NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 43 draft remits and draft scopes and summary of comments and discussions at scoping workshops

Item number	Batch 43
5.1	Collagenase clostridium histolyticum and potassium para-aminobenzoate for treating Peyronie's disease
5.2	Daclizumab for treating relapsing-remitting multiple sclerosis
5.3	Everolimus, lanreotide and sunitinib for treating advanced or metastatic, unresectable gastroentero-pancreatic neuroendocrine tumours
5.4	Obeticholic acid for treating primary biliary cirrhosis
5.5	Elotuzumab for previously treated multiple myeloma
5.6	Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer
5.7	Adalimumab and etanercept for treating severe, chronic plaque psoriasis in children and adolescents
5.8	Ticagrelor for secondary prevention of atherothrombotic events after myocardial infarction
5.9	Cediranib for treating relapsed, platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer
5.10	Pembrolizumab for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy
5.11	Masitinib for treating systemic mastocytosis
5.12	Obinutuzumab in combination with bendamustine for treating rituximab-refractory follicular lymphoma
5.13	Necitumumab for untreated advanced, metastatic, squamous non-small-cell lung cancer
5.14	Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer

Provisional Title	Collagenase clostridium histolyticum and potassium para-aminobenzoate for treating Peyronie's disease		
Topic Selection ID Number	7629	**Wave / Round**	R129
TA ID Number	849		
Company	SOBI (Collagenase clostridium histolyticum and potassium [CCH]) Cheplapharm (para-aminobenzoate [PPA])		
Anticipated licensing information	Already granted for both. CCH: indicated for treating adult men with Peyronie's disease with a palpable plaque and deformity of at least 30 degrees at the start of therapy PPA: indicated for treating Peyronie's disease		
Draft remit	To appraise the clinical and cost effectiveness of collagenase clostridium histolyticum and potassium para-aminobenzoate within their marketing authorisations for treating Peyronie's disease.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of collagenase clostridium histolyticum and potassium para-aminobenzoate for treating Peyronie's disease is <u>not appropriate</u>. Attendees considered that as a result of the small population size (no more than 500 patients likely to be eligible for CCH), and individualised approach to patient care (because of the heterogeneous nature of the condition), that a short clinical guideline for Peyronie's disease would provide more value to the NHS, and should be considered for development. Both companies confirmed that the budget impact to the NHS of their treatments is very small. The manufacturer of CCH highlighted that they expect the budget impact of their technology would be less than £1 million to the NHS, and that in their opinion, an appraisal is of little value to the NHS. They also highlighted that they will not be actively promoting this indication (their focus is on the primary indication for Dupuytren's contracture) and to date only 10 vials have been sold privately since the marketing authorisation was granted in April 2015. At the Decision Point 4 meeting, attendees agreed that a remit should not be sought.		
Population size	CCH is expected to be suitable for some patients who are candidates for shortening surgical procedures. In England this represents a total population of approximately 1000 patients per year (source SOBI, confirmed by clinicians at scoping workshop). No more than half of these patients (n=500) would be suitable for CCH (best case scenario). If considering the whole population of adults with active and stable Peyronie's disease for both PPA and CCH (as a short clinical guideline) – there are between 84,000 and 1.89 million men in the UK with the condition, of whom many do not require/seek treatment.		

Process (MTA/STA/HST)	N/A – A referral is not sought
Proposed changes to remit (in bold)	N/A – A referral is not sought
Costing implications of remit change	It is estimated that a maximum of 500 patients would be suitable for this technology. The cost of CCH for a maximum of eight injections over four treatment cycles would cost £5,200. The only currently licensed non-surgical treatment of this indication, Potassium para-aminobenzoate, costs between £1,250 and £1,630 per annum. Therefore the incremental cost of CCH is around £3800 per person, equivalent to around £1.9m for 500 people.
Timeliness statement	N/A – A referral is not sought

