

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

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

**Consultation on Batch 52 draft remits and draft scopes and  
summary of comments and discussions at scoping workshops**

Topic ID	Topic title
1055	Sofosbuvir-velpatasvir-voxilaprevir for treating chronic hepatitis C
1068	Bezlotoxumab for treating <i>Clostridium difficile</i> infection
1064	Eculizumab for treating refractory myasthenia gravis
1037	Empagliflozin for reducing the risk of death from cardiovascular disease in people with type 2 diabetes and established cardiovascular disease
1051	Tocilizumab for treating giant cell arteritis
1061	Furosemide micro-pump for treating oedema associated with heart failure
1002	Sirukumab for previously treated moderate to severe active rheumatoid arthritis

<b>Provisional Title</b>	Sofosbuvir-velpatasvir-voxilaprevir for treating chronic hepatitis C		
<b>Topic Selection ID Number</b>	7882	<b>Round</b>	152
<b>TA/HST ID Number</b>	ID 1055		
<b>Company</b>	Gilead Sciences		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of sofosbuvir–velpatasvir–voxilaprevir within its marketing authorisation for treating chronic hepatitis C.		
<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 sofosbuvir-velpatasvir-voxilaprevir for treating chronic hepatitis C is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>No material issue was raised during consultation.</p> <p>NICE has recently published several pieces of guidance on new direct-acting antivirals (DAAs) for treating chronic hepatitis C, including the double regimen of sofosbuvir-velpatasvir. However, this triple regimen is expected to provide additional benefit as the marketing authorisation could potentially include people previously treated with a DAA.</p>		
<b>Population size</b>	Currently around 10,000 people have treatment for hepatitis C and this is estimated to increase to around 15,000 in the next 5 years. It is not known how many people would be eligible for treatment with sofosbuvir–velpatasvir–voxilaprevir, because the company has not informed NICE of the anticipated place in the treatment pathway, or the target patient groups. The anticipated MA is broad.		
<b>Process TA/HST</b>	TA		
<b>Proposed changes to remit (in bold)</b>	None		
<b>Costing implications of remit change</b>	Currently around 10,000 people have treatment for hepatitis C and this is estimated to increase to around 15,000 in the next 5 years. There are alternative treatment options which offer similar effectiveness and treatment durations. These include other sofosbuvir combination therapies which cover similar population groups.		
<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>	Bezlotoxumab for treating <i>Clostridium difficile</i> infection		
<b>Topic Selection ID Number</b>	8406	<b>Round</b>	192
<b>TA/HST ID Number</b>	ID 1068		
<b>Company</b>	Merck Sharp & Dohme		
<b>Anticipated licensing information</b>	Marketing authorisation received in January 2017 for the prevention of recurrence of <i>Clostridium difficile</i> infection (CDI) in adults at high risk for recurrence of CDI		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of bezlotoxumab for preventing recurrent <i>Clostridium difficile</i> infection		
<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 bezlotoxumab for treating <i>Clostridium difficile</i> infection is <u>appropriate</u>.</p> <p>The proposed remit is not appropriate and should be amended inline with the marketing authorisation.</p> <p>Bezlotoxumab is to be used in combination with standard of care antibiotics which are 'treating' the infection. Consultees considered the word 'preventing' to be confusing in this context because it implied that it could be used after the infection had resolved for preventing a subsequent infection. The topic selection group agreed that the scope is the place to clarify this.</p> <p>Other minor issues around comparators and outcomes have been addressed directly in the scope.</p>		
<b>Population size</b>	Approximately 14,000 people were diagnosed with <i>C. difficile</i> infection between March – April 2016 in England. It is not clear what proportion of patients would be classed as having a high risk for recurrence of CDI.		
<b>Process (TA/HST)</b>	TA		
<b>Proposed changes to remit (in bold)</b>	To appraise the clinical and cost effectiveness of bezlotoxumab within its marketing authorisation for <b>preventing the recurrence of preventing recurrent</b> <i>Clostridium difficile</i> infection		
<b>Costing implications of remit change</b>	Bezlotoxumab is a new treatment option and is administered alongside standard care of antibiotics as a single intravenous infusion. The cost of bezlotoxumab is not yet known. Increased drug treatment costs are likely to be accompanied by reduced costs from decreased disease recurrence and fewer surgeries for extreme cases.		
<b>Timeliness statement</b>	Considering that this product is shortly due to receive a marketing authorisation for use in the UK, publication of timely guidance will not be possible.		

