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

Role	NHS Professional
Location	England
Conflict	Yes
Notes	I have consulted for and received honorarium for speaking at educational meetings for Gsk and Amgen.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	My concern is the limitation to patients who have undergone splenectomy. Response rates for splenectomy are only 60%. This exposes up to 40% of patients to the risk of surgery and the risk of sepsis and infections without any benefit from the surgery.
Section 4 (Consideration of the evidence)	As a clinical expert who was present at the consultation, I disagree with some of these comments. The committee presented the Bayesian analysis comparing romiplostim and eltrombopag and asked us to comment on
Section 5 (Implementation)	We strongly recommend these agents are only prescribed by haematologists who are in a position to monitor efficacy and safety.

Role	NHS Professional
Location	England
Conflict	No
Notes	Amgen supported registration/accommodation at a scientific meeting (BSH) in 2012
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The thrombomimetics are clinically similar in their response rates. Splenectomy should not be part of the requirement as it is not for romiplostim. Patients in the UK do not accept splenectomy 2nd line and as a major treatment centre (Leeds), we have carried out NO splenectomies in the last 5 years (mainly patient choice)
Section 4 (Consideration of the evidence)	I do not agree that the evidence supports the arguement that eltrombopag is less effective that romiplosim and although a direct comparison is lacking, available evidence suggests they should be considered as having the same effectiveness.

Role	NHS Professional
Location	England
Conflict	no
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The preliminary recommendations are different from those for Romiplostim TA221, where there is no insistence on prior splenectomy. These agents are essentially similar in their clinical response and their licenses are also similar. By having differing recommendations it suggests that these are different agents with different indications, which is not the case. For Romiplostim there is also the recommendation that the agent should be supervised by a haematologist. I would strongly

	recommen this is included in TA205 as lack of this could lead to inappropriate use.
Section 4 (Consideration of the evidence)	The response to splenectomy is lower than quoted especially in the long term. Literature suggests that Indium labelled platelet studies are an effective way of predicting which patients are likely to respond to splenectomy. As splenectomy is associated an increased risk of infection related morbidity and mortality it does not seem reasonable to subject patients who have a low likelihood of responding (ie >40% and those who have a -ve Indium labelled test) to such surgery. 4.11 states Committee agreed with the clinical specialists that the available evidence suggested that romiplostim was likely to be more effective than eltrombopag rather than equally effective?. I think our comments have been misinterpreted . In my opinion in terms of clinical effectiveness i.e achieving a haemostatically meaningful response the agents are similar and should be treated as such. The stringent end-point for the randomised studies did demonstrate that the platelet response rate was marginally less in the eltrombopag studies but as we stressed in our comments it is the bleeding symptoms that are of far more relevance than the actual platelet count in patients with ITP.
Section 6 (Proposed recommendations for further research)	I am disappointed to read that there was little enthusiasm to support an ITP registry rather than a strong recommendation that all patients on these drugs should be monitored by a specialist haematologist AND be registered for long term follow up so that real world outcomes and comparisons of treatments can be obtained
Section 7 (Related NICE guidance)	The technology appraisals for 221 and the current one should cross refer and be giving the same message and advice.

Role	Patient
Location	England
Conflict	no
Notes	I have suffered from severe, refractory ITP since June 2008 (platelet count below 10). Although my clinician (and others he has asked) believes I am eligible for Romiplostim on account of the seriousness of my disease, my local PCT has continually denied me access to that drug on account of the fact that I have not undergone splenectomy. My clinician is completely supportive of my decision not to have a splenectomy, informed by concerns of its impact on work-related travel to areas of the world with a higher risk of infectious diseases, combined with the unpredictability of splenectomy in treating the disease. The PCT has consistently interpreted the wording of the NICE guidance for Romiplostim in such a way as to block every appeal, even though patients in a similar situation to myself are already getting access to the drug in other parts of the country. I am concerned that the current wording of the guidance for Eltrombopag will raise a similar problem, and that patients in my situation may be denied access also to this.
Comments on individual sections of the ACD:	

Section 1 (Appraisal Committee's preliminary recommendations)	The position of splenectomy in the care pathway and clinicians? role in determining this urgently needs to be clarified to ensure patient access. Similar ambiguity for Romiplostim is proving an obstacle, further hampered by non-uniform application of NICE guidance. Currently Eltrombopag is recommended only for asplenic patients unless surgery is contra-indicated. This forces splenectomy even when there is strong justification against. This highly prescriptive model is contrary to recognized best practice: (Point 4.3) ?managing ITP depends on individual circumstances, and the specialists could not define a single treatment pathway as routine practice?. Also: ?The Committee heard that splenectomy would be considered as first-line, second-line or subsequent-line treatment?. Many specialists actively avoid it (eg Royal London Hospital, tertiary UK referral centre) as it irreversibly removes a healthy organ with an important immunological function and its success is relatively low (especially long term) and unpredictable. Risk benefit analysis must be tailored to a patient?s circumstances that may make splenectomy inadvisable (e.g. higher risk of infection due to work-related travel).
Section 4 (Consideration of the evidence)	Please see comments for Section 1 concerning the position of splenectomy in the pathway of care, and the key role of clinicians in determining this with reference to an individual patient.

Role	Patient
Location	England
Conflict	no
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Eltrombopag needs to be made available to ITP patients regardless of whether or not they have already had a splenectomy. Many iTP patients who do not have a splenectomy (often it is shown by indium label test for example that a splenectomy will not work for them so no point in having it) should surely be entitled to Eltrombopag as an alternative where other treatments have not worked

Role	NHS Professional
Location	England
Conflict	yes
Notes	I have undertaken clinical trials with both licensed Thrombopoietin receptor agonists, in addition to early studies with some of the newer agents now available.□
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	"The preliminary recommendations are different from those for Romiplostim TA221, where there is no insistence on prior splenectomy. These agents are essentially similar in their clinical response and their licenses are also similar. By having differing recommendations it suggests that these are different agents with different indications, which is not the case. For Romiplostim there is also the recommendation that the agent should be supervised by a haematologist. These should

	be emphasised here as this could lead to inappropriate use."
Section 3 (The manufacturer's submission)	"The response to splenectomy not as high as quoted and long term is less than 60%. In patients who have failed splenectomy and require further treatment there is well recognised increased morbidity and mortality primarily due to infection, which is treatment related. Now that Indium labelled platelt studies can identify patients who will fail surgery patients should not be forced into surgery we know will fail. This is currently the case where commissioners are insisting on surgery before agreeing funding. Clinically this is indefensible and the recommendations perpetuate this state of affairs. The recommendation for TA 221 are much more appropriate."
Section 4 (Consideration of the evidence)	In terms of clinical effectiveness the two products available are interchangeable. The stringent end-point for the randomised studies did demonstrate that the platelet response rate was marginally less in the eltrombopag studies however interms of achieving haemostatically meaningfull responses the agents were similar and should be treated as such.
Section 6 (Proposed recommendations for further research)	While this is an ideal good quality studies are expensive and difficult to perform. Prior to the recent studies in the TPO receptor agonists most studies were small scale and rarely randomised or either placebo or Standard of Care controlled. It is worth bearing in mind that in the Amgen-sponsored trial of romiplostim treatment for ITP required 85 sites in 14 countries to enrol 234 patients in 22 months. The ITP Clinical Centres group in the UK is committed to developing good quality research projects but the numbers required to achieve good quality data in large treatment studies may be difficult and is likely to require pharma support as these rarely gain central funding.
Section 7 (Related NICE guidance)	The technology appraisals for 221 and the current one should cross refer and be giving the same message and advice.