Provisional Title	Daclizumab for treating relapsing-remitting multiple sclerosis		
Topic Selection ID Number	7515	**Wave / Round**	R122
TA ID Number	827		
Company	Biogen Idec		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of daclizumab within its marketing authorisation for treating relapsing-remitting multiple sclerosis.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of daclizumab for treating relapsing-remitting multiple sclerosis is appropriate. The proposed remit is considered appropriate. No changes required. Comparators: The comparators listed in the scope are appropriate. Attendees suggested splitting the comparators as follows: For patients who have not received treatment previously • alemtuzumab • beta-interferon • dimethyl fumarate • glatiramer acetate • teriflunomide For patients who have received previous treatment • alemtuzumab • dimethyl fumarate • teriflunomide For patients with rapidly-evolving severe relapsing-remitting multiple sclerosis • alemtuzumab • natalizumab For patients with highly active relapsing-remitting multiple sclerosis despite previous treatment • alemtuzumab • fingolimod		
Population size	There are conflicting sources of incidence and prevalence data available in the literature. The General Practice Research Database, estimates 6003 new cases of MS were diagnosed in 2010. Other sources estimate a much lower number of new cases - Horizon scanning estimates 2500 each year. The London School of Hygiene in conjunction with MS society estimated 100,000 people were living with MS.		
Process (MTA/STA/HST)	STA		

Proposed changes to remit (in bold)	None
Costing implications of remit change	Daclizumab high yield process (DAC HYP) is an additional treatment option for the long-term first or second line treatment of relapsing forms of multiple sclerosis (MS). It is estimated that 89,000 people in England have MS, of these people 35.5% have relapsing-remitting multiple sclerosis (around 31,500) and 38.75% are eligible for treatment with DAC HYP (around 12,000). The cost of DAC HYP is not yet known; the annual cost of alternative treatments ranges from £8,500 to £35,200. No additional administration costs are anticipated. The number of people that would switch from existing comparator treatments is not known, but any incremental costs or savings will depend on the existing treatment option used.
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	Everolimus, lanreotide and sunitinib for treating advanced or metastatic, unresectable gastroentero-pancreatic neuroendocrine tumours		
Topic Selection ID Number	7624 and 3396	**Wave / Round**	R128
TA ID Number	858		
Company	Ipsen (lanreotide) Novartis (everolimus) Pfizer (sunitinib)		
Anticipated licensing information	Lanreotide has a marketing authorisation in the UK for the treatment of Grade 1 and a subset of Grade 2 (Ki67 index up to 10%) gastroentero pancreatic neuroendocrine tumours (GEP-NETs) of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in adult patients with unresectable locally advanced or metastatic disease. Everolimus has a marketing authorisation in the UK for the treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumours of pancreatic origin in adults with progressive disease. ***CONFIDENTIAL INFORMATION REMOVED*** Sunitinib has a marketing authorisation in the UK for the treatment of unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours with disease progression in adults.		
Draft remit	To appraise the clinical and cost effectiveness of everolimus, lanreotide and sunitinib within their marketing authorisations for treating advanced or metastatic, unresectable gastro-enter-pancreatic tumours.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of everolimus, lanreotide and sunitinib for treating advanced or metastatic, unresectable gastroentero-pancreatic neuroendocrine tumours is appropriate. <u>Remit</u> Attendees agreed that the wording of the draft remit is <u>not appropriate.</u> Attendees discussed the wording of the draft remit in relation to the wording of the marketing authorisations for the 3 technologies. They highlighted the following differences between the marketing authorisations: • The marketing authorisation for lanreotide includes both pancreatic and gastroentero neuroendocrine tumours (NETS) whereas the marketing authorisations for everolimus and sunitinib are for pancreatic NETs only. • The marketing authorisation for lanreotide is more restrictive than the marketing authorisations for everolimus and sunitinib as it includes people with grade 1 and only a subset of grade 2 (Ki67 up to 10%). • The marketing authorisations for everolimus and		

	sunitinb specify progressive disease while the marketing authorisation for lanreotide does not. The study protocol for the CLARINET trial (pivotal regulatory trial for lanreotide) specified that randomisation would be stratified by the absence or presence of progressed disease, however 96% of people enrolled had non-progressed tumours. Attendees accepted that the evidence base for lanreotide for progressed disease would be limited. Based on the differences between the marketing authorisations, it was agreed that it was reasonable to assume that there were 4 relevant populations covered by the marketing authorisations: pancreatic NETs without disease progression; gastroentero NETs without disease progression; pancreatic NETs with disease progression; gastroentero NETs with disease progression. Attendees agreed that the wording of the remits should reflect the populations covered by the marketing authorisations for the 3 technologies and the clinical evidence on which they were based. Non-progressed disease: • It was agreed that it would be appropriate to have a single remit which covered both populations without disease progression and that the remit should consider lanreotide only. Progressed disease: • It was agreed that it would not be appropriate to have a single remit for the 2 populations with disease progression. • **Pancreatic NETs**: It was agreed that it was appropriate to consider everolimus, lantreotide and sunitinib in a remit for pancreatic NETs with disease progression. • **Gastroentero NETs**: Attendees noted that only lanreotide currently has a marketing authorisation that covers this population. Attendees heard from Novartis that it intended to submit for a licence extension for everolimus for the treatment of gastro intestinal NETs. There was no clear agreement as to whether it would be appropriate to undertake an appraisal of lanreotide for this population (because of the limited evidence available for the progressed population from the CLARINET trial) or to undertake an MTA to coincide with everolimus receiving its marketing authorisation for this population. <u>Populations</u> In their discussions, attendees took account of their recommendation to split the draft remit into 2 separate remits

