

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

**CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals**

**Consultation on Batch 63 draft remits and draft scopes and
summary of comments and discussions at scoping workshops**

Topic ID	Topic title
ID1463	Anakinra for treating Still's disease
ID1486	Lumacaftor with ivacaftor for treating cystic fibrosis in children aged 2 to 11 years old homozygous for the F508del mutation
ID740	Liraglutide for managing overweight and obesity
ID1065	Pitolisant hydrochloride for treating excessive daytime sleepiness caused by obstructive sleep apnoea
ID1400	Upadacitinib for treating moderate to severe rheumatoid arthritis
ID1410	Lenadogene nolparvovec for treating Leber's hereditary optic neuropathy

Provisional Title	Anakinra for treating Still's disease		
Topic Selection ID Number	9818	TA ID Number	1463
Company	Swedish Orphan Biovitrum		
Licensing information	<p>Marketing authorisation (granted April 2018): Anakinra is indicated "in adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above for the treatment of Still's disease, including Systemic Juvenile Idiopathic Arthritis (SJIA) and Adult-Onset Still's Disease (AOSD), with active systemic features of moderate to high disease activity, or in patients with continued disease activity after treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids."</p>		
Draft remit	To appraise the clinical and cost effectiveness of anakinra within its marketing authorisation for treating Still's disease.		
Main points from consultation	<p>Following the consultation exercise, NICE is of the opinion that an appraisal of anakinra for treating Still's disease is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>A clinical commissioning policy for use of anakinra for Adult Onset Still's Disease (AOSD) in patients who failed DMARDs has recently been approved by NHS England and adopted into clinical practice. This did not include systemic juvenile idiopathic arthritis (SJIA), which is included in the juvenile idiopathic arthritis policy.</p> <ul style="list-style-type: none"> • The company argued that SJIA and AOSD share common clinical manifestations, and are increasingly recognised as a single disease. • The Royal College of Pathologists argued that the clinical commissioning policy was based on a robust evaluation of the clinical and cost effectiveness of anakinra for AOSD, and so the proposed STA would constitute "unnecessary duplication of the work". However, the comment acknowledged that there is scope to extend the indication to SJIA based on the evidence that was already gathered for AOSD policy. <p>The company would like the appraisal to focus on treatment in patients with inadequate response to DMARDs (as per NHSE policy) rather than first-line therapy (as per indication).</p>		
Population size	<p>Approximately 600 people in England would be eligible for treatment with anakinra.</p> <p>This estimate is based on an estimated prevalence of AOSD (400-800) and SJIA (1,000) in England, of whom up to a third may be eligible for treatment with biologics.</p>		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		

Costing implications	Anakinra is already marketed in the UK for the treatment of rheumatoid arthritis with an NHS indicative price of £734 for 28 pre-filled disposable 100mg/0.67 solution injections. Using the indicative price, the annual cost of treatment for an adult will be around £9,600. Using a weighted average weight for a child, and the same indicative price for anakinra, the annual cost of treatment will be around £4,500. The total resource impact of anakinra will depend on the uptake of both adults and children.
Timeliness statement	Considering that this product has received a marketing authorisation for use in the UK, publication of timely guidance will not be possible.

Provisional Title	Lumacaftor with ivacaftor for treating cystic fibrosis in children aged 2 to 11 years old homozygous for the F508del mutation		
Topic Selection ID Number	9831	TA ID Number	1486
Company	Vertex		
Licensing information	<p>Current marketing authorisation (extension granted Jan 2018): “Orkambi is indicated for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who are homozygous for the F508del mutation in the CFTR gene.” (tablet formulation)</p> <p>Marketing authorisation expected: No update received from company but on 16 November, CHMP positive opinion was granted “Orkambi granules [in sachet] are indicated for the treatment of cystic fibrosis (CF) in children aged 2 years and older who are homozygous for the F508del mutation in the CFTR gene.”</p>		
Draft remit	To appraise the clinical and cost effectiveness of lumacaftor in combination with ivacaftor within its marketing authorisation for treating cystic fibrosis in children ages 2 to 11 years old who are homozygous for the F508del mutation		
Main points from consultation	<p>Following the consultation exercise, NICE is of the opinion that an appraisal of lumacaftor and ivacaftor for cystic fibrosis (CF) in children aged 2 to 11 years who are homozygous for the F508del mutation in the CFTR gene is <u>appropriate</u>.</p> <p>Vertex did not engage in the consultation.</p> <p>One particular issue highlighted that if the drug were to be approved for under 12s but not over 12s it could be considered that there was inequity of access based on age.</p> <p>British Thoracic Society were pleased that the scope is for the whole age range but noted that lung function in terms of spirometry is not available for the youngest age group and it would be ‘lung clearance index’ instead.</p>		
Population size	<p>Based on information from the UK Cystic Fibrosis Registry 2015 dataset, approximately 1227 people (aged 2-11) in England would be eligible for treatment with lumacaftor-ivacaftor.</p> <p>See https://www.cysticfibrosis.org.uk/~media/documents/the-work-we-do/uk-cf-registry/data-request-269--2015--v4.ashx?la=en</p>		
Process (TA/HST)	TA		
Proposed changes to remit	None		
Costing implications	Treatment with lumacaftor with ivacaftor is administered as 2 tablets orally every 12 hours. The cost of lumacaftor with ivacaftor is £8,000 for 112 tablets. Lumacaftor with ivacaftor is also available as granules for younger children, however the unit cost is unknown so the resource impact for treatment with this new formulation cannot currently be estimated.		
Timeliness statement	Considering that this product has received a marketing authorisation for use in the UK, publication of timely guidance will not be possible.		