<b>Provisional Title</b>	Eculizumab for treating refractory myasthenia gravis		
<b>Topic Selection ID Number</b>	8239	<b>Wave / Round</b>	174
<b>TA/HST ID Number</b>	ID 1064		
<b>Company</b>	Alexion		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of eculizumab within its marketing authorisation for treating refractory myasthenia gravis.		
<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 eculizumab for treating refractory myasthenia gravis is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p><u>Process</u></p> <p>The company provided extensive comments on why eculizumab for this indication meets all the HST prioritisation criteria and therefore should be evaluated through HST. The group accepted that the topic is not suitable for HST for the following reasons:</p> <ul style="list-style-type: none"> <li>• The clinicians stated that gMG is currently managed in 50 specialist neuroscience centres in England. The population size is uncertain and may be large.</li> <li>• Treatment of gMG is currently not organised or commissioned as a highly specialised service. NHS England have no intention to commission as a highly specialised service.</li> <li>• The target group is not clinically distinct; it is a subgroup of the overall gMG population. In particular treatment refractory gMG is not a distinct entity. The clinicians stated that some refractory patients have not been properly managed with current treatment and therefore not truly refractory, also the drug can, in theory, be used at any stage of the disease and regardless of the anti-AChR antibody status.</li> </ul>		
<b>Population size</b>	<ul style="list-style-type: none"> <li>• Myasthenia gravis affects 15 in every 100,000 people in the UK (<a href="#">NHS Choices website</a>), which equates to ~8200 people based on the ONS population estimate for England (54.8 million)</li> <li>• 75% of patients with myasthenia gravis progress to gMG (n=6150) <ul style="list-style-type: none"> <li>○ Company estimate (Roberston et al., 2009)</li> </ul> </li> <li>• Estimates for the percentage of people that are likely to be refractory range from up to 15% (n=923) to as low as Between 1% (n=62) <ul style="list-style-type: none"> <li>○ <a href="#">Alexion website</a> suggests 10-15% people</li> <li>○ A clinical expert who attended the workshop suggested in <a href="#">email correspondence</a> that the truly refractory population may be as low as 1%</li> </ul> </li> </ul> <p>The population will be smaller if the marketing authorisation</p>		

	specifies 'anti-acetylcholine receptor (anti-AChR) antibody-positive'.
<b>Process (TA/HST)</b>	TA
<b>Proposed changes to remit (in bold)</b>	None
<b>Costing implications of remit change</b>	Eculizumab is an orphan drug and represents a new treatment option for this condition. Eculizumab is administered by IV infusion. The cost per patient is estimated to be around £327,600 based on a unit cost of £3,150 per 300mg vial, administered at a dose of 1200mg every 2 weeks. Therefore the annual price could be up to £302m, depending on the percentage of refractory patients. There would also be administration costs for IV.
<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>	Empagliflozin for reducing the risk of death from cardiovascular disease in people with type 2 diabetes and established cardiovascular disease.		
<b>Topic Selection ID Number</b>	8421	<b>Wave / Round</b>	194
<b>TA ID Number</b>	ID 1037		
<b>Company</b>	Boehringer Ingelheim		
<b>Anticipated licensing information</b>	<p>Marketing authorisation: In Dec 2016 the CHMP adopted a positive opinion to change the existing indication, and regulatory approval was granted in Feb 2017.</p> <p>Updated wording of marketing authorisation from Feb 2017: 'Empagliflozin for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise</p> <ul style="list-style-type: none"> <li>- as monotherapy when metformin is considered inappropriate due to intolerance</li> <li>- in addition to other medicinal products for the treatment of diabetes'.</li> </ul> <p>Note that the wording of the marketing authorisation is different from the proposed indication discussed at DP3, that is, there is now no specific reference to reducing the risk of cardiovascular death as part of the main indication.</p>		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of empagliflozin within its marketing authorisation for reducing the risk of death from cardiovascular disease in people with type 2 diabetes.		
<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 empagliflozin for reducing the risk of death from cardiovascular disease in people with type 2 diabetes is appropriate.</p> <p>The proposed remit is not appropriate and should be amended as follows: To appraise the clinical and cost effectiveness of empagliflozin within its marketing authorisation for reducing the risk of death from cardiovascular disease in people with type 2 diabetes and established cardiovascular disease.</p> <p>Empagliflozin is already used in clinical practice in type 2 diabetes for glycaemic control. However, stakeholders considered that there would be value in appraising empagliflozin for its additional cardiovascular benefits, which they believe are significant. Stakeholders also felt that it would be worthwhile exploring whether the appraisal could be combined with another drug (liraglutide) that is being investigated for the prevention of death from cardiovascular disease in people with type 2 diabetes ***CONFIDENTIAL INFORMATION REMOVED***</p>		
<b>Population size</b>	<p>Approximately 1.75 million people in England (diagnosed and undiagnosed with type 2 diabetes) may be eligible for treatment with this technology. This estimate is based on:</p> <ul style="list-style-type: none"> <li>- there being approximately 2.9 million adults in England with diabetes, of whom 90% have type 2 diabetes (2.61</li> </ul>		