	(without disease progression and with disease progression). <u>Comparators</u> In their discussions regarding the appropriate comparators, attendees took account of their recommendation to split the draft remit into 2 separate remits and the proposed populations. Remit 1: Gastroentero-pancreatic NETs without disease progression The comparators should be amended to only best supportive care/watchful waiting for people with pancreatic NETs and octreotide long-acting release for people with gastroentero NETs. Remit 2: Pancreatic NETs with progressed disease The comparators should be amended to the following: • Interventions will be compared with each other, • Chemotherapy (streptozocin, 5-FU, doxorubicin, temozolomide, capecitabine), • Lutetium-177 (available on the CDF, not appraised by NICE).
Population size	Gastroentero neuroendocrine tumours (progressed and non-progressed combined): up to 2700 people Pancreatic neuroendocrine tumours (progressed and non-progressed combined): up to 900 people
Process (MTA/STA/HST)	Remit 1 – Gastroentero–pancreatic NETs without disease progression There was no clear agreement amongst attendees as to whether the potential appraisal should be an STA or MTA. The options to be considered are: • An STA of lanreotide for treating unresectable locally advanced or metastatic gastroentero-pancreatic neuroendocrine tumours without disease progression. • An MTA of lanreotide and octreotide long-acting release for treating unresectable or metastatic gastroentero-pancreatic neuroendocrine tumours without disease progression. Remit 2 – Pancreatic NETs with disease progression Attendees agreed that progressed pancreatic NETs should be considered through the MTA process. However, there was no clear agreement as to whether lutetium-177 should be included as an intervention in the MTA. Options to be considered are: • An MTA of everolimus, lanreotide and sunitinib for treating unresectable or metastatic pancreatic neuroendocrine tumours with disease progression. • An MTA of everolimus, lanreotide, lutetium-177 and sunitinib for treating unresectable or metastatic pancreatic neuroendocrine tumours with disease

	progression to coincide with lutetium-177 receiving its marketing authorisation. Gastroentero NETs with disease progression There was no clear agreement amongst the attendees as to whether it may be appropriate to undertake an appraisal of lanreotide for the population with gastroentero NETs at all or to delay an appraisal to coincide with everolimus and lutetium-177 receiving their respective marketing authorisations for this population. Attendees did not discuss the remit for this population. Options to be considered are: • No appraisal of gastroentero NETs with progressed disease. • An STA of lanreotide for gastroentero NETs with progressed disease • MTA of lanreotide and everolimus to coincide with everolimus receiving its marketing authorisation for gastroentero NETs. • MTA of lanreotide, everolimus and lutetium-177 to coincide with both everolimus and lutetium-177 receiving their respective marketing authorisations. *At the Decision Point 4 meeting, attendees agreed that 2 remits should be sought.* • *An STA of lanreotide for unresectable locally advanced or metastatic gastroentero-pancreatic tumours without disease progression* • *An MTA of everolimus, lanreotide, lutetium-177 and sunitinib for unresectable or metastatic neuroendocrine tumours with disease progression.*
Proposed changes to remit (in bold)	Remit 1: To appraise the clinical and cost effectiveness of **lanreotide** within **its** marketing authorisation for treating **unresectable locally** advanced or metastatic gastroentero-pancreatic tumours **without disease progression.** Remit 2: To appraise the clinical and cost effectiveness of everolimus, lanreotide, **lutetium-177** and sunitinib within their marketing authorisations for treating **unresectable or metastatic neuroendocrine tumours with disease progression**
Costing implications of remit change	<u>Remit 1:</u> <u>Gastroentero–pancreatic NETs without disease progression</u> It is estimated that there are up to 2700 people with gastroentero neuroendocrine tumours (progressed and non-progressed combined) and up to 900 people with pancreatic neuroendocrine tumours (progressed and non-progressed combined). Of these, it is unclear how many people will have tumours without disease progression. The estimated cost of lanreotide based on the cost for other indications is £12,181 per person per annum, although there will be savings from other treatments avoided. However, since the eligible population is unknown, the cost impact cannot be

