

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

**Consultation on Batch 49 draft remits and draft scopes and
summary of comments and discussions at scoping workshops**

Topic ID	Topic title
967	Masitinib for treating amyotrophic lateral sclerosis
937	Ocrelizumab for treating relapsing multiple sclerosis
938	Ocrelizumab for treating primary progressive multiple sclerosis
913	Betrixaban for preventing venous thromboembolism in people hospitalised for acute medical conditions
953	Tenofovir alafenamide for treating chronic hepatitis B
828	Peramivir for treating influenza
979	Baricitinib for treating moderate to severe rheumatoid arthritis
942	Glycerol phenylbutyrate for treating urea cycle disorders

Provisional Title	Masitinib for treating amyotrophic lateral sclerosis		
Topic Selection ID Number	7769	Wave / Round	R140
TA ID Number	967		
Company	AB Science		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of masitinib within its marketing authorisation for treating the amyotrophic lateral sclerosis form of motor neurone disease.		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of masitinib for treating amyotrophic lateral sclerosis is <u>appropriate</u>.</p> <p>The proposed remit is not appropriate and should be amended as follows: for treating the amyotrophic lateral sclerosis form of motor neurone disease. The change is needed because the company could not confirm whether masitinib will be licensed for the narrow UK definition of amyotrophic lateral sclerosis or the wider international definition of the disease. The original remit implied that the marketing authorisation uses the narrow UK definition. The revised remit is broader and will be appropriate for whichever definition is in the indication and SmPC.</p> <p>Similarly, the population, comparators and outcomes in the scope are appropriate for both definitions of the disease.</p> <p>Consultees viewed this appraisal as high priority. There is only one disease-modifying treatment available for amyotrophic lateral sclerosis (riluzole, technology appraisal guidance 20).</p>		
Population size	<p>Between 3200 and 4000 people in England have amyotrophic lateral sclerosis and would be eligible for treatment with masitinib.</p> <p>This was calculated using NICE guideline 42. The exact population size depends on the disease definition in the indication and SmPC.</p>		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of masitinib within its marketing authorisation for treating the amyotrophic lateral sclerosis form of motor neurone disease .		
Costing implications of remit change	Masitinib is administered orally, on a continuous basis, and dosed according to patient bodyweight. The cost of masitinib is not known, but as an add-on treatment its use will lead to increased drug costs. Where treatment reduces symptoms or disability, some treatment costs may be avoided; treatment may also extend length of survival - the size of these resource impacts is unknown at this stage. No administration costs anticipated as it's orally administered.		
Timeliness statement	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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Provisional Title	Ocrelizumab for treating relapsing multiple sclerosis		
Topic Selection ID Number	7530	Wave / Round	R123
TA ID Number	937		
Company	Roche Products		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of ocrelizumab within its marketing authorisation for treating relapsing forms of multiple sclerosis.		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ocrelizumab for treating relapsing forms of multiple sclerosis is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>NICE recommends an STA because combining this topic with other ongoing scopes could delay issuing guidance and would make a complicated appraisal. There are 2 multiple sclerosis topics in scoping:</p> <ul style="list-style-type: none"> Batch 49: ID938 ocrelizumab for primary progressive multiple sclerosis; same licensing timelines as for this scope. Batch 47: ID919 biotin for primary and secondary progressive multiple sclerosis; launch expected *** Commercial in confidence text removed*** 		
Population size	<p>Approximately 76–80,000 people in England would be eligible for treatment with ocrelizumab. Each year, approximately 3,500 more people would be eligible.</p> <p>These estimates are based on 89,000 people in England having multiple sclerosis, with 4,000 people being diagnosed each year. 85–90% have relapsing-remitting disease (MS Society; Murray 2006; Scolding et al. 2015).</p>		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	*** Commercial in confidence text removed*** Existing treatments cost between £6,000 and £19,000 annually so the resource impact of this topic will depend on the comparators currently used by the people that switch treatments.		
Timeliness statement	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.		

Provisional Title	Ocrelizumab for treating primary progressive multiple sclerosis		
Topic Selection ID Number	7531	Wave / Round	R123
TA ID Number	938		
Company	Roche Products		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of ocrelizumab within its marketing authorisation for treating primary progressive multiple sclerosis.		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ocrelizumab for treating primary progressive multiple sclerosis is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>Consultees view this appraisal as high priority. *** Commercial in confidence text removed***</p>		
Population size	<p>Approximately, 8,900 people in England would be eligible for treatment with ocrelizumab. Each year, approximately 400 more people would be eligible.</p> <p>These estimates are based on 89,000 people in England having multiple sclerosis, with 4,000 people being diagnosed each year. 10% have primary progressive disease (MS Society; Murray 2006; Scolding et al. 2015).</p>		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	*** Commercial in confidence text removed***The use of this technology would represent an additional cost to the NHS because there are currently no licensed disease-modifying drugs or similar therapies for this indication. There are also likely to be additional costs for intravenous administration and dosage monitoring. There is potential for delayed progression of disease rather than avoiding progression so costs may be deferred rather than avoided.		
Timeliness statement	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.		

