For debate
New therapeutic products and difficult decisions. The case of recombinant factor VIII in the management of haemophilia A
Colin Green and Ron Akehurst

Summary

New and expensive therapeutic products can place great pressure on health care purchasers. Often, evidence to support the inclusion of such products in the purchasing process is lacking or confusing, yet demand can be organized and forceful. In this paper we use the example of the introduction of recombinant factor VIII (rFVIII) in the management of haemophilia A, to highlight some problems purchasers face in deciding whether to fund its use. The introduction of rFVIII involves substantial extra funding requirements and the benefits afforded by its use are unclear. Although a case can be made for the use of rFVIII on the grounds of subjective future theoretical risks and intangible benefits, the purchasers of health care are charged with maximizing the present and obtainable benefits of the community at large, given finite resources. Guidelines produced by the United Kingdom Haemophilia Centre Directors Organization state rFVIII to be its treatment of choice for all haemophilia A patients, but offer no insight into the benefits attainable through the use of rFVIII, in terms of health outcomes. We report summary findings of Purchaser Intelligence Groups examining the use of rFVIII and offer comment on the problems associated with the implementation of therapeutic products such as rFVIII.

Keywords: haemophilia, purchaser guidance

There are a growing number of newly introduced therapeutic products which involve a substantial increase in funding but which offer an unclear picture of the benefits being purchased. These products, often marketed aggressively, are placing increasing pressure on health care purchasers. One such product currently receiving attention is recombinant factor VIII (rFVIII), used in the treatment of haemophilia A (severe or classical haemophilia A).

Treatment of haemophilia A, an X-linked recessive genetic disorder of blood coagulation caused by diminished or abnormal production of factor VIII (FVIII), has been managed through FVIII replacement therapy with the infusion of plasma-derived FVIII (pdFVIII). The availability, and increased public awareness, of a recombinant alternative to pdFVIII, for the management of haemophilia A, has focused attention on the potential costs and consequences of the recombinant product.

The United Kingdom Haemophilia Centre Directors Organization (UKHCDO) has recently published ‘guidelines on therapeutic products to treat haemophilia and other hereditary disorders’. In its specific recommendations for haemophilia A the UKHCDO states rFVIII to be its treatment of choice for all patients. It also indicates its order of patient priority, based on ‘ability to benefit’, should the introduction of rFVIII not be across all patients. Further to these guidelines, members of the UKHCDO have responded to regional variations in purchasing policy, with respect to the use of rFVIII, by raising awareness of the potential problems associated with ‘treatment by postcode’, whereby treatment choice may be dependent upon the patient’s postcode.

Although clinical opinion favours the use of rFVIII, issues related to the costs and the consequences associated with the use of rFVIII have proved to be less than clear, given the evidence available from the haemophilia literature. In response to the conflicting viewpoints surrounding rFVIII, a number of ‘Purchaser Intelligence Groups’ have produced guidance notes to synthesize the available literature and offer policy advice. Such Purchaser Groups have found that rFVIII involves substantial extra funding but offers no immediate benefit, in terms of health status or health gain. Work recently undertaken within the Trent Working Group on Acute Purchasing (TWGAP) estimated that a purchaser community (population approximately 500 000) wishing to fund the use of rFVIII as the treatment of choice for haemophilia A, as advocated through the UKHCDO guidelines, would be required to devote in excess of

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£250 000 extra per year to the treatment of haemophilia A. In return for devoting such a level of additional resource to the treatment of haemophilia A, purchasers of health care could expect no direct benefit, in terms of health outcomes, from the use of rFVIII.

The perceived benefit stemming from the use of rFVIII lies in the clinical belief that it is better placed to contend with the next, as yet unknown, virus or agent. This potential benefit is based on what can only be the subjective assessment of unknown risk, and may be much influenced by the great hardship undoubtedly suffered within the haemophilic population through previous experiences with the transmission of HIV and the hepatitis C virus.7

Purchasers are charged with considering the health of the community at large, given budget constraints, and must assess the potential benefit of any new therapy in the light of its 'opportunity cost'. In the resource constrained National Health Service (NHS) and in the absence of national guidance or additional earmarked funding to facilitate the use of rFVIII, purchasers are directed to make their own evaluation of the benefits of rFVIII. Those seeking funding for the use of rFVIII must accept that decision-makers are placed in an unenviable position whereby they must either (1) decide not to fund the use of rFVIII and expose themselves to the consequences of the unquantifiable possibility of future infection-causing viruses being transmitted through pdFVIII (assuming rFVIII is better placed to contend with the unknown virus or agent) or (2) decide to fund the use of rFVIII (across all patients or across certain patient categories), thereby foregoing the opportunity of maximizing the immediate purchase of health gain. Given the current financial climate, the decision to fund rFVIII would ultimately require the withdrawal of health care services currently purchased for other sectors of the community.

A telephone survey of Health Authorities in England was undertaken in mid-1997 to gauge the regional variations in purchaser policy with respect to rFVIII. The findings from this survey are shown in Table 1. It would appear that the significant financial investment required through the use of rFVIII as the treatment of choice was being judged as too high in relation to the associated opportunity costs.

The case of rFVIII highlights the problems faced in the interpretation and implementation of so-called evidence-based guidelines. When guidelines on therapeutic products fail to demonstrate their significance in terms of quantifiable health gain, as is the case with those guidelines recently published by the UKHCDO, and fail to address the issue of the opportunity cost of treatment, it should be no surprise that difficulties arise in their acceptance and implementation, and that regional variations in purchasing policy create problems such as 'treatment by postcode'.

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### References


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### Table 1 Recombinant factor VIII in the management of haemophilia A: the policy position of Health Authorities in England*

<table>
<thead>
<tr>
<th>Policy position of Health Authorities</th>
<th>Health Authorities numbers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding the use of recombinant factor VIII across all patients</td>
<td>4 (4.1)</td>
</tr>
<tr>
<td>Funding the use of recombinant factor VIII across some patient categories</td>
<td>27 (27.5)</td>
</tr>
<tr>
<td>Not funding the use of recombinant factor VIII</td>
<td>50 (51.0)</td>
</tr>
<tr>
<td>Health authorities not responding</td>
<td>17 (17.3)</td>
</tr>
<tr>
<td>Total</td>
<td>98 (100)</td>
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</tbody>
</table>

*Health Authorities were contacted in May 1997.*