	<p>million)</p> <ul style="list-style-type: none"> <li>- there being an estimated 1 million adults in the UK (840,000 in England) with undiagnosed type 2 diabetes</li> <li>- CVD is a major cause of death and disability in people with diabetes and accounts for 52% of deaths.</li> </ul>
<b>Process (TA/HST)</b>	TA (possible MTA with another drug that is expected to be licensed for the prevention of death from cardiovascular disease in people with type 2 diabetes (liraglutide, batch 55, TS ID8967))
<b>Proposed changes to remit (in bold)</b>	To appraise the clinical and cost effectiveness of empagliflozin within its marketing authorisation for reducing the risk of death from cardiovascular disease in people with type 2 diabetes <b>and established cardiovascular disease</b> .
<b>Costing implications of remit change</b>	The annual cost of empagliflozin per person is estimated to be around £480. This would be an additional cost on top of other diabetes medication. Of the total of potentially eligible 1.75 million people, it is not known how many would receive this technology. For every 100,000 people using this technology in addition to existing treatments, the additional annual drug cost would be around £48 million. There are likely to be savings from a reduction in cardiovascular events as a result of using the technology.
<b>Timeliness statement</b>	Considering that this product already has a marketing authorisation for use in the UK, publication of timely guidance will not be possible.

<b>Provisional Title</b>	Tocilizumab for treating giant cell arteritis		
<b>Topic Selection ID Number</b>	7203	<b>Round</b>	92
<b>TA ID Number</b>	1051		
<b>Company</b>	Roche Products		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of tocilizumab within its marketing authorisation for treating giant cell arteritis.		
<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 tocilizumab for treating giant cell arteritis is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>Giant cell arteritis is not well defined and some consultees asked whether the remit should include large vessel vasculitis (such as Takayasu's arteritis). At the scoping workshop, attendees (including the company) agreed that the expected marketing authorisation was specific to giant cell arteritis and no change to remit was required.</p> <p>Other minor issues (including the description of the condition, the current treatment pathway, comparators and subgroups) have been addressed directly in the scope.</p>		
<b>Population size</b>	<p>Approximately 6,050 people in England would be eligible for treatment with tocilizumab.</p> <p>This estimate is based on 1 in 4,500 people aged 40 years or older being diagnosed in the UK each year, and Office for National Statistics (ONS) 2015 mid-year estimates of the population of England. ONS estimate of England population is 55 million, of which 27 million are aged 40 years or older.</p>		
<b>Process (TA/HST)</b>	TA		
<b>Proposed changes to remit (in bold)</b>	None		
<b>Costing implications of remit change</b>	<p>The cost of tocilizumab for GCA is unknown. The annual cost of treatment is based on the cost of a subcutaneous injection of tocilizumab licensed for rheumatoid arthritis. The annual cost per patient has been estimated to be between £5,940 and £11,870 depending on whether it is given weekly or every 2 weeks. Applying this range to the estimated 6,050 eligible patients would give a cost of between £35.9m and £71.8m, excluding any savings from other treatments avoided.</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>	Furosemide micro-pump for treating oedema associated with heart failure		
<b>Topic Selection ID Number</b>	8360	<b>Wave / Round</b>	189
<b>TA ID Number</b>	1061		
<b>Company</b>	scPharmaceuticals		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of furosemide micro-pump within its marketing authorisation for treating oedema associated with heart failure.		
<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 furosemide micro-pump for treating oedema associated with heart failure is <u>appropriate</u>.</p> <p>The proposed remit is <u>appropriate</u>.</p> <p><u>Technology</u></p> <ul style="list-style-type: none"> <li>• The furosemide micro-pump consists of a device which contains a replaceable cartridge of furosemide. The device adheres to the skin and contains a needle which delivers the furosemide subcutaneously over a number of hours.</li> <li>• Furosemide has been reformulated to make it pH neutral and less likely to irritate the skin. The company is seeking a marketing authorisation in the UK for the reformulation of furosemide, as the current marketing authorisation for furosemide does not include subcutaneous administration.</li> <li>• The company is seeking a CE mark for the device.</li> <li>• The company stated that it did not plan to make the re-formulated furosemide available separately to the delivery device.</li> </ul> <p>Issues relating to the population, comparators and outcomes have been addressed directly in the scope.</p>		
<b>Population size</b>	<p>Approximately 7,000-10,500 people in England would be eligible for treatment with this technology.</p> <p>There were 70,000 hospital admissions in 2014/15 with a primary diagnosis of heart failure. According to the National Heart Failure Audit Annual Report 2014-2015, approximately half of hospital admissions where the primary diagnosis was heart failure were associated with moderate or severe oedema.</p> <p>The scoping workshop attendees thought that 20-30% of people currently admitted to hospital with oedema would be suitable for treatment with the furosemide micro-pump.</p>		
<b>Process (TA/HST)</b>	TA		

