2 May 2001

Dear Colleague,

Re: **Shortage of Recombinant Factor VIII:**

I am writing to you to update you on the latest information available on the supply of FVIII to the UK. Dr Hill is currently ill and I am deputising for him during his absence, anticipated to be at least two months.

The reduction in supply of both Kogenate and Helixate, which began last Autumn, has worsened considerably this year. There have been no significant releases of Kogenate and Helixate since January. This has been caused by a failure of the Bayer, Berkley, plant to comply with FDA requirements for monitoring of bacterial counts in the air and water at a very early stage in manufacture. Although this should not affect the safety of the final product in any way, since bacteria are filtered out of the water at an early stage, some of the batches manufactured during this period will never be released. Additional quality control steps and pyrogen testing of the final product have been introduced. These steps have effectively prolonged the manufacturing process and will slow release further.

It is anticipated that production and releases of Kogenate/Helixate during 2001 will consequently fall significantly below the levels achieved during 2000. Projected production levels for 2002 are currently unknown. It is expected that a batch of Kogenate and Helixate will be released from the Bayer packing plant in Rosea, Italy, in the next few days. This will be distributed around Europe on a pro rata basis and amounts to about four weeks normal supply. Apart from this, no large releases of Kogenate or Helixate are anticipated for a further hundred days or so. After that time, a normal rate of release of Kogenate is expected to resume. The supply of Helixate is expected to remain significantly reduced until early 2002, however.

Normally, approximately13.5 million units of all brands of recombinant factor VIII are supplied to the United Kingdom each month. Kogenate and Helixate make up approximately 6.5 million units of this. This shortfall can currently be met by high-purity plasma-derived factor VIII, increased supplies of which are available from BPL, Baxter, Aventis Behring and Grifols. It is also possible that Alpha Therapeutic may be in a position to re-introduce Alphanate to the marketplace in the next few weeks. Although we anticipate a slow improvement, and a 30% increase in the supply of Recombinate (Baxter) in July, the overall supply of recombinant factor VIII will probably be reduced for the rest of this year.

For this reason, following an extraordinary meeting of the Advisory Committee of UKHCDO on the 26th of March, we introduced a guidance document which set out a

framework for an orderly reduction in the use of recombinant factor VIII for the duration of this crisis (copy enclosed). This document follows similar principles to those adopted by other national organisations. Although this policy provides a useful framework for a consensual approach to this issue, there is an urgent need to agree specific action to ensure continued supply of recombinant factor VIII to all Centres. Some centres, previously heavily dependent on Kogenate/Helixate, will very soon exhaust their supplies of rFVIII. We must avoid, at all costs, the situation where these Centres may be forced to treat patients, previously exposed only to recombinant FVIII, with plasma derived products. It is essential that we agree a mechanism to allow some redistribution of supplies of RVIII to these patients. There may be several options whereby this may be achieved.

Patients currently treated with recombinant factor VIII who have previously been treated with plasma-derived factor VIII may be changed back to these products. It may also be possible for some centres, having taken these steps, to allow their stock-levels of recombinant factor VIII to fall. This should release sufficient recombinant factor VIII to redirect to centres currently in need. Similar schemes have already been introduced in mainland Europe. It is anticipated that such a scheme would be co-ordinated by UKHCDO independently the manufacturers but with their co-operation. This proposed approach has been endorsed by DOH.

These possibilities and any further suggestions that you may care to make in the interim will be discussed further at the next meeting of the UKHCDO Advisory Committee. This has been brought forward to **Tuesday 15/5/01 at 10.30, and will be held at the Lansdowne Club, Berkley Square.** The current guidance document will also be reviewed. A representative of the DOH and the Haemophilia Society will attend this part of the meeting.

In the meantime, it would be very helpful if all centres could write to me giving me details of their normal and current usage of all brands of recombinant factor VIII, and their projected usage for pups, children who have never received plasma-derived factor VIII, children under 10 yrs of age and children under the age of 16. An estimate of current stock levels and usual rate of supply would also be very useful. I need this information as soon as possible, even from those centres who have already provided limited information to Dr Hill so that it can be collated prior to The Advisory Committee meeting in mid-May. I can assure you that this data will be handled confidentially and that details will ***not*** be shared with the pharmaceutical industry. Those whose stock levels may be in excess of current, reduced, requirements should contact me directly.

Finally, I am sure you will join me in wishing Frank Hill a speedy recovery.

Yours sincerely,

Dr Charles RM Hay
Acting Chair, UKHCDO.

CC: All Haemophilia Centre Directors,
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