	quantified. <u>Remit 2: Neuroendocrine tumours with disease progression</u> There is no firm evidence available on the incidence of neuroendocrine tumours with progressed disease. Since the eligible population is unknown, the cost impact cannot be quantified. Any cost impact will depend on the uptake for each technology, which also cannot be quantified with any degree of certainty with currently available data.
Timeliness statement	Remit 1: Gastroentero-pancreatic NETs without disease progression: As lanreotide has received its marketing authorisation, issuing timely guidance will not be possible. Remit 2: Neuroendocrine tumours with progressed disease: As everolimus, lanreotide and sunitinib have received their marketing authorisations, issuing timely guidance will not be possible. Timely guidance may be possible for lutetium-177 and the license extension of everolimus.

Provisional Title	Obeticholic acid for treating primary biliary cirrhosis		
Topic Selection ID Number	6884	**Wave / Round**	R79
TA ID Number	785		
Company	Intercept Pharmaceuticals		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of obeticholic acid within its marketing authorisation for treating primary biliary cirrhosis.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of obeticholic acid for treating primary biliary cirrhosis is appropriate. Remit is appropriate but the name of the disease will change in the future to 'primary biliary cholangitis'. Comparators should be amended to include fibrates, and to specify the comparators for each population: - Those who have had an inadequate response to ursodeoxycholic acid - People who are unable to tolerate ursodeoxycholic acid Outcomes should be amended to: - Specify liver function measurement - Include 'fatigue' as a symptom - Remove high-density lipoprotein metabolism - Include primary biliary cirrhosis related events, including ascites, varices, encephalopathy and hepatic cell carcinoma		
Population size	Total population with primary biliary cirrhosis: - 18,900 people in England (35 people per 100,000) Estimated population for obeticholic acid (ursodeoxycholic acid failed or not tolerated): - 3,800 - 13,200 people		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	Obeticholic acid is intended to be used as second line therapy for the treatment of primary biliary cirrhosis in patients who have an inadequate response to or are unable to tolerate ursodeoxycholic acid (UDCA); monotherapy or in combination with UDCA. Obeticholic acid represents a potential alternative treatment option for these people. It is estimated that around 4,500 people would be eligible to use obeticholic acid. The cost of obeticholic acid is unknown, so the potential cost impact is unknown. Some savings due to reduced or delayed liver transplantations may also be possible.		

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	Elotuzumab for previously treated multiple myeloma		
Topic Selection ID Number	7020	**Wave / Round**	R81
TA ID Number	855		
Company	Bristol-Myers Squibb		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of elotuzumab within its marketing authorisation for previously treated multiple myeloma.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of elotuzumab for previously treated multiple myeloma is appropriate. Some comparators (bendamustine, pomalidomide and conventional chemotherapies) should be removed because: - They are not used in clinical practice at this line of treatment - They would be used for multiple myeloma that is refractory to lenalidomide (Elotuzumab is used in combination with lenalidomide) It was agreed that the most relevant comparators for elotuzumab in clinical practice were: - bortezomib (with or without dexamethasone) - lenalidomide in combination with dexamethasone		
Population size	Approximately 4000 people diagnosed per year. Population eligible for treatment will be less.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	Elotuzumab is intended to be used in combination with lenalidomide and dexamethasone for the treatment of relapsed or refractory multiple myeloma (MM). Around 4000 people are diagnosed with MM each year. Treatment regimens for MM are patient specific and dependent on performance status, eligibility for high dose chemotherapy with stem cell transplantation support, and frailty. It is estimated that around 40% (1,600) of people relapse or are refractory after a first line treatment, and could be eligible to choose elotuzumab. It is expected that elotuzumab will be administered intravenously (IV). The cost of elotuzumab is not yet known and the number of people who will change from other treatment options is also uncertain. The cost impact of this technology is therefore 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.		

