

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**CENTRE FOR HEALTH TECHNOLOGY EVALUATION**  
**Technology Appraisals**

**Consultation on Batch 47 draft remits and draft scopes and  
summary of comments and discussions at scoping workshops**

Item	Topic ID	Topic title
5.1	766	Dimethyl fumarate for treating moderate to severe chronic plaque psoriasis
5.2	906	Midodrine for treating severe orthostatic hypotension
5.3	908	Etelcalcetide for treating secondary hyperparathyroidism
5.4	843	Ustekinumab for treating moderately to severely active Crohn's disease after prior therapy
5.5	927	Afamelanotide for treating erythropoietic protoporphyria
5.6	919	Biotin for primary and secondary progressive multiple sclerosis

<b>Provisional Title</b>	Dimethyl fumarate for treating moderate to severe chronic plaque psoriasis		
<b>Topic Selection ID Number</b>	7127	<b>Wave / Round</b>	R87
<b>TA ID Number</b>	766		
<b>Company</b>	Almirall SA		
<b>Anticipated licensing information</b>	***Confidential information removed***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of dimethyl fumarate (LAS41008) within its marketing authorisation for treating moderate to severe plaque psoriasis.		
<b>Main points from consultation</b>	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of dimethyl fumarate for treating moderate to severe plaque psoriasis is <u>appropriate</u>.</p> <p>The proposed remit is not appropriate and should be amended as follows: the population of the remit should be changed to moderate to severe <b>chronic</b> plaque psoriasis which is consistent with the trial population.</p> <p>Fumaric acid esters have been recommended for treating moderate to severe chronic plaque psoriasis in European guidelines and Fumaderm has also been used off-label in the UK this population. Fumaric acid esters have been included as a comparator. Infliximab has been removed as a comparator as it is used in a different population (very severe psoriasis).</p>		
<b>Population size</b>	Approximately 7000 people in England would be eligible for treatment with dimethyl fumarate (NICE commissioning support document for psoriasis quality standard).		
<b>Process (MTA/STA/HST)</b>	STA		
<b>Proposed changes to remit (in bold)</b>	To appraise the clinical and cost effectiveness of dimethyl fumarate (LAS41008) within its marketing authorisation for treating moderate to severe <b>chronic</b> plaque psoriasis		
<b>Costing implications of remit change</b>	It is estimated that approximately 7,000 people in England have severe psoriasis and would be eligible to use dimethyl fumarate. The list price of dimethyl fumarate is £343 for a pack of 14 tablets of 120mg. There may be reduced administration costs compared with alternative treatments because dimethyl fumarate is administered orally.		
<b>Timeliness statement</b>	Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.		

<b>Provisional Title</b>	Midodrine for treating severe orthostatic hypotension		
<b>Topic Selection ID Number</b>	7886	<b>Wave / Round</b>	R152
<b>TA ID Number</b>	906		
<b>Company</b>	Brancaster Pharma Limited		
<b>Anticipated licensing information</b>	Midrodine has a marketing authorisation for this indication, which is in 'adults for the treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate'.		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of midodrine within its marketing authorisation for treating severe orthostatic hypotension.		
<b>Main points from consultation</b>	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of midrodine for treating orthostatic hypotension is <u>not appropriate</u>.</p> <p>The attendees at the SW considered that an appraisal of midodrine would not be a good use of NHS resources. Unlicensed midodrine has been available to patients for over 10 years and has been used by clinicians where required without access issues and the clinical experts consider there to be even fewer barriers now midodrine has a licence and the price has reduced (the company says the price has been reduced by approximately 60% from that of the unlicensed midodrine).</p> <p>The clinical experts explained that there is no issue with access to midodrine except that some GPs do not like writing repeat prescriptions and patients therefore have to go to hospital for their prescriptions. It was considered that NICE guidance was unlikely to change this.</p> <p>The proposed remit is appropriate. No changes are required.</p>		
<b>Population size</b>	Approximately 3500 people in England would be eligible for treatment with midrodine based on the NICE advice (ESNM61) October 2015.		
<b>Process (MTA/STA/HST)</b>	STA		
<b>Proposed changes to remit (in bold)</b>	None		
<b>Costing implications of remit change</b>	Estimates of the prevalence of orthostatic hypotension range from 440,000 to 2,620,000 (5% to 30%) of people aged over 65 years. Many cases can be treated with non-pharmacological approaches and it is estimated that around 3500 people in England would be eligible for treatment with midrodine. The annual cost for midodrine at the maximum dose of 10mg 3 times daily is £1,643 per person and would represent additional costs for the NHS. There may be off-setting savings from a reduction in admissions because of better management of the condition.		
<b>Timeliness statement</b>	As this technology has already received a marketing authorisation, issuing timely guidance for this technology will not		

