



Royal Pharmaceutical Society of Great Britain

Helping pharmacists achieve excellence

To:

Dr Carole Longson
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Dear Dr Longson,

Review of NICE Technology Appraisal Guidance No 84; drotrecogin alfa (activated) for severe sepsis; Proposal to defer the review

Thank you for the opportunity to comment on the above proposal and please accept my delay in responding at this late stage.

The RPSGB supports the views of the UK Clinical Pharmacists Association (UKCPA); Critical Care Group, regarding the deferral to review drotrecogin alfa guidelines. We feel that there is a need to review the current available guidance *before* the pending randomised controlled trial is published. As the proposed manufacturer's trial is still in the planning stage, it is likely to be three to four years or even more before data from these trials are available.

There has been considerable debate in the published literature on how drotrecogin alfa should be used, as well as several papers providing information on its safety and efficacy. A recent US study showed that 'real life' actual usage did not reflect guidelines developed from the original PROWESS trial, with incidences of adverse effects higher than predicted.¹ There is similar anecdotal evidence in the UK; the wide disparity in how drotrecogin alfa is used within the NHS, suggests that existing guidelines are not being followed.

A follow up study of the PROWESS subjects, published in November 2004, highlighted the differences in effect on mortality, depending on the definitions used in subgroup analysis.² The specific definitions were used to set the thresholds for receiving drotrecogin in septic patients, however, they differ in the USA and Europe, which is reflected in the product license. In addition, the definition of sepsis induced 'multi-organ failure' and the resulting treatment effect needs further examination, as this effect appears to be small.

In summary, there is a need to reduce the variability in current practice. We would recommend NICE to review the current guidance, taking into account the data from the PROWESS follow up study. Any new guidance could then be updated with data from the pending trial when published in three to four years time.

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Jeremy Holmes MA Chief Executive and Registrar

Patron: Her Majesty The Queen

We are willing to actively support NICE in a review of the current guidance and hope that the issues raised as above will be taken into consideration.

If you have any further questions please do not hesitate to contact me on the above number.

Yours sincerely



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Practice Pharmacist

Ref:

1. Crit Care Med 36(1):14-23
2. Crit Care Med 32(11):2207-2218

Cc:

Mr Mark Borthwick
Consultant Pharmacist
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