Provisional Title	Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer		
Topic Selection ID Number	7232	**Wave / Round**	R98
TA ID Number	767		
Company	Roche products		
Anticipated licensing information	Pertuzumab has a marketing authorisation in the UK 'in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence'. **Marketing authorisation granted:** July 2015		
Draft remit	To appraise the clinical and cost effectiveness of pertuzumab within its marketing authorisation for the neoadjuvant treatment of human epidermal growth factor receptor 2 (HER2) positive breast cancer.		

Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer is appropriate
	
	The comparators should be amended to:
	- remove 'no neoadjuvant treatment' as this would not be an option for this population
	- To specify the neoadjuvant treatments:
	  o 5 fluorouracil, epirubicin, and cyclophosphamide followed by docetaxel plus trastuzumab
	  o trastuzumab, docetaxel and carboplatin.
	
	The subgroup 'people with inflammatory or locally advanced breast cancer' should be considered as these populations may gain more benefit, and are more clearly defined in clinical practice, than those with 'early (high risk of recurrence)' breast cancer		

Population size	Approximately 8700 people		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	Pertuzumab is intended to be used as a HER2-positive locally advanced, inflammatory or early breast cancer – neo-adjuvant in combination with trastuzumab. The prevalence is estimated at 16 per 100,000, equivalent to 8,700 people in England. The cost of pertuzumab is £2,395 for 30 a mg/mL, 14-mL vial. The cost of treatment with pertuzumab in combination with		

	trastuzumab is around £21,000 per person, excluding infusion costs. Were all eligible people to switch, the estimated drug cost impact of pertuzumab in combination with trastuzumab for England is £182 million, or for pertuzamab alone, £125 million. However this population is currently likely to be receiving one of a range of other high-cost treatments, so there would be significant offsetting savings.
Timeliness statement	As the technology has received a marketing authorisation, issuing timely guidance will not be possible.

Provisional Title	Adalimumab and etanercept for treating severe, chronic plaque psoriasis in children and adolescents		
Topic Selection ID Number	7694	**Wave / Round**	R131
TA ID Number	854		
Company	Abbvie (adalimumab) Pfizer (etanercept)		
Anticipated licensing information	**Adalimumab** has a marketing authorisation in the UK for treating severe chronic plaque psoriasis in children and adolescents from 4 years of age who have an inadequate response to or are inappropriate candidates for topical therapy and phototherapies. **Etanercept** has a marketing authorisation in the UK for treating chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.		
Draft remit	To appraise the clinical and cost effectiveness of adalimumab and etanercept within their marketing authorisations for treating severe chronic plaque psoriasis in children and adolescents.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of adalimumab and etanercept for treating severe, chronic plaque psoriasis in children and adolescents is appropriate. Ustekinumab should be included within this MTA and the remit updated accordingly. To do so, a further scope consultation is needed to include the manufacturer of ustekinumab (suggested this is done post-referral, as part of the appraisal process) - Following the scoping workshop, the manufacturer of ustekinumab (Janssen-Cilag) contacted NICE stating that they had been awarded (on 29/6/15) an MA extension to cover *'the treatment of moderate to severe plaque psoriasis in adolescent patients from the age of 12 years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies'.* - Ustekinumab was B listed at DP2 in March 2014 (TS ID 6807). This decision was made because *'The group noted that the adult population is covered in TA180, but that in the future it might be worthwhile re-considering this topic as a MTA with other biologics that have paediatric and adolescent indications'* <u>Comparators</u> The scoping workshop noted the differences in the marking authorisation wording for adalimumab and etanercept but agreed that they were generally used in the same point in the treatment pathway and therefore it was appropriate to compare them to each other. The comparators should be amended as follows:		

	- Topical therapies included for those for whom non-biological systemic treatments are not appropriate - Biological treatment that are used off label should be included o this could include infliximab, but also etanercept, and ustekinumab if used at ages not included within respective MAs – adalumimab MA is from age 4+, etanercept age 6+, ustekinumab for age 12+ <u>Sequencing</u> Sequencing of treatments was discussed, it was suggested that if evidence allows, the appraisal should consider the sequential use of anti-TNF inhibitors. <u>Subgroups</u> Subgroups according to the specific line of treatment were discussed and it was suggested that if evidence allows the clinical and cost effectiveness should be considered separately for people receiving treatments: - after topical therapy - after non-biological systemic therapy - after biological therapy.
Population size	Approximately 1000
Process (MTA/STA/HST)	MTA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of adalimumab, ~~**and**~~ etanercept, **and ustekinumab** within their marketing authorisations for treating severe chronic plaque psoriasis in children ~~**and**~~ **or** adolescents. *Change to 'or' suggested as ustekinumab has a marketing authorisation for adolescents only*
Costing implications of remit change	The three technologies offer different treatment options for severe chronic plaque psoriasis in children and adolescents, which is inadequately controlled by or contraindicated for topical therapy and/or phototherapy. The population in this age group with severe chronic plaque psoriasis is around 1,150. Assuming the costs of each of the technologies are similar to each other and existing treatment options, the appraisal is expected to be broadly cost neutral.
Timeliness statement	As adalimumab and etanercept have received a marketing authorisation, and that this will be referred as an MTA, issuing timely guidance will <u>not</u> be possible.