Provisional Title	Betrixaban for preventing venous thromboembolism in people hospitalised for acute medical conditions		
Topic Selection ID Number	7529	Wave / Round	R123
TA ID Number	913		
Company	Portola Pharmaceuticals		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of betrixaban within its marketing authorisation for preventing venous thromboembolism in people hospitalised for acute medical conditions		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of betrixaban for preventing venous thromboembolism in people hospitalised for acute medical conditions 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>		
Population size	It is difficult to accurately estimate the number of people who are both hospitalised and at risk of venous thromboembolism. Estimates suggest that between 25,000 and 32,000 people could be dying each year in the UK from preventable hospital-acquired venous thromboembolism including patients admitted to hospital for medical care and surgery. However, there is some debate about whether the figures are as high as this (National Statistics for England records the recognised figure on death certificates in 2010 as 6,000).		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	Betrixaban is intended to be used for the first-line prevention of venous thromboembolism (VTE) in acute medically ill patients. VTE has an annual incidence of approximately 2 in 1,000 population (107,000 people in England). The number of people who are hospitalised or post discharge with a relevant condition (congestive heart failure, acute respiratory failure, acute infection without septic shock, acute rheumatic disorders or acute ischemic stroke with lower extremity hemiparesis or hemiparalysis) and would therefore be eligible for treatment with betrixaban is not known. The cost of betrixaban is not known, but where it is used in place of another type of oral anti-coagulant the cost will be at least partially offset. As it is orally administered, there may be savings on administration costs when used in place of one of the subcutaneously administered treatment options. The cost of oral anticoagulation treatments may be under £100 for the suggested treatment period of up to		

	35 days.
Timeliness statement	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.

Provisional Title	Tenofovir alafenamide for treating chronic hepatitis B		
Topic Selection ID Number	7724	Wave / Round	R139
TA ID Number	953		
Company	Gilead Sciences		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of tenofovir alafenamide within its marketing authorisation for treating chronic hepatitis B.		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of tenofovir alafenamide for treating chronic hepatitis B is <u>appropriate, but not urgent</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>At the DP3 meeting on 6 May 2016, it was decided that this appraisal will focus on a direct comparison with tenofovir disoproxil (TA173) only given that tenofovir alafenamide and tenofovir disoproxil are both prodrugs of tenofovir. Therefore other NICE recommended treatments were not included as comparators. The consultees and scoping workshop attendees generally agreed with the concept and rationale for this approach. However they stated that there are people who cannot take tenofovir disoproxil, such as people with or at risk of renal disease or osteoporosis. This group would normally have entecavir. Therefore entecavir was included as a comparator only for people who cannot take tenofovir disoproxil.</p>		
Population size	Approximately 326,000 people in England have chronic hepatitis B and could potentially be eligible for treatment with tenofovir alafenamide. However only a small proportion of people are diagnosed and receive treatment.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	<p>Approximately 326,000 people in England have chronic hepatitis B but only a small proportion are diagnosed (26%) and receive anti-viral treatment (5%).</p> <p>If licensed, tenofovir alafenamide monotherapy will provide an additional oral treatment option for these people. The cost of tenofovir alafenamide is not yet known. Comparator treatments tenofovir disoproxil and entecavir cost around £2,500 and £4,600 each year respectively. The resource impact of this topic depends on the number of people that would switch treatments and the difference in cost.</p>		
Timeliness statement	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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Provisional Title	Peramivir for treating influenza		
Topic Selection ID Number	7516	Wave / Round	R122
TA ID Number	828		
Company	Sequirus Vaccine (previously BioCryst Pharmaceuticals)		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of peramivir within its marketing authorisation for treating acute, uncomplicated influenza.		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of peramivir for treating influenza is <u>appropriate</u>.</p> <p>The proposed remit is <u>not</u> appropriate. The clinical expert at the workshop stated that uncomplicated influenza would be treated in primary care, whereas peramivir would be used in a hospital setting for more severe complicated influenza. Given that the anticipated marketing authorisation does not specify the severity of disease, the remit should be kept broad to specify 'influenza' only.</p> <p>Issues relating to the marketing authorisation *** Commercial in confidence text removed*** <u>Note:</u> The MTA of oseltamivir and zanamivir (TA168) includes both adults and children, but does not cover circumstances of a pandemic or impending pandemic.</p> <p>At the decision point 4 meeting, it was agreed that a referral should be sought *** Commercial in confidence text removed***</p>		
Population size	It is difficult to estimate the number of people in England who would be eligible for treatment with peramivir. In 2014, the peak weekly rate of GP consultations in England and Wales for influenza-like illness was 28.3 per 100,000. However clinical advice suggests that peramivir would mostly be used in hospitals rather than primary care because of its intravenous mode of administration. Therefore the population size would be smaller.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of peramivir within its marketing authorisation for treating acute, uncomplicated influenza.		
Costing implications of remit change	The estimated number of people in England who may be prescribed treatment for influenza in a non-epidemic year is around 4,600. This is significantly lower than the numbers who may develop influenza in any one year because many people use symptomatic relief rather than visit their GP for treatment. The number who may receive treatment in hospital is not		

