NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 59 draft remits and draft scopes and Summary of comments and discussions at scoping workshops

Topic ID	Topic title
1276	Selective internal radiation therapies for treating hepatocellular carcinoma.
1149	Lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing elective surgery
1196	Intravenous zanamivir for treating influenza in hospital
1150	Clostridium botulinum neurotoxin type A for treating chronic sialorrhea
1294	Ozanimod for treating relapsing-remitting multiple sclerosis

Provisional Title	Selective internal radiation therapies for treating hepatocellular carcinoma (new title post scoping) TheraSphere for treating advanced hepatocellular carcinoma (previously title pre scoping)		
Topic Selection ID Number	N/A	**Wave / Round**	Routed from MTEP
TA ID Number	1276		
Company	BTG		
CE Mark information	TheraSphere received its CE mark in 2005, available in the UK since 2009. It is indicated for 'the treatment of hepatic neoplasia'.		
Draft remit	To appraise the clinical and cost effectiveness of TheraSphere within its approved indication for treating advanced hepatocellular carcinoma.		

Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of selective internal radiation therapies for treating hepatocellular carcinoma is appropriate:
	
	Rationale:
	SIRT is not routinely commissioned for people with hepatocellular carcinoma (HCC). An appraisal may provide evidence for NHS E to up-date its interim commissioning policy on SIRT (Interim Clinical Commissioning Policy Statement: Selective Internal Radiotherapy (SIRT) June 2013 B01/PS/a)
	
	The proposed remit is not appropriate and should be amended as follows:
	• Broadened to include all SIRT technologies. There are currently 2 other SIRT technologies (SIR-Sphere and QuiremSpheres) available with CE markings that cover hepatocellular carcinoma and are similar in terms of their mechanism of action.
	  ○ SIR-Sphere is indicated for 'non-operable liver cancer'.
	  ○ QuiremSpheres is indicated for 'advanced unresectable cancers in the liver'.
	• Broadened to 'treating hepatocellular carcinoma'. SIRT would be used for patients with potentially resectable hepatocellular carcinoma (i.e. as a bridge to resection) or for patients with unresectable hepatocellular carcinoma irrespective of the grade of the cancer.
	
	The population and comparators in the scope have been amended to be consistent with the SIRT technologies CE markings and expected use in people with potentially resectable or unresectable hepatocellular carcinoma.		

Population size	The number of people in England who would be eligible for treatment with SIRT is uncertain. SIRT could be used to treat patients with potentially resectable and unresectable hepatocellular carcinoma, as an adjunct or alternative to options currently available. The resource impact template for Technology appraisal guidance 474 'Sorafenib for treating advanced hepatocellular carcinoma' estimated that there were 4049 people with hepatocellular carcinoma (estimate based on the total liver cancer registrations in England in 2015).		

Process (TA/HST)	TA (MTA)
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of ~~**TheraSphere**~~ **selective internal radiation therapies (SIRT)** within ~~**its**~~ **their** approved indication**s** for treating ~~**advanced**~~ hepatocellular carcinoma.
Costing implications	Unknown. The exact costs of using SIRT technologies for this indication are unknown and the resource impact is therefore unknown. An illustrative example of the price used to reimburse NHS centres using SIRT technologies for other indications is £21,550.
Timeliness statement	Considering that these products have all received a CE Mark for use in the UK, publication of timely guidance will not be possible

Provisional Title	Lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing elective surgery		
Topic Selection ID Number	8379	**Wave / Round**	R191
TA ID Number	1149		
Company	Shionogi		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of lusutrombopag within its marketing authorisation for treating thrombocytopenia in people with chronic liver disease needing elective surgery		
Main points from consultation	Following the consultation exercise, NICE is of the opinion that an appraisal of lusutrombopag for treating thrombocytopenia is appropriate. The proposed remit is appropriate. No changes are required. The company suggested that this should be included within an update of NICE guideline NG24 because 1) there is a low budget impact due to small patient numbers and dosing [once-daily for 7 days] and 2) there is a potential preservation of platelet resources that might not be captured in an STA. However, on 1) it is not clear what the drug cost will be so we do not know the budget impact, on 2) although the population in this scope is a subset of the population covered in NG24, this group (severe thrombocytopenia **and** liver disease) is not currently considered in NG24 and the guideline will only be considered for an update in November 2020.		
Population size	Approximately 3,071 people in England would be eligible for treatment with lusutrombopag. This is based on company market research which suggests that 11% of the 27,927 hospital admissions (HES data) for people with liver disease in England could receive lusutrombopag.		
Process (TA/HST)	TA (MTA combine with ID1105)		
Proposed changes to remit (in bold)	None		
Costing implications	Unknown - If licensed, lusutrombopag will offer an additional oral treatment option for people with thrombocytopenia associated with chronic liver disease who are undergoing an elective invasive procedure. The cost of lusutrombopag is unknown and therefore the resource impact is unknown. If used, savings may result from a reduction in the need for platelet transfusions.		