Provisional Title	Ticagrelor for secondary prevention of atherothrombotic events after myocardial infarction		
Topic Selection ID Number	6511	**Wave / Round**	R53
TA ID Number	813		
Company	AstraZeneca		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of ticagrelor within its marketing authorisation to reduce atherothrombotic events in people who have had a prior myocardial infarction.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ticagrelor within its marketing authorisation to reduce atherothrombotic events in people who have had a prior myocardial infarction is appropriate. The draft remit should be amended in line with the marketing authorisation to clarify that ticagrelor should be used when the myocardial infarction occurred at least 12 months ago and that the population only includes adults who are at an increased risk of atherothrombotic events. The company confirmed that the marketing authorisation will stipulate that ticagrelor should be given in combination with aspirin. Therefore, the proposed comparator of 'clopidogrel (for those hypersensitive to aspirin)' is not appropriate and should be removed from the scope, as people with aspirin hypersensitivity will not be eligible for treatment with ticagrelor. Clinical experts highlighted that clopidogrel in combination with aspirin is given to some patients beyond 12 months after a myocardial infarction. They acknowledged an ongoing study that has shown significant benefits of long-term treatment with dual anti-platelet therapy and considered that more patients may be treated with clopidogrel plus aspirin in the future as clinical practice is expected to change once the trial is completed. Attendees concluded that clopidogrel in combination with aspirin should be included as a comparator in the scope.		
Population size	The incidence of myocardial infarction in England and Wales in 2013/14 was 81,000.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost-effectiveness of ticagrelor within its marketing authorisation to reduce atherothrombotic events in **adults** who have had a ~~**prior**~~ myocardial infarction **at least 12 months ago and are at increased risk of atherothrombotic events.**		
Costing implications of remit change	Ticagrelor is intended to be used in combination with aspirin for the prevention of cardiovascular disease events in adults who have had a prior myocardial infarction (MI) at least 12 months ago and are at increased risk of atherothrombotic events. The		

	number of people who have experienced MI at some point is estimated at around 1.1 million in England, and the estimated incidence of MI in England is around 81,000 per annum. Since ticagrelor is intended to be used in adults who have had a prior myocardial infarction (MI) at least 12 months ago and are at increased risk of atherothrombotic events, the total eligible population is unknown, but likely to be large. The cost per annum per person using ticagrelor is around £710. Another treatment option, prasugrel, costs around £620 for per year. The uptake of ticagrelor cannot be estimated, but where people switch, there would be offsetting savings from other drugs avoided, and from costs associated with the treatment of cardiovascular diseases. From the information available and the variety of the unknowns, the cost impact cannot be accurately 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	Cediranib for treating relapsed, platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer		
Topic Selection ID Number	7343	**Wave / Round**	R107
TA ID Number	790		
Company	AstraZeneca		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of cediranib within its marketing authorisation for treating relapsed, platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of cediranib for treating relapsed, platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer is appropriate. The proposed remit is appropriate. No changes are required. Consultees confirmed that cediranib would be suitable for patients whose disease was either partially or fully platinum sensitive. Consultees confirmed that the most appropriate comparators, which reflect current clinical practice are: • carboplatin monotherapy • paclitaxel in combination with platinum chemotherapy (subject to ongoing NICE appraisal) • pegylated liposomal doxorubicin hydrochloride in combination with platinum (subject to ongoing NICE appraisal; not licensed in the UK for this indication) • gemcitabine in combination with carboplatin (not recommended by NICE and on the CDF)		
Population size	In 2012, there were approximately 6500 people diagnosed with ovarian cancer in England. The population eligible for treatment with cediranib is estimated to be 3000 patients per year.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	Ovarian cancer is the fifth most common cancer in women in the UK. Most women (approximately 70%) present with advanced disease and undergo a combination of debulking surgery and 6 cycles of platinum-based chemotherapy. Cediranib is intended for the treatment of patients with ovarian cancer relapsing more than 6 months following completion of first line platinum-based treatments (platinum-sensitive). The eligible population is estimated at around 3000 patients per year. The cost of cediranib is not yet known. Any cost impact will		