Provisional Title	Liraglutide for managing overweight and obesity		
Topic Selection ID Number	7045	TA ID Number	740
Company	Novo Nordisk		
Licensing information	<p>Marketing authorisation gained in 2015. ***Confidential information removed***</p> <p>Adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients with an initial Body Mass Index (BMI) of</p> <ul style="list-style-type: none"> • $\geq 30 \text{ kg/m}^2$ (obese), or • $\geq 27 \text{ kg/m}^2$ to $<30 \text{ kg/m}^2$ (overweight) in the presence of at least one weight-related comorbidity such as dysglycaemia (pre-diabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea. 		
Draft remit	<p>To appraise the clinical and cost effectiveness of liraglutide within its marketing authorisation, in addition to diet and physical activity, for the management of people with obesity or overweight with risk factors</p>		
Main points from consultation	<p>Following the consultation exercise, NICE is of the opinion that an appraisal of liraglutide for treating overweight and obesity is appropriate.</p> <p>The proposed remit should be amended to make clear that liraglutide is given in addition to a reduced calorie diet and increased physical activity, and to reflect the wording of the MA.</p> <p>Stakeholders strongly support referring this topic to NICE. Many consider this is urgent because of the high prevalence of obesity, the health impact associated with it, and the limited medication treatment options available.</p> <p>The company is seeking a NICE recommendation for a subgroup of patients within the current licensed indication; adult patients with a BMI ≥ 35 with prediabetes (HbA1c measurement 42-47 mmol/mol) and high risk CVD in specialist Tier 3 services. Based on the clinical and cost effectiveness evidence, the company believes that this subgroup of patients would benefit the most from liraglutide.</p>		
Population size	<p>Approximately 11,905,680 people in England may be eligible for treatment with this technology. This is based on information from the company submission for TA494 (naltrexone-bupropion; same position in pathway) using estimates from the 2014 Health Survey for England which suggested that 11,126,000 adults (aged ≥ 16) were obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). 15,825,000 adults were overweight (with around 30% or 4,747,500 having a $\text{BMI} \geq 27 \text{ kg/m}^2$); of these, an estimated 16% will have one or more weight-related comorbidity, equivalent to 779,680 patients.</p>		
Process (TA/HST)	TA		
Proposed changes to remit	<p>To appraise the clinical and cost effectiveness of liraglutide within its marketing authorisation, in addition to diet and</p>		

(in bold)	physical activity a reduced calorie diet and increased physical activity, for the management of people with obesity or overweight with risk factors.
Costing implications	Liraglutide is administered by subcutaneous injection at 3mg once daily. The annual cost of liraglutide is around £7,200 (NHS Drug Tariff). The only other active drug, orlistat, is administered at 120mg 3 times a day. The annual cost of treatment with orlistat is around £200 (NHS Drug Tariff) which gives an incremental cost of around £7,000 per person, per annum. However, orlistat is not widely used in clinical practice because it is not well tolerated. Therefore the incremental cost may be different if standard management is the comparator treatment that is used in current practice instead of orlistat.
Timeliness statement	Based on marketing authorisation for use in the UK, publication of timely guidance will not be possible. However, if the date of commercial availability within the UK NHS for this indication is used, timely guidance will be possible.

