

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

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

**Consultation on Batch 45 draft remits and draft scopes and  
summary of comments and discussions at scoping workshops**

Item	Topic
5.1	Erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia
5.2	Ibrutinib for treating Waldenstrom's macroglobulinaemia
5.3	Rociletinib for previously treated locally advanced or metastatic, EGFR T790M - positive non-small-cell lung cancer
5.4	Golimumab for treating non-radiographic axial spondyloarthritis
5.5	Ex vivo expanded autologous human corneal epithelial cells for treating moderate to severe limbal stem cell deficiency due to ocular burns
5.6	Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma
5.7	Teduglutide for treating short bowel syndrome

<b>Provisional Title</b>	Erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia		
<b>Topic Selection ID Number</b>	7706	<b>Wave / Round</b>	R136
<b>TA ID Number</b>	864		
<b>Company</b>	Orphan Europe		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of erythrocyte encapsulated asparaginase within its marketing authorisation for treating acute lymphoblastic leukaemia.		
<b>Main points from consultation</b>	<p>Following the consultation exercise and the scoping teleconference, the Institute is of the opinion that an appraisal of erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia is appropriate.</p> <p>Consultees at the scoping teleconference stated that they were unaware of any patient in the UK receiving this drug, even as part of the clinical trials. They considered that the most beneficial use of erythrocyte encapsulated asparaginase would be in people with previous allergic reaction to asparaginase. The company stated that there was little evidence for this group of people from the available clinical trial. However, another clinical trial evaluating this drug in people who are “double allergic” (allergic reactions to both E.coli and Erwinase derived asparaginase) is planned and will report in 2018. The consultees (including the company) agreed that it would be better for this topic to be referred when the data for the relevant patient group is available.</p> <p>At the decision point 4 meeting, it was decided that an appraisal is appropriate and a referral should be sought at this stage, noting that the remit is broad and the technology will be appraised within its marketing authorisation. It was also noted that there is an option to pause the appraisal after referral and re-start it when data for the relevant patient group becomes available. <u>The NICE team would need to discuss this with the company at the Decision Problem meeting after the topic has been referred for appraisal.</u></p> <p><u>Remit:</u> The proposed remit is appropriate. No changes required.</p> <p><u>Population:</u> Consultees agreed that the population in the scope should be ‘people who are intolerant or allergic to asparaginase or have disease that has relapsed on asparaginase treatment.</p>		
<b>Population size</b>	<p>Approximately 500-550 people in England would be eligible for frontline treatment for acute lymphoblastic leukaemia. Therefore it is expected that the number of people with relapsed disease or allergic reaction to asparaginase would be smaller.</p> <p>The company stated during the scoping teleconference that it is anticipated that approximately 3 people a year in England would</p>		

	be treated with erythrocyte encapsulated asparaginase.
<b>Process (MTA/STA/HST)</b>	STA
<b>Proposed changes to remit (in bold)</b>	None
<b>Costing implications of remit change</b>	In England there were 529 new diagnoses of ALL registered in 2012. The company estimate that around 3 people may be eligible for treatment with erythrocyte encapsulated asparaginase in England each year. The cost of erythrocyte encapsulated asparaginase is not yet known. The treatment is administered intravenously, so there are likely to be tariff costs associated with the drug administration. It is understood that this erythrocyte encapsulated asparaginase would be administered alongside current chemotherapy treatments.
<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. If the appraisal is scheduled to coincide with the results from the clinical trial evaluating this drug in people who are "double allergic" (allergic reactions to both E.coli and Erwinase derived asparaginase), issuing timely guidance will not be possible.