	depend on the cost in relation to current treatment options such as bevacizumab (£2,577 per cycle) and paclitaxel (£902 per cycle).
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	Pembrolizumab for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy		
Topic Selection ID Number	7140	**Wave / Round**	R90
TA ID Number	840		
Company	Merck Sharp & Dohme		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of pembrolizumab for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy is appropriate. The proposed remit is appropriate. No changes are required. Clinical experts noted that there are different methods currently available that test for expression of PD-L1 which has resulted in a lack of consistency and difficulty in defining people who are PD-L1 positive. The company noted that outcomes in the pivotal trial were assessed in people who expressed PD-L1 levels greater than 50%, which the clinical experts agreed would represent people in UK clinical practice who are considered PD-L1 positive. Given the clinical uncertainty around the PD-L1 biomarker, scoping workshop attendees agreed that it would be better to be inclusive at this stage and not to exclude comparators on the basis that they do not target PD-L1 expression. They considered that the most appropriate comparators are: • Docetaxel • Erlotinib (subject to ongoing NICE review) • Nintedanib in combination with docetaxel • Ramucirumab (subject to proposed NICE appraisal) • Nivolumab for people with squamous tumour histology only (subject to ongoing NICE appraisal) • Best supportive care		
Population size	The company's estimate for the population size is 6 per 100,000 people.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of	In 2010, there were around 34,000 new cases of lung cancer in England, of whom around 90% (30,600) were NSCLC, and 78%		

remit change	(23,900) were stage III or IV at diagnosis. Pembrolizumab is intended to be used as second-line therapy for the treatment of PD-L1 positive, advanced (stage IIIB/IV) or recurrent non-small cell lung cancer, in patients who have progressed following platinum-based chemotherapy. This population is estimated to be around 3200 for England. If licensed, it will provide an additional targeted treatment option for this patient group. The cost of pembrolizumab is £1315 per 50mg vial. Comparator treatments cost around £900 (docetaxel) to £1,600 (erlotinib and pemetrexed) per dose.
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	Masitinib for treating systemic mastocytosis		
Topic Selection ID Number	6479	**Wave/Round**	R52
TA ID Number	781		
Company	AB Science		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of masitinib within its marketing authorisation for treating systemic mastocytosis		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of masitinib for treating systemic mastocytosis is appropriate. The proposed remit is appropriate. No changes are required. The population should be amended to 'people with smouldering or indolent systemic mastocytosis with **severe** disability as a result of their condition **despite maximal symptomatic treatment**'. The sole comparator 'established clinical management' should specify the following examples: antihistamines, sodium cromoglicate, corticosteroids, bisphosphonates, leukotriene receptor antagonists and analgesics. The list of outcomes should be amended by adding corticosteroid use and including anaphylactic episodes as a symptom.		
Population size	According to the company, the estimated UK population of adults with indolent systemic mastocytosis with severe disability is 270 patients.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	There is uncertainty around the eligible population. It is estimated that there is an incidence of 1 in 150,000 people diagnosed with mastocytosis giving around 340 cases per year. There is also a prevalence of around 2500 people who may be eligible to receive masitinib. The company estimates the eligible population with indolent systemic mastocytosis with severe disability is around 230 patients for England. The cost of masitinib is also not yet known. There are no fully effective or well tolerated therapeutic options currently available for people with mastocytosis and therefore if masitinib was found to be effective, the uptake could be a substantial proportion of the eligible population. There could be offsetting		