Provisional Title	Pitolisant hydrochloride for treating excessive daytime sleepiness caused by obstructive sleep apnoea		
Topic Selection ID Number	8238	TA ID Number	1065
Company	Bioprojet		
Anticipated licensing information	***Confidential information removed***		
Draft remit	<p>To appraise the clinical and cost effectiveness of pitolisant hydrochloride within its marketing authorisation for treating excessive daytime sleepiness caused by obstructive sleep apnoea</p>		
Main points from consultation	<p>Following the consultation exercise, NICE is of the opinion that an appraisal of pitolisant hydrochloride for treating EDS in patients with OSA is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <p>Stimulants similar to pitolisant hydrochloride, such as modafinil, are used to treat EDS related to other conditions. However, pitolisant hydrochloride is the first licensed treatment for EDS caused by OSA.</p> <p>Two responses and one endorsement from consultees were received (company and British Thoracic Society endorsed by Royal College of Physicians).</p> <p>British Thoracic Society (endorsed by RCP) made the following comments:</p> <ul style="list-style-type: none"> • This does not seem high priority for NICE. • Pitolisant is not expected to make a significant and substantial impact and it might even discourage CPAP use. • Pitolisant costs more than the other current stimulants currently used off label. • There are concerns about CPAP refusers being in the same group as those with excessive daytime sleepiness despite CPAP; these are two different patient groups and many would opt not to use/refuse CPAP if a tablet was an option. <p>The company commented that:</p> <ul style="list-style-type: none"> • It is important to refer this topic to NICE for appraisal, because there are some OSA patients treated with CPAP (5 to 10%), with good adherence, that have residual EDS: in that case, pitolisant could benefit these patients. 		
Population size	<p>The exact population size of people with ODS is somewhat uncertain but significant in size.</p> <p>An estimated 1.5 million adults in the UK are affected by OSA, but up to 85% (1.275m) are undiagnosed and untreated.</p> <p>It has been estimated that 87.2% people with OSA also</p>		

	<p>demonstrate EDS.</p> <p>Therefore, the population eligible for treatment with pitolisant hydrochloride could be as high as 1.31m. However, the number known to the health service is approximately 225,000.</p> <p>The population that could benefit from pitolisant is the OSA patient with <i>good adherence to CPAP treatment</i>, presenting with a residual EDS. This appears to represent approximately 5 to 10% of the OSA patient population (source: company), so 11,000 to 23,000 patients in the UK.</p>
Process (TA/HST)	TA
Proposed changes to remit	None
Costing implications	<p>Pitolisant hydrochloride is currently available in 4.5mg and 18mg tablets, however in clinical trials for pitolisant hydrochloride for obstructive sleep apnoea, pitolisant hydrochloride was administered orally at 10, 20 or 40mg per day for a duration of 12 weeks. The cost of this initial 12 week treatment is between around £900 and £1,700 per person.</p> <p>Maintenance treatment is administered orally at 10, 20 or 40mg per day for a duration of 39 weeks. The cost of maintenance treatment is between around £2,800 and £5,600.</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.

Provisional Title	Upadacitinib for treating moderate to severe rheumatoid arthritis		
Topic Selection ID Number	9189	TA ID Number	1400
Company	AbbVie		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for previously treated moderate to severe active rheumatoid arthritis.		
Main points from consultation	<p>Following the consultation exercise, NICE is of the opinion that an appraisal of upadacitinib for treating moderate to severe rheumatoid arthritis is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p>		
Population size	<p>Approximately 441,000 people in England would be eligible for treatment with upadacitinib. Severe RA population is around 66,000. A range of treatment options are already available for this population.</p> <p>This estimate is based on the prevalence of RA in the UK and approximately 15% of people with severe diagnosis (figure from previous NICE RA appraisals)</p>		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	The unit cost of upadacitinib is unknown so the resource impact of this technology cannot currently be estimated.		
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	Lenadogene nolparvovec for treating Leber's hereditary optic neuropathy		
Topic Selection ID Number	9139	TA ID Number	1410
Company	GenSight Biologics		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of lenadogene nolparvovec within its marketing authorisation for treating Leber's hereditary optic neuropathy.		
Main points from consultation	<p>Following the consultation exercise, NICE is of the opinion that an appraisal of lenadogene nolparvovec for treating Leber's hereditary optic neuropathy is <u>appropriate</u>.</p> <p>The proposed remit is appropriate. No changes are required.</p> <ul style="list-style-type: none"> • There is only one treatment licensed for this condition, idebenone. • Idebenone was considered at DP2 in November 2011 (TS ID 5432), and it was decided not to proceed to appraisal due to difficulties in defining the exact small population in this condition, even with specialist advice. It was noted that this topic could potentially be reviewed by AGNSS. • NHS England are currently putting a clinical commissioning policy for idebenone in its licensed indication through the NHS England process. This will be in the CSP programme and is a full policy. 		
Population size	Largely unknown but thought to be small. In the UK, it is estimated that 1,500–2,000 people in the UK are affected with LHON, but it unknown what proportion of these patients will be eligible for lenadogene nolparvovec treatment.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	The unit cost of lenadogene nolparvovec is unknown so the resource impact of this technology cannot currently be estimated.		
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.		