<b>Provisional Title</b>	Ibrutinib for treating Waldenstrom's macroglobulinaemia		
<b>Topic Selection ID Number</b>	7811	<b>Wave / Round</b>	R146
<b>TA ID Number</b>	884		
<b>Company</b>	Janssen		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of ibrutinib within its marketing authorisation for treating Waldenstrom's macroglobulinaemia.		
<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 ibrutinib for treating Waldenstrom's macroglobulinaemia is appropriate.</p> <p><u>Remit:</u> The proposed remit is appropriate. No changes required.</p> <p><u>Process:</u> Consultees at the scoping workshop agreed that an STA would be appropriate. It was suggested that this topic would be an ideal candidate for the proposed new technology appraisals process which allows commissioning with research.</p> <p>The marketing authorisation was granted based on the results of a single arm phase 2 study in people who received at least one prior therapy. There is an ongoing phase 3 clinical trial comparing ibrutinib+rituximab versus rituximab alone. This study also includes an open-label substudy of ibrutinib monotherapy in people who failed to achieve a molecular response or have relapsed within 12 months of receiving rituximab-containing therapy. This phase 3 trial will report interim findings mid 2016. However, neither of the studies compares ibrutinib monotherapy against placebo or any active intervention, which will make any direct or indirect comparisons challenging.</p>		
<b>Population size</b>	<p>Approximately 500-700 people in England would be eligible for treatment with ibrutinib.</p> <p>According to the Waldenstrom's UK website, at any one time 4000 people have Waldenstrom's macroglobulinaemia. The vast majority of people have symptomatic disease. Because ibrutinib is licensed for second line therapy for most patients, this will represent a relatively small proportion of patients (10-15% -- approximately 400-600 people). The proportion of patients who are unsuitable for chemo-immunotherapy due to fitness or comorbidities is unknown, but expected to be very small (2-3% of people with Waldenstrom's macroglobulinaemia) – between 80-120 people. However, adoption could potentially be higher, as there is no set treatment pathway for Waldenstrom's macroglobulinaemia and treatment decisions are based largely on patient and physician choice.</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>Waldenstrom's macroglobulinaemia is relatively rare with an age standardised incidence rate of 0.55 per 100,000 per year in the UK, equating to around 300 people in England diagnosed each year.</p> <p>The target group for treatment is patients who are relapsed/refractory and in treatment-naïve for whom chemotherapy is inappropriate. Approximately 500-700 people in England would be eligible for treatment with ibrutinib.</p> <p>The list price of ibrutinib is £4,599 for a pack of 90 x 140mg tablets. Each 4 week cycle of treatment with ibrutinib would cost £4,292 based on 420mg per day.</p> <p>The average number of cycles per patient per year is not known however the company has estimated a cost for the treatment of &gt;£30,000 per patient per year.</p> <p>It is anticipated that the treatment is more expensive than current treatments, but should treatment prove effective, the single agent therapy would replace infused therapy in relapsed and refractory patients which may reduce chemotherapy infusion costs.</p>
<b>Timeliness statement</b>	<p>As the technology has received a marketing authorisation, issuing timely guidance will <u>not</u> be possible. The Topic Selection programme was not informed of the topic in time to allow appropriate consideration in line with the anticipated marketing authorisation date for the product.</p>

<b>Provisional Title</b>	Rociletinib for previously treated locally advanced or metastatic, EGFR T790M -positive non-small-cell lung cancer		
<b>Topic Selection ID Number</b>	7696	<b>Wave / Round</b>	R132
<b>TA ID Number</b>	883		
<b>Company</b>	Clovis Oncology		
<b>Anticipated licensing information</b>	*** <b>CONFIDENTIAL INFORMATION REMOVED</b> ***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of rociletinib within its marketing authorisation for previously treated locally advanced or metastatic, EGFR T790M-positive non-small-cell lung cancer (NSCLC).		
<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 rociletinib for previously treated locally advanced or metastatic, EGFR T790M -positive non-small-cell lung cancer is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>No significant changes were made to the PICO table, although the comparators have been split to clarify that there are two possible positions for this treatment: after one TKI therapy; and after two prior treatments (a TKI and one other therapy).</p> <p>A brief discussion took place regarding diagnostic testing and it was confirmed that current methods of testing for the EGFR mutation can also be used for testing for T790M mutation, usually at the point of progression.</p>		
<b>Population size</b>	<p>Approximately 215 people in England would be eligible for treatment with rociletinib.</p> <p>This estimate is based on approximately 430 people a year in England who are eligible to receive first-line treatment with an EGFR-TKI therapy (taken from costing statement for TA258). Of these approximately 50% have the T790M mutation. If all of these fail treatment then approximately 215 people would be eligible for rociletinib.</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 215 people in England would be eligible for treatment with rociletinib.</p> <p>The cost of treatment with rociletinib is not known. It is orally administered and savings on drug administration and avoidance of alternative treatment options are anticipated.</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.
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<b>Provisional Title</b>	Golimumab for treating non-radiographic axial spondyloarthritis		
<b>Topic Selection ID Number</b>	7213	<b>Wave / Round</b>	R148
<b>TA ID Number</b>	903		
<b>Company</b>	MSD		
<b>Anticipated licensing information</b>	<p>Marketing authorisation received in June 2015 as a license extension.</p> <p>Wording of marketing authorisation: For treating adults with severe, active non radiographic axial spondyloarthritis with objective signs of inflammation (including elevated C-reactive protein and/or evidence from magnetic resonance imaging) whose disease has responded inadequately to, or who are intolerant to, non-steroidal anti-inflammatory drugs.</p>		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of golimumab within its marketing authorisation for treating non-radiographic axial spondyloarthritis.		
<b>Main points from consultation</b>	<p>Following the consultation exercise, the Institute is of the opinion that an appraisal of golimumab for treating non-radiographic axial spondyloarthritis is <u>appropriate</u>.</p> <p>Consideration as to the most appropriate process in which to appraise golimumab within this indication should be explored further by NICE following the recent publication of TA383; TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>No changes were made to the scope.</p>		
<b>Population size</b>	<p>Approximately 6100 people in England would be eligible for treatment with golimumab.</p> <p>This is based on the draft costing report for the ongoing MTA of TNF-inhibitors (ID694): Ankylosing spondylitis and axial spondyloarthritis (non-radiographic) - adalimumab, etanercept, infliximab and golimumab (inc rev TA143 and TA233).</p>		
<b>Process (MTA/STA/HST)</b>	TA (to allow for exploration of most appropriate process for the appraisal)		
<b>Proposed changes to remit (in bold)</b>	None		
<b>Costing implications of remit change</b>	<p>Approximately 6100 people in England with axial spondyloarthritis would be eligible for treatment with TNF-inhibitors.</p> <p>Golimumab is an additional option alongside adalimumab, etanercept and infliximab. It is a similar price to comparators so it is anticipated there would not be a resource impact for this topic.</p>		
<b>Timeliness statement</b>	As the technology has received a marketing authorisation, issuing timely guidance will <u>not</u> be possible.		