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	Intravenous zanamivir for treating influenza in hospital		
Topic Selection ID Number	8777	**Wave / Round**	R211
TA ID Number	1196		
Company	GlaxoSmithKline		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of intravenous zanamivir within its marketing authorisation for treating influenza in hospital.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of intravenous zanamivir for treating influenza in hospital is not appropriate. The company believes that this product does not require a NICE appraisal because of: the small population size, limited data availability, and that there is already consensus on where to use the product in the UK (there is Public Health England (PHE) guidance for its use). ***Confidential information removed*** The product has been available in the UK since 2009. In February 2010, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion (EMA/CHMP/32815/2010) on the compassionate use of IV zanamivir in accordance with Article 83 of regulation (EC) 726/2004[2]. ***Confidential information removed*** Zanamivir IV is covered in the 2017 PHE guidance on the use of antiviral agents for the treatment and prophylaxis of seasonal influenza. This guidance document positions zanamivir IV for the treatment of complicated – which is synonymous with hospitalised – ***Confidential information removed***Once the marketing authorisation is granted, it is expected that this guidance document would be updated in due course to be in line with the approved SmPC ***Confidential information removed*** The British Thoracic Society comments that are endorsed by the Royal College of Physicians suggest an appraisal is appropriate. They envisage its use would be used for the 'Critically ill, significant immune-compromise, those in whom GI absorption is a concern, poor clinical response, or strain specific therapy'.		
Population size	The population likely to be eligible to receive zanamivir IV could not be estimated from available published sources. In 2014-15 there were 4,122 hospital admissions for influenza in England. The target group is patients who are not responding to oral or inhaled products or patients for whom drug delivery via other routes not feasible.		

	Confidential information removed
Process (TA/HST)	N/A – referral not sought
Proposed changes to remit (in bold)	N/A – referral not sought
Costing implications	Zanamivir IV is a treatment option for influenza that will offer an additional treatment option for people who have been hospitalised. The cost of zanamivir IV is not yet known, but zanamivir powder for inhalation is already marketed as Relenza in the UK; a pack of 20 x 5mg inhalation powder blisters costs £16.36 (Dictionary of Medicines and Devices). There may be offsetting savings from people transferring from current treatments.
Timeliness statement	N/A – referral not sought

Provisional Title	Clostridium botulinum neurotoxin type A for treating chronic sialorrhea		
Topic Selection ID Number	7809	**Wave / Round**	R145
TA ID Number	1150		
Company	Merz Pharma UK		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of clostridium botulinum neurotoxin type A within its marketing authorisation for treating hypersalivation associated with neurological conditions.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of clostridium botulinum neurotoxin type A for treating chronic sialorrhoea is appropriate. The proposed remit is not appropriate and should be amended as follows: To appraise the clinical and cost effectiveness of clostridium botulinum neurotoxin type A within its marketing authorisation for treating ~~hypersalivation~~ ***chronic sialorrhoea*** ~~associated with neurological conditions~~. Stakeholders considered the remit to be broadly appropriate but suggested that it should be aligned to the marketing authorisation (MA) wording. In addition, the term 'hypersalivation' suggested over-production of saliva, which is not always the case. At the workshop it was deemed that sialorrhoea (unintentional loss of saliva through the mouth) is a more accurate term. Attendees also agreed that the mention of neurological conditions was not necessary because sialorrhoea occurs in a wide range of conditions, such as motor neurone disease, strokes, head and neck injuries as well as in those with a tracheostomy. Sialorrhoea can be also be a side effect of taking benzodiazepines, neuroleptics, cholinesterase inhibitors. Clinical experts stated an appraisal of this treatment would be worthwhile. They said that, although botulinum toxin A is recommended in NICE guidelines, it is not widely accessible in clinical practice because of a lack of funding (because it is off-label). Also, it is NICE recommendations are restricted to those with Parkinsons' disease or cerebral palsy (under 25s) only. There is therefore still a clinical unmet need for people with other conditions associated with hypersalivation/sialorrhea. This proposed licensed preparation was 100 units /cycle in the clinical trial supporting the MA. Clinicians stated that the dose used (off-label) in current practice is typically 60 units. Issue for DP4 to consider: • the value of an appraisal given existing NICE clinical guidelines • an alternative could be to update the relevant guidelines		

Population size	Approximately 100,000 or more people in England could be eligible for treatment with this technology. Approximately one in two people with motor neuron disease (~1875) is affected by hypersalivation and one in five needs continuous saliva elimination. Its prevalence up to 70% in Parkinson's disease (~88,000) and between 10-80% in people with cerebral palsy (~11,000 - 88,000).
Process (TA/HST)	TA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of clostridium botulinum neurotoxin type A within its marketing authorisation for treating ~~hypersalivation~~ ***chronic sialorrhoea*** ~~associated with neurological conditions~~.
Costing implications	Unknown. The cost per treatment cycle, based on four injections of 100 units per injection is around £520. The average number of treatment cycles per person is unknown and there the resource impact is also unknown. Alternative treatments used off-label, such as oral glycopyrronium bromide costs approximately £2,100 per year.
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	Ozanimod for treating relapsing multiple sclerosis		
Topic Selection ID Number	8383	**Wave / Round**	R191
TA ID Number	1294		
Company	Celgene		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of ozanimod within its marketing authorisation for treating relapsing multiple sclerosis		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of ozanimod for treating relapsing multiple sclerosis is appropriate. The proposed remit is appropriate. No changes are required. Daclizumab has been removed from the scope following withdrawal of its marketing authorisation. Based on publically available feedback from the company on their application, the population of 'people with secondary progressive multiple sclerosis with active disease, evidenced by relapses' has been removed from the scope. Other populations and comparators have not changed, but the groups have been reordered for clarity based on feedback from consultation. The outcome 'freedom from disease activity' has been amended to 'no evidence of disease activity' to reflect changing terminology, and the 9 hole peg test has been specified as a measure of disability.		
Population size	Approximately 72,000 to 81,000 people in England would be eligible for treatment with ozanimod. This estimate is based on 90,000 people in England having multiple sclerosis, of which 80-90% have relapsing forms of the disease.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	Unknown - If licensed, ozanimod will offer an additional oral treatment option for people with relapsing remitting multiple sclerosis. However, it is unknown what proportion of these people will use ozanimod over other existing treatment options. The cost of ozanimod is not yet known so any potential resource impact is also unknown.		
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.		