	known. The cost of peramivir is unknown. Peramivir is intended for use as a treatment option and requires a single IV dose which completes a full treatment course. There are additional costs associated with this treatment option compared with other options which are administered orally or inhaled. These costs relate to increased clinical time and preparation for IV administration. The cost of comparator treatments ranges from £10.27 to £16.36 per person. The resource impact depends on the cost of peramivir compared with comparator treatments.
Timeliness statement	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.

Provisional Title	Baricitinib for treating moderate to severe rheumatoid arthritis		
Topic Selection ID Number	7791	Wave / Round	R142
TA ID Number	979		
Company	Eli Lilly and Company		
Anticipated licensing information	*** Commercial in confidence text removed***		
Draft remit	To appraise the clinical and cost effectiveness of baricitinib within its marketing authorisation for treating moderate to severe active rheumatoid arthritis.		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of baricitinib for treating moderate to severe active rheumatoid arthritis is appropriate.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>There were no substantive changes to the scope following consultation.</p>		
Population size	<p>Approximately 520,000 people in England would be eligible for treatment with baricitinib.</p> <p>This is the full estimated population of people with RA in England. *** Commercial in confidence text removed***</p>		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	Not applicable		
Costing implications of remit change	The cost of baricitinib is not yet known. If licensed, baricitinib will be the first JAK1/2 inhibitor to be licensed in the treatment of moderate to severe RA. A number of other treatments cost around £9,000 -£13,000. Baricitinib is administered orally and so is likely to reduce administration costs compared with other treatments.		
Timeliness statement	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.		

Provisional Title	Glycerol phenylbutyrate for treating urea cycle disorders		
Topic Selection ID Number	7926	Wave / Round	R161
TA ID Number	942		
Company	Horizon Pharma		
Anticipated licensing information	<p>Marketing authorisation granted: November 2015</p> <p>Wording of marketing authorisation:</p> <p>RAVICTI is indicated for use as adjunctive therapy for chronic management of adult and paediatric patients ≥ 2 months of age with urea cycle disorders (UCDs) including deficiencies of carbamoyl phosphate-synthase-I (CPS), ornithine carbamoyltransferase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase I (ARG) and ornithine translocase deficiency</p> <p>hyperornithinaemiahyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. RAVICTI must be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements).</p>		
Draft remit	To appraise the clinical and cost effectiveness of glycerol phenylbutyrate within its marketing authorisation for treating urea cycle disorders		
Main points from consultation	<p>Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of glycerol phenylbutyrate for treating urea cycle disorders is not appropriate.</p> <p>The proposed remit would be appropriate, if an appraisal were to proceed. No changes are required.</p> <p>Consultees considered that an STA would not be appropriate and would be of limited value, and noted that the main uncertainties concerned how to select treatment options and understand the many unlicensed drugs available for this condition. Scoping workshop attendees and the technical team recommend that the suitability of this topic for a Commissioning Support Document or evidence summary for new medicines is considered.</p>		
Population size	<p>Approximately 115 people in England would be eligible for treatment with glycerol phenylbutyrate.</p> <p>This figure is based on estimates from clinical and patient experts: approximately 350 people are known to have urea cycle disorders in the UK, of whom one-third are considered for nitrogen scavengers (such as glycerol phenylbutyrate or its comparators, sodium benzoate and sodium phenylbutyrate).</p>		
Process (TA/HST)	<p>N/A – referral not sought</p> <p>May be considered for a Commissioning Support Document or evidence summary for new medicines.</p>		
Proposed changes to remit (in bold)	N/A – referral not sought		

Costing implications of remit change	People whose disease cannot be managed by dietary protein restriction with amino acid supplementation would be considered for second line pharmaceutical treatment. The cost of glycerol phenylbutyrate is unknown but it represents an alternative treatment option. The cost of a sodium phenylbutyrate preparation (current treatment option) for a year is estimated to be £25,000–29,000 per patient (based on the list price).
Timeliness statement	N/A – referral not sought