<b>Provisional Title</b>	Ex vivo expanded autologous human corneal epithelial cells for treating moderate to severe limbal stem cell deficiency due to ocular burns		
<b>Topic Selection ID Number</b>	7864	<b>Wave / Round</b>	R148
<b>TA ID Number</b>	899		
<b>Company</b>	Chiesi Farmaceutici		
<b>Anticipated licensing information</b>	Conditional marketing authorisation received: February 2015 *** <b>CONFIDENTIAL INFORMATION REMOVED</b> ***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of ex vivo expanded autologous human corneal epithelial cells containing stem cells within its marketing authorisation for treating moderate to severe limbal stem cell deficiency due to ocular burns.		
<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 ex vivo expanded autologous human corneal epithelial cells containing stem cells for treating moderate to severe limbal stem cell deficiency due to ocular burns is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p><u>STA/HST process:</u> The company suggested that this technology fits best under the HST programme. It noted that the commissioning of Holoclar is expected to be included by NHS England as a specialised/highly specialised service, and that only a very small population would be eligible to have Holoclar (90-100 patients). It also noted the chronic and severely disabling nature of the condition and highlighted that it is expected that only few centres in the NHS would provide the treatment. During the scoping workshop the NICE team described the criteria that need to be met for a technology to be considered under the HST programme and noted that at least one of the criteria was not met (that is, the technology does not have the potential for life long use). The clinical expert also noted that it is expected that many centres would express interest in using this technology. The company noted that because of the complexities in treatment delivery (the ex vivo expansion occurs in Italy and treatment should be immediately surgically implanted in the patient's eye once it sent back to the hospital), it is expected that only very few centres in the NHS would provide this treatment (the company anticipates 2 centres will be designated by NHSE and trained by the company deliver the intervention).</p>		
<b>Population size</b>	<p>Approximately 90-100 people per year in England will be eligible for treatment with ex vivo expanded autologous human corneal epithelial cells containing stem cells based on the company's estimates.</p> <p>The estimated prevalence of LSCD due to ocular burns in Europe is 0.3 in 10,000 people, which is equivalent to about 1800 people in England.</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>It is estimated that around 1,800 people in England are affected by LSCD. Of these around 90-100 may be eligible for holoclar. The cost of holoclar is not known, but it is expected to be on the high-cost drug exclusion list.</p> <p>The number of corneal transplants performed for ocular surface burns is thought to be very small, probably no more than around 20 cases per annum in the UK. Where transplants are avoided there may be offsetting savings.</p>
<b>Timeliness statement</b>	As the technology has received a marketing authorisation, issuing timely guidance will <u>not</u> be possible.

<b>Provisional Title</b>	Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma.		
<b>Topic Selection ID Number</b>	7263	<b>Wave / Round</b>	R100
<b>TA ID Number</b>	807		
<b>Company</b>	Takeda		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of ixazomib citrate within its marketing authorisation for relapsed or refractory multiple myeloma.		
<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 ixazomib citrate for treating refractory multiply myeloma is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>No significant changes were made to the PICO table, although the comparators have been split by line of treatment: people who have received at least 1 therapy and people who have received at least 2 therapies.</p>		
<b>Population size</b>	<p>Approximately 1669 to 2999 people in England would be eligible for treatment with ixazomib citrate. If ixazomib citrate is recommended for people who have had at least 3 prior therapies the patient population would be smaller than 1669.</p> <p>These figures are taken from the costings templates for lenalidomide (TA171), which is recommended as an option or the treatment of multiple myeloma only in people who have received two or more prior therapies and bortezomib (TA129) which is recommended as an option for the treatment of progressive multiple myeloma in people who are at first relapse having received one prior therapy.</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>There are approximately 10,300 people with multiple myeloma in England. Of these approximately 39% (4,000) have relapsed disease. It is anticipate that around 1669 to 2999 people in England would be eligible for treatment with ixazomib citrate.</p> <p>The cost of ixazomib citrate is not yet known. Treatment costs for comparators such as bortezomib; bortezomib plus dexamethasone and lenalidomide plus dexamethasone are £3,050, £3,073 and £4,368 per cycle respectively. Ixazomib citrate represents an additional treatment cost to some therapy regimens, but where used in place of another drugs there are offsetting savings, as well as administration savings due to</p>		

