Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	Clinical Academic Researcher
Location	England
Conflict	yes
Notes	I run a tertiary referral centre for Thrombocytopenic purpura. I undertake clinical and laboratory based studies and have received financial support for my department from Amgen, GSK (who have a competing technology)and from other companies have an interest in the condition (Baxter, Bayer, Celgene, Genetech, Shionogi). I was organiser and co-author of a consensus document on the treatment of Immune thrombocytopenia published earlier this year in BLOOD.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I welcome the recommendations from the appraisal committee, which would bring treatment into line with Europe and North America. Treatment using thrombopoietin receptor agonists in Immune Thrombocytopenia (ITP)is one of the few treatments in this condition that has good quality, randomised, placebo controlled studies confirming its utility. This is in accord with the published concensus document on the management of ITP published earlier this year in BLOOD. There has been some misconceptions over the status of this document. This was produced independently by a writing group and assessment group of over 20 international experts in the condition. Unrestricted grants were obtained from Amgen, Baxter and GSK to support the meetings and logistics of producing the consensus guidelines, however, none of the companies were involved in any way with the production of the document and had no access to it prior to publication. Â This has been acknowledged recently by means of a letter published in the New England Journal of Medicine.
Section 2 (The technology)	1 year is now accepted as the cut-off point for diagnosing chronic ITP (2.1)as even in adults spontaneous remissions may occur up to this point.
Section 3 (The manufacturer's submission)	There have been disappointingly few comparative studies using conventional treatments in ITP. Most are open labelled studies in small numbers. Most use platelet count to recruit, which is also a surrogate for response. Randomised comparative studies using bleeding episodes, as well, have only been seen in TPO studies. Thus there are few analysise of cost and clinical effectiveness (3.3, 3.10). In the TPO studies most patients had relapsed or refractory disease and fell into the category where treatment would be expected. In this sub-group of ITP although there may be a policy of watch and rescue many, because of previous bleeding history will go straight onto a new treatment. There is a reluctance to withdraw previous treatments and as such many

	patients end up on multiple treatments without a clear therapeutic rationale. Following initial therapy there is no general agreement on treament policy, this being individual to each clinician, and is reflected in the consensus document where treatments are described alphabetically. No conventional treatments are effective in more than 25-30% explaining the lack of clear consensus (3.22, 3.28)
Section 4 (Consideration of the evidence)	There is an assumption that ITP mainly impacts on life-style. In the group we are considering for treatment it is much more a health issue. 40% of patients require no treatment with minor or no problems but 20% fall into the relapsed or refractory category and half of these will require treatment for bleeding. First line treatments are generally agreed but the main side-effects that patients complain about in our Adult ITP Registry relate to the long (and short) term effects of steroids, which need to be stopped at the earliest opportunity. IVIG is now severely restricted and anti-D immunoglobulin is not available in Europe for ITP. It is worth noting that 50% of deaths in ITP are due to infection relating to immune-suppressive treatment (often in association with splenectomy) not bleeding. Safer treatments are desperately required. The non-licensed treatment Rituximab while effective immediately in much greater numbers than other treatments (50-60%) has long term responses of 20%, no more than conventional treament. Its association with Progressive Multifocal Leucoencephalopathy has led to a swing against its use in non-malignant conditions in Europe and N America.
Section 5 (Implementation)	As stated in the preliminary recommendatiosn treatment should be restricted to specialists in haematology and good practice will be disseminated through the specialist society, the British Society for Haematology.
Section 6 (Related NICE guidance)	Although NICE did not recommend use of eltrombopag in ITP in pratical terms there is no significant clinical difference between the two agents at the level of clinical response required. Each agent shows a response that is haemaostatically worthwhile (increments of up to 50) in over 80% but the drugs are not interchangeable. As an oral agent it has some benefits and if the final recommendations for romiplostim are positive NICE should have further discussions with GSK on a patient access scheme that will make eltrombopag available as an alternative.
Section 7 (Proposed date of review of guidance)	
Date	09/01/2011 14:20

Name	[redacted]
Role	NHS Professional
Other role	Cancer Pharmacist
Location	England
Conflict	no

Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Given this is a therapy for a long term condition, consideration should be given to the use of shared care arrangements between the specialist in haematology and the patients GP to aid access to therapy Also need to define "standard active treatments" i.e. is it splenectomy/steroids/immunoglobulins What about rituximab, esp. as mentioned in DH policy for immunoglobulins?
Section 2 (The technology)	Costs are inaccurate as they presume no waste As dosing is weekly and reconstituted vials have a 24 hour shelf life, it is inevitable that each weekly dose will require its own vial Therefore at a dose of 1 microgram/kg there will be significant waste from a 250 microgram vial unless the vial is manipulated in a licenced aseptic unit and patients are seen as cohorts to enable vial sharing as each vial should provide doses for 2-3 patients depending upon their weight (more if the 500 microgram vial is used) Given the proportion of non-repsonders in the RCT would it not be prudent to propose stopping criteria?
Section 3 (The manufacturer's submission)	I would suggest that in clinical practice immunoglobulins are a standard therapy (not rescue therapy as per RCT) Reference is given to comparison with rituximab, what dose was used in the comparison as ritux is not licenced here and is often used at a dose of 100mg (rather than 375mg/m2) which has a marked impact on cost comparison
Section 4 (Consideration of the evidence)	
Section 5 (Implementation)	
Section 6 (Related NICE guidance)	
Section 7 (Proposed date of review of guidance)	
Date	01/12/2010 21:24