easy to control.

In a surgical patient, notify the surgeon of the intent to use aPC.

Monitoring of coagulation status
Beware of the unpredicable effects of aPC on APTT assays. The latter are not useful to indicate ongoing drug effect or lack of the same.

Anticoagulant therapy.
Heparin administered at >15 i.u./kg/hr is a contra-indication for aPC use.
When patients require CRRT, attempt to run it without heparin, or indeed any anticoagulants other than aPC. If further anticoagulation proves necessary, consider low dose heparin. APTT should not be regarded as useful in guiding heparin dose in this situation.