	being oral rather than IV administered.
<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>	Teduglutide for treating short bowel syndrome		
<b>Topic Selection ID Number</b>	4549	<b>Wave / Round</b>	n/a
<b>TA ID Number</b>	885		
<b>Company</b>	Shire		
<b>Anticipated licensing information</b>	<p>Marketing authorisation (received in 2012): “for the treatment of adult patients with Short Bowel Syndrome. Patients should be stable following a period of intestinal adaptation after surgery.”</p> <p>Posology and method of administration: “Optimisation and stabilisation of intravenous fluid and nutrition support should be performed before initiation of treatment.”</p> <p>Teduglutide has been commercially available in the UK for the treating short bowel syndrome since September 2014.</p>		
<b>Draft remit</b>	To evaluate the benefits and costs of teduglutide within its licensed indication for treating short bowel syndrome 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 teduglutide for treating short bowel syndrome is appropriate.</p> <p>The proposed remit is not appropriate and should be amended as follows: To appraise the clinical and cost effectiveness of teduglutide within its marketing authorisation for treating short bowel syndrome. 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> <p>The estimate of population size in the draft scope before consultation was 194 people in England. Endorsed by NHS England, it was based on 2013 population data from the Office for National Statistics and the company’s estimate of the prevalence of non-malignant long-term parenteral support-dependent short bowel syndrome in England. At the workshop, it was indicated that a larger group (&gt;270 patients) might be treated with teduglutide in clinical practice (see ‘Population size’ section below).</p>		
<b>Population size</b>	<p><b>More than 270 people</b> in England would be eligible for treatment with teduglutide. This number comprises approximately <b>270 people</b> who are dependent on parenteral support plus an unknown number of people who are not dependent on parenteral support (data unavailable).</p> <p>The current estimate is based on unpublished data from The British Artificial Nutrition Survey (BANS) (provided by clinician):</p> <ul style="list-style-type: none"> <li>• Period prevalence for people on home parenteral nutrition (HPN) in UK was 1310 in 2013;</li> <li>• 89–93% were from England</li> <li>• Projecting this to 2015, there will have been 1350 HPN patients in England (this is in keeping with the clinical impression from the national intestinal failure centres)</li> </ul>		

	<ul style="list-style-type: none"> <li>• 52% patients on HPN have an underlying short bowel → 675 patients on HPN had short bowel in 2015</li> <li>• Fewer patients will be suitable for teduglutide. It is contraindicated in patients with malignancy: exclude 60% of patients → leaves 270 patients.</li> </ul> <p>Note: this population estimate reflects the subgroup scoped (people who are dependent on parenteral support i.e. they have type III intestinal failure). The clinical expert advised that there are no data on the number of patients with short bowel syndrome who are not on parenteral support, so we do not have a population estimate that reflects the full breadth of the marketing authorisation. Because the marketing authorisation is broader than the evidence base, the number of people potentially eligible for teduglutide would be more than 270.</p>
<b>Process (MTA/STA/HST)</b>	STA (instead of HST)
<b>Proposed changes to remit (in bold)</b>	To <b>evaluate appraise</b> the <del>benefits and costs</del> <b>clinical and cost effectiveness</b> of teduglutide within its <del>licensed indication</del> <b>marketing authorisation</b> for treating short bowel syndrome <del>for national commissioning by NHS England</del> .
<b>Costing implications of remit change</b>	Around 270 people could have non-malignant short bowel syndrome that is home parenteral nutrition dependent, and be eligible for treatment with teduglutide (the number of potentially eligible patients with short bowel syndrome who are not on parenteral support is unknown). The company estimates that around 80 of these would receive treatment after 5 years. The cost of teduglutide is £190,000 per patient per year, although some of this cost may be offset by a reduction in provision of home parenteral nutrition. The company estimates that by 2020, the incremental cost to the NHS will be around £15m if teduglutide is approved.
<b>Timeliness statement</b>	As the technology has received a marketing authorisation, issuing timely guidance will <u>not</u> be possible.