	savings from other NHS services avoided. The cost impact of this topic 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	Obinutuzumab in combination with bendamustine for treating rituximab-refractory follicular lymphoma		
Topic Selection ID Number	7257	**Wave/Round**	R99
TA ID Number	841		
Company	Roche Products		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of obinutuzumab in combination with bendamustine within its marketing authorisation for treating rituximab-refractory follicular lymphoma.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of obinutuzumab in combination with bendamustine for treating rituximab-refractory follicular lymphoma <u>is appropriate</u>. The proposed remit should be changed to: To appraise the clinical and cost effectiveness of obinutuzumab in combination with bendamustine within its marketing authorisation for treating follicular lymphoma that is refractory to rituximab or a rituximab-containing regimen. The intervention should be amended to specify obinutuzumab in combination with bendamustine, followed by obinutuzumab maintenance therapy. No changes to the population are needed. The comparators have been updated to Chemotherapy regimens without rituximab. If evidence allows, consideration should be given to subgroups based on people whose disease relapses during rituximab induction therapy and those whose disease relapses during, or within 6 months of completing, rituximab maintenance therapy. The outcomes should be amended to specify 'response rates' and 'adverse effects of treatment (including immunosuppression and infections)'.		
Population size	800 (company estimate)		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of obinutuzumab in combination with bendamustine within its marketing authorisation for treating **<u>follicular lymphoma that is refractory to rituximab or a rituximab-containing regimen</u>**		
Costing implications of remit change	Obinutuzumab in combination with bendamustine is intended to be used as second line therapy for the treatment of follicular lymphoma that is refractory to rituximab or a rituximab-containing regimen. There were around 10,700 cases of NHL in 2011 and approximately 1,800 cases of follicular lymphoma. The number of people who are refractory to rituximab is uncertain but will be a subset of 1500 people and is estimated		

	by the company to be around 800 people per year. The cost of obinutuzumab is not yet known but assuming a midpoint annual cost of £22,500, and an eligible population of 800, the annual cost impact could be around £18m prior to savings from other treatment options 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	Necitumumab for untreated advanced, metastatic, squamous non-small-cell lung cancer		
Topic Selection ID Number	7233	**Wave/Round**	R98
TA ID Number	835		
Company	Eli Lilly		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of necitumumab within its marketing authorisation for untreated advanced, metastatic, squamous non-small-cell lung cancer.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of necitumumab in combination with gemcitabine and cisplatin chemotherapy for first-line treatment of locally advanced or metastatic squamous non-small cell lung cancer is appropriate. The proposed remit is appropriate. No changes are required. No changes to the scope were requested by the stakeholders.		
Population size	Approximately 3500 patients have untreated advanced, metastatic, squamous non-small-cell lung cancer.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	Necitumumab is intended to be used in combination with gemcitabine and cisplatin as first line therapy for the treatment of advanced and metastatic squamous cell non-small cell lung cancer. The prevalence of advanced and metastatic squamous cell non-small cell lung cancer who could be treated with necitumumab is estimated at around 3,500 people in England. The cost of necitumumab is not known - the cost impact of this technology can therefore not be calculated. Necitumumab may offer an additional treatment option for this patient group, potentially relieving symptoms, controlling disease progression, improving quality of life and increase survival. Other treatments exist, and if there is a switch from them, there will be offsetting savings.		
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	**Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer**		
Topic Selection ID Number	7767	**Wave / Round**	B44
T ID Number	865		
Company	Pfizer		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of crizotinib within its marketing authorisation for untreated, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small cell lung cancer.		
Main points from consultation	An appraisal would address unmet need in ALK-positive NSCLC, with no first-line targeted therapy currently available <u>Population</u> All of the trial data was conducted in the non-squamous population. The population should be changed to people with untreated, non-squamous, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer. <u>Comparators</u> 1. The company do not consider platinum-based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine to be relevant comparators for people who would receive crizotinib because they are mainly used to treat patients with squamous histology. However, the company acknowledged that gemcitabine may be an alternative treatment offered to a small number of patients with non-squamous disease who cannot tolerate pemetrexed. 2. Pemetrexed and **cisplatin** as specified in the marketing authorisation and the recommendations of TA181 is the most appropriate comparator. The company consider that cisplatin and carboplatin are used equally in combination with pemetrexed for the first line treatment of non-squamous NSCLC in clinical practice and recommend that the scope not specify the cisplatin combination, and instead use 'cisplatin/carboplatin' or 'platinum-based chemotherapy'		
Population size	Approximately 450 people in England would be eligible for treatment with crizotinib. ALK incidence is approximately 3.6% in the UK. Based on 34,889 diagnosed cases of non-small-cell lung cancer (NSCLC) in England, and assuming 60% of patients are tested, this estimates 754 patients with ALK-positive, advanced NSCLC. Typically, only 60% of patients are fit for chemotherapy, so this would result in 452 patients eligible for treatment.		
Process (MTA/STA/HST)	STA		

Proposed changes to remit (in bold)	None
Costing implications of remit change	
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.