	<p>be possible. NICE were only notified of the development of the product close to the marketing authorisation date, which is not early enough in its development cycle in order to provide the opportunity to issue timely guidance.</p>
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<b>Provisional Title</b>	Etelcalcetide for treating secondary hyperparathyroidism		
<b>Topic Selection ID Number</b>	7204	<b>Wave / Round</b>	R92
<b>TA ID Number</b>	908		
<b>Company</b>	Amgen		
<b>Anticipated licensing information</b>	***Confidential information removed*** Expected wording of marketing authorisation: The treatment of secondary hyperparathyroidism in patients with chronic kidney disease on haemodialysis.		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of etelcalcetide within its marketing authorisation for treating secondary hyperparathyroidism in people with chronic kidney disease		
<b>Main points from consultation</b>	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of etelcalcetide for treating secondary hyperparathyroidism in patients with chronic kidney disease on haemodialysis is <u>appropriate</u>.</p> <p>The proposed remit is not appropriate and should be amended as follows:</p> <p>To appraise the clinical and cost effectiveness of etelcalcetide within its marketing authorisation for treating secondary hyperparathyroidism in people with chronic kidney disease, <b>receiving haemodialysis</b> to reflect the anticipated wording of the marketing authorisation.</p> <p>Minor changes to the comparators and outcomes were suggested.</p>		
<b>Population size</b>	<p>Approximately 23,500 people in England would be eligible <b>in theory</b> for treatment with etelcalcetide.</p> <p>All patients receiving haemodialysis will be eligible for etelcalcetide as per the anticipated marketing authorisation, and according to the UK Renal Registry 17th Annual Report, the number of people receiving haemodialysis in 2013 was approximately 23,500.</p> <p>However in clinical practice, the number would be far less as the clinical experts envisage that etelcalcetide would be used in place of cinacalcet, in people who have very high level of parathyroid level (despite having conventional therapy with or without cinacalcet).</p>		
<b>Process (MTA/STA/HST)</b>	STA		
<b>Proposed changes to remit (in bold)</b>	To appraise the clinical and cost effectiveness of etelcalcetide within its marketing authorisation for treating secondary hyperparathyroidism in people with chronic kidney disease, <b>receiving haemodialysis</b>		
<b>Costing implications of remit change</b>	There are around 3,050 people in England that are receiving dialysis for CKD and have secondary hyperparathyroidism and PTH >300pg/ml. This may represent the eligible population. The cost of cinacalcet (a currently available treatment for this group of people) is between £1,600 and £9,000 per year. The		

	cost of etelcalcetide is not yet known and so the overall resource impact cannot be estimated.
<b>Timeliness statement</b>	Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.

<b>Provisional Title</b>	Ustekinumab for treating moderately to severely active Crohn's disease after prior therapy		
<b>Topic Selection ID Number</b>	7518	<b>Wave / Round</b>	R122
<b>TA ID Number</b>	843		
<b>Company</b>	Janssen		
<b>Anticipated licensing information</b>	***Confidential information removed***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of ustekinumab within its marketing authorisation for treating moderately to severely active Crohn's disease in people who are intolerant of, or whose disease has not responded or is resistant to either conventional therapy or a tumour necrosis factor-alpha inhibitor.		
<b>Main points from consultation</b>	<p>Following the consultation exercise the Institute is of the opinion that an appraisal of ustekinumab for treating moderately to severely active Crohn's disease is appropriate.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>Only minor changes to the scope were proposed during consultation.</p>		
<b>Population size</b>	<p>Approximately 17,000 people in England would be eligible for treatment with this technology.</p> <p>This is based on the costing statement for vedolizumab (TA352), which estimates that there are approximately 17,000 people with moderate to severe Crohn's disease in whom conventional treatment is ineffective or not tolerated.</p> <p>Of the 17,000 people, it is estimated that approximately 7,700 cannot tolerate or have contraindications to infliximab or adalimumab.</p>		
<b>Process (MTA/STA/HST)</b>	STA		
<b>Proposed changes to remit (in bold)</b>	None		
<b>Costing implications of remit change</b>	<p>Approximately 17,000 people in England with moderate to severely active Crohn's disease would be eligible for treatment with ustekinumab. The average annual cost of ustekinumab is around £10,000 per year. The cost of a comparator treatment, vedolizumab (which is approved by NICE for the same population), is not known because there is a patient access scheme with a confidential discount to the list price. Therefore the resource impact cannot be estimated. There are no anticipated changes in administration costs.</p>		
<b>Timeliness statement</b>	<p>Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.</p>		

