

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Drotrecogin alpha (activated) for severe sepsis

Scope

Objective: to appraise the clinical and cost effectiveness of the new pharmaceutical treatment drotrecogin alfa-activated (Xigris) in its licensed indications for the treatment of severe sepsis.¹

Background: Severe sepsis is defined as sepsis associated with acute organ dysfunction. It usually results from bacterial infections, but it may occur in response to other pathogens, such as fungi, viruses, and parasites. Severe sepsis may develop as a result of events such as trauma, surgery and extensive burns, or illnesses such as cancer and pneumonia. Severe sepsis is a progressive condition and the risk of death increases as the severity of the sepsis increases. In the most severe form, it triggers a chain of events involving systemic inflammation and activation of clotting that can result in multiple organ failure and death. Multiple organ failure exists when two or more of the body's organs or systems start to dysfunction; this can include cardiovascular failure, which may result in septic shock. A recent study suggested that the criteria for severe sepsis was satisfied in the first 24 hours in the intensive care unit by 27.7% admissions in England, Wales and Northern Ireland.² It is estimated that the rate of death from severe sepsis ranges from 30% to 50% despite advances in critical care.

Severe sepsis often arises outside the intensive care unit, as a consequence of infection in medical or surgical patients. Routine management of the septic patient includes use of suitable antibiotics, taking into account any positive microbiological culture results, the likely source of infection and likely tissue uptake of the antibiotic and supportive treatments.

The technology: Drotrecogin alfa (activated) is a recombinant version of the natural plasma-derived protein C. The activated protein C inhibits cofactors Va and VIIIa, which are integral components of the coagulation cascade and thus, inhibits clot formation. It can also decrease inflammation and increase fibrinolysis.

Intervention(s)	Drotrecogin alfa (activated)
Population(s)	Adult patients with severe sepsis with multiple organ failure
Current standard treatments (comparators)	Supportive treatments including fluids, inotropes and vasopressors.

<p>Other considerations:</p>	<p>If the evidence allows, optimal timing and duration of drotrecogin alpha (activated) treatment should be defined.</p> <p>If the evidence allows, the appraisal will attempt to identify the criteria for selecting patients for whom this treatment would be particularly appropriate.</p> <p>Relevant outcome measures include overall mortality, length of ICU stay, functional status and quality of life in the long-term.</p> <p>Where the evidence allows the appraisal will consider how the severity of the disease affects the suitability for treatment with drotrecogin alpha (activated).</p>
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¹ Original remit from the Department of Health " *to appraise the clinical and cost effectiveness of the new pharmaceutical treatments including, drotrecogin alfa-activated (Xigris) and afelimomab (Segard), in their licensed indications for the treatment of severe sepsis and/or septic shock.*"

(Afelimomab will not receive a marketing authorisation within the time-span of this appraisal, and will therefore not be included.)

² Padkin AJ et al (2001) *The prevalence of severe sepsis in the first 24 hours in the ICU, in England, Wales and Northern Ireland.* Intensive Care Medicine 27:S458.