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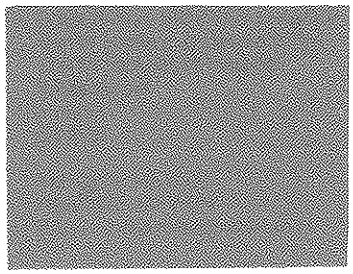

19 November, 2009

Professor David Barnett
Chair, Appraisal Committee
National Institute for Health & Clinical Excellence
MidCity Place
71 High Holborn
London
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Dear Professor Barnett

Re: Single Technology Appraisal: Romiplostim for the treatment of chromic immune or idiopathic thrombocytopenic purpura, appraisal consultation document

I am writing to you following the invitation to comment on the ACD for Romiplostim for the treatment of ITP which was recently issued by NICE. This document provides a clear summary of data to date.

I am the Chair and the lead writer of the recently published **international consensus report on the investigation and management of primary immune thrombocytopenia** (*Blood First Edition Paper, prepublished online October 21, 2009; DOI 10.1182/blood-2009-06-225565*).

I appreciate that you will have reviewed much data in preparing the ACD but I felt that I should write to you concerning the current management of ITP which has changed considerably over the last few years, and I wanted to bring some of these issues to your attention:

1. **ITP is uncommon and there have been very few good RCTs**. The biggest and best studies ever conducted in ITP are those of Amgen (romiplostim) and GSK (eltrombopag).

2. **Most drugs for the treatment of ITP are used off-label**: apart from corticosteroids, IVIG and anti-D (WinRho). The efficacy of most of our current treatments is low, but toxicities are significant.

3. **Anti-D (WinRho), one of our few licensed treatments has now been withdrawn from the European market**. We have lost one of our best evidence-based treatments.

4. **Morbidity and mortality studies in ITP** have shown that at least 50% of the deaths in patients with chronic ITP are caused by treatment-related toxicities rather than by the ITP itself; patients are succumbing to infection induced by the immunosuppressants such as mycophenolate, azathioprine, cyclosporine and others. There is therefore greater reluctance amongst the physicians caring for patients with ITP to use immunosuppressive therapies.

5. **Splenectomy is declining in popularity**, both from the point of view of patients but also the physicians looking after them. Splenectomy has long been a standard second line treatment option, but a substantial proportion (~50%) of patients who respond to splenectomy will subsequently relapse.

6. **The new TPO-receptor agonists** including romiplostim and eltrombopag offer a non-immunosuppressive method of management which obviates the need for immunosuppressive and other low efficacy treatments. The RCTs for both romiplostim and eltrombopag are the largest ever conducted in ITP. The efficacy of both drugs appears to be high and the toxicity profile is low, making these highly attractive treatments. The

recent RCTs used a platelet endpoint of 50 x 10^9/l but in clinical practice, for long term treatment, we would be happy with a platelet count of around 15–20 x 10^9/l; for short term support we would aim for platelets of ≥50 x 10^9/l for minor surgery, and ≥80 x 10^9/l for major surgery.

7. **Placement of the TPO receptor agonists within the new International Consensus document**: the TPO receptor agonists have been placed firmly within the **second line** category in our International Consensus document. We feel, as a group of 22 experienced ITP experts, that the romiplostim data are compelling enough for us to use romiplostim after first line therapy has failed. We have appraised the TPO receptor agonist data and we feel that these drugs offer significant advantages over existing therapies for the management of ITP.

I have enclosed a copy of the International Consensus Document as it appears on the *Blood* website. There are additional tables online which provide an appraisal of all the treatments used for ITP to date recommendation boxes, etc. This Consensus Document will be adopted the haematology community Internationally for the diagnosis and management of ITP, and as a Consensus Group we feel strongly that romiplostim should be available as a second line option for patients with chronic ITP.

If you require any further information please do not hesitate to contact me.

Yours sincerely