<b>Provisional Title</b>	Afamelanotide for treating erythropoietic protoporphyria		
<b>Topic Selection ID Number</b>	7867	<b>Wave / Round</b>	R149
<b>HST ID Number</b>	927		
<b>Company</b>	Clinuvel UK		
<b>Anticipated licensing information</b>	<p>Marketing authorisation date: December 2014</p> <p>Marketing authorisation: Afamelanotide has a UK marketing authorisation under exceptional circumstances for 'prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP)'</p>		
<b>Draft remit</b>	To evaluate the benefits and costs of afamelanotide within its licensed indication for treating erythropoietic protoporphyria for national commissioning by NHS England.		
<b>Main points from consultation</b>	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of afamelanotide for treating erythropoietic protoporphyria is <u>appropriate</u>.</p> <p>The proposed remit is not appropriate and should be amended as follows:</p> <p>To appraise the clinical and cost effectiveness of afamelanotide within its marketing authorisation for treating erythropoietic protoporphyria.</p> <p>This is because, following input from consultees and commentators, it was decided that the STA process would be more appropriate for this technology than the HST process.</p>		
<b>Population size</b>	EPP prevalence has been estimated at 25.4 cases per million people in the UK (Elder et al., 2013). Therefore, approximately 1300 people in England would be eligible for treatment with afamenalotide.		
<b>Process (MTA/STA/HST)</b>	STA (instead of HST)		
<b>Proposed changes to remit (in bold)</b>	To <b>evaluate appraise</b> the <b>benefits and costs clinical and cost effectiveness</b> of afamelanotide within its <b>licensed indication marketing authorisation</b> for treating erythropoietic protoporphyria <b>for national commissioning by NHS England</b> .		
<b>Costing implications of remit change</b>	The proposed remit change does not affect the population size. Afamelanotide is administered as a subcutaneous implant every 60 days. The drug price is not available on the PPA drug tariff, eMit or BNF. There are currently no pharmacological treatments licensed for this condition. There may be some savings from the avoidance of treatment costs for liver failure, which occurs in 1-4% of people with EPP.		
<b>Timeliness statement</b>	As this technology has already received a marketing authorisation, issuing timely guidance for this technology will <u>not</u> be possible. NICE were only notified of the development of the product post the CHMP opinion, which is not early enough in its development in order to provide the opportunity to issue timely guidance.		



<b>Provisional Title</b>	Biotin for primary and secondary progressive multiple sclerosis		
<b>Topic Selection ID Number</b>	7779	<b>Wave / Round</b>	919
<b>Company</b>	Medday Pharmaceuticals		
<b>Anticipated licensing information</b>	***Confidential information removed***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of biotin within its marketing authorisation for treating primary and secondary progressive multiple sclerosis.		
<b>Main points from consultation</b>	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of biotin for primary and secondary progressive multiple sclerosis is appropriate.</p> <p>Changes to the comparators and outcomes were suggested.</p> <p>The proposed remit is appropriate. No changes are required.</p>		
<b>Population size</b>	Approximately 30,000 people (around 21,000 people with secondary progression disease and 8700 people with primary progressive disease)		
<b>Process (MTA/STA/HST)</b>	STA		
<b>Proposed changes to remit (in bold)</b>	None		
<b>Costing implications of remit change</b>	<p>The total population potentially eligible for treatment is around 30,000. The number of people receiving treatment at any one time will be a subsection of this group, but the actual population likely to be treated cannot be estimated accurately with available data.</p> <p>Biotin is estimated to cost €2,100 (approximately £1,650 as at May 2016) per 28 days treatment and can be used for up to 24 months. The annual cost for treatment with Biotin is therefore approximately £21,500 per person. Prescribing Biotin could decrease the use of other medication and services; the reductions in these costs are uncertain and therefore have not been off-set against the cost of Biotin.</p>		
<b>Timeliness statement</b>	Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.		