<b>Proposed changes to remit (in bold)</b>	None
<b>Costing implications of remit change</b>	<p>It is estimated that 7,000-10,500 people in England would be eligible for treatment with this technology each year. The target price for the drug-device combination including the novel furosemide formulation and all device components is €150.00 (approximately £128). It is estimated that a typical patient would use 1.25 of the units, at a cost of around £160, equivalent to £1.1m - £1.7m for the eligible population in England each year.</p> <p>Some of these costs will be offset by people transferring from alternative treatments. The technology may also help to reduce the need for inpatient care for people with heart failure by preventing hospital admissions or reducing length of stay when people are admitted, thus creating savings for the NHS. Each heart failure hospital admission avoided will save between £1,300 and £5,600 for commissioners and around £200 will be saved for each bed-day avoided.</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.

<b>Provisional Title</b>	Sirukumab for previously treated moderate to severe active rheumatoid arthritis.		
<b>Topic Selection ID Number</b>	7816	<b>Round</b>	146
<b>TA ID Number</b>	1002		
<b>Company</b>	Janssen Cilag		
<b>Anticipated licensing information</b>	***CONFIDENTIAL INFORMATION REMOVED***		
<b>Draft remit</b>	To appraise the clinical and cost effectiveness of sirukumab within its marketing authorisation for previously treated moderate to severe active rheumatoid arthritis		
<b>Main points from consultation</b>	<p>Following the consultation exercise, the Institute is of the opinion that an appraisal of sirukumab for previously treated moderate to severe active rheumatoid arthritis is <u>appropriate</u>.</p> <p>The proposed remit is <u>appropriate</u>. No changes are required. In response to consultation, the company suggested that the remit should be amended so that it did not specify that people must have had previous treatment. ***CONFIDENTIAL INFORMATION REMOVED***</p> <p>There were no substantive changes to the scope following consultation.</p> <p>At the DP3 meeting, it was suggested that sirukumab would be an appropriate topic to go through the TA process that uses cost comparison. The majority of consultees and commentators (including the company) considered this process appropriate for sirukumab.</p>		
<b>Population size</b>	<p>Based on the populations enrolled in the trials, between 10,400 and 34,600 people would be eligible for treatment with sirukumab.</p> <p>The prevalence of rheumatoid arthritis in the UK estimated to be 0.44% in males and 1.16% in females; when applied to the England population, this is approximately 530,500 people.</p> <p>Approximately 34,600 people have an inadequate response/intolerance to DMARDs (NICE costing statement TA225-10% of people with rheumatoid arthritis). Approximately 10,380 people with have an inadequate response/intolerance to DMARDs &amp; have an inadequate response to TNF-a inhibitors (Company estimate of 30% of inadequate response or intolerance to DMARDs population).</p>		
<b>Process (TA/HST)</b>	TA		

<b>Proposed changes to remit (in bold)</b>	None
<b>Costing implications of remit change</b>	The cost of the technology is not yet known, but comparable annual treatment costs range from approximately £9.2k to £13.6k per patient. As sirukumab is an additional treatment option for this group of patients, if the cost of sirukumab is similar to the comparable treatments it is unlikely that there will be a resource impact for the NHS.
<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.