NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 40 draft remits and draft scopes and summary of comments and discussions at scoping workshops

Item number	Batch 40
5.1	Bevacizumab for treating recurrent, or persistent, or metastatic cervical cancer
5.2	Nivolumab for previously treated locally advanced or metastatic non-small-cell lung cancer
5.3	Lenalidomide for treating relapsed or refractory mantle cell lymphoma
5.4	Carfilzomib for treating multiple myeloma in people who have received at least 1 prior therapy
5.5	Talimogene laherparepvec for treating metastatic melanoma
5.6	Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia
5.7	Dinutuximab for treating high-risk neuroblastoma
5.8	Lesinurad in combination with a xanthine oxidase inhibitor for treating chronic hyperuricaemia in gout

Provisional Title	**Bevacizumab for treating recurrent, or persistent, or metastatic cervical cancer**		
Topic Selection ID Number	7373	**Wave / Round**	R110
TA ID Number	797		
Company	Roche		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication for treating recurrent, persistent or metastatic cervical cancer.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of bevacizumab for treating recurrent, or persistent, or metastatic cervical cancer is not appropriate, unless bevacizumab can be appraised outside of its marketing authorisation. The proposed remit is not appropriate. Bevacizumab in combination with paclitaxel is intended to be used as an add-on to current practice (which is treatment with carboplatin), *****CONFIDENTIAL INFORMATION REMOVED***** DH approval would be needed to appraise this technology outside of its marketing authorisation. Intervention and comparators The intervention, bevacizumab, is currently available on the Cancer Drugs Fund for the first line treatment of recurrent or persistent metastatic cervical cancer in combination with chemotherapy (paclitaxel and either cisplatin or carboplatin). Clinical experts at the scoping workshop explained that bevacizumab in combination with paclitaxel will be an add-on to existing clinical practice, which is usually carboplatin. *****CONFIDENTIAL INFORMATION REMOVED*****. The scope has been amended to state that the intervention is bevacizumab in combination with paclitaxel and a platinum compound to keep it broad at this stage. The wording of the intervention has therefore been amended to state: • Bevacizumab in combination with paclitaxel and a platinum agent (such as cisplatin or carboplatin); • Bevacizumab in combination with paclitaxel and topotecan. Population: The wording of the population has been amended to state 'people with metastatic, or persistent, or recurrent carcinoma of the cervix' to reflect that there are 3 distinct populations and to differentiate newly diagnosed metastatic disease from recurrent and persistent disease. Comparators:		

	The comparator 'Topotecan in combination with paclitaxel' has been added to reflect that this is also used in clinical practice. <u>Innovation</u> Workshop attendees all considered that this product was innovative.
Population size	In England in 2011, there were 2511 new diagnoses of cervical cancer. Up to 15% of people with newly diagnosed cervical cancer have stage III/IV disease.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	*Subject to DH agreement to appraise bevacizumab outside of its marketing authorisation:* To appraise the clinical and cost effectiveness of bevacizumab, **in combination with either paclitaxel and a platinum agent (such as cisplatin or carboplatin), or in combination with paclitaxel and topotecan** for treating **metastatic, or recurrent, or persistent** cervical cancer.
Costing implications of remit change	The estimated number of women eligible to receive treatment each year is around 375. Bevacizumab is intended for use in combination with paclitaxel and a platinum agent or topotecan which are regimens currently in use so any costs would be additional to current practice. The cost of bevacizumab for six cycles at a dose of 10mg/kg is approximately £11,088. If the total women eligible for treatment take up bevacizumab the cost would be around £4 million.
Timeliness statement	Considering that this technology has been granted a positive CHMP opinion by the EMA*****CONFIDENTIAL INFORMATION REMOVED*****and the expected referral date of this topic, issuing timely guidance for this technology will not be possible.

Provisional Title	**Nivolumab for previously treated locally advanced or metastatic non-small cell lung cancer**		
Topic Selection ID Number	6932	**Wave / Round**	R80
TA ID Number	811		
Company	Bristol-Myers Squibb		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of nivolumab within its licensed indication for previously treated locally advanced or metastatic 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 nivolumab for previously treated locally advanced or metastatic non-small cell lung cancer is appropriate The proposed remit is appropriate. No changes are required <u>Population</u> Updated to include people with stage IIIA disease: 'people with previously treated locally advanced or metastatic (stage III or IV) non-small cell lung cancer' • Clinical experts clarified that locally advanced or metastatic disease would also include people with stage IIIA non-small cell lung cancer. <u>Comparators</u> Updated to include: • best supportive care has been included for every subgroup • In people with non-squamous EGFR-TK mutation positive tumours after one prior therapy (if the previous therapy was not a TKI due to delayed confirmation of mutation status) - other EGFR-TKIs (erlotinib and gefitinib) should be included in addition to afatinib. • In people with non-squamous EGFR-TK mutation positive tumours after two prior therapies - erlotinib and nintedanib have been included • In people with non-squamous EGFT-TK mutation negative tumours - crizotinib and ceritinib have been included (crizotinib is available on the CDF, and ceritinib is currently being appraised by NICE) • In people with squamous tumours after one and two prior therapies erlotinib, docetaxel monotherapy and best supportive care should be listed • Where nintedanib is listed it has been amended to state 'nintedanib in combination with docetaxel'.		
Population size	The number of people diagnosed with NSCLC in England is approximately 26,800 per year, of whom 3551 (13.2%) had stage IIIA, 2527 (9.4%) had stage IIIB and 12,229 (45.6%) had stage IV disease.		

Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of nivolumab within its **marketing authorisation** for previously treated locally advanced or metastatic non-small cell lung cancer.
Costing implications of remit change	Nivolumab is intended to be used as second line treatment for advanced or metastatic stage IIIA/IIIB/IV non-small cell lung cancer (NSCLC). Each year around 26,800 people in England are diagnosed with NSCLC lung cancer, of which around 68% (18,300 people) have stage IIIA/IIIB/IV cancer. The number of these people that will need second line treatment and would take up treatment with nivolumab cannot be estimated from available data. The cost of nivolumab is not known so the potential cost impact of this technology cannot be estimated. There are a range of alternative second line treatments – two of these docetaxel and erlotonib cost around £1070 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	**Lenalidomide for treating relapsed or refractory mantle cell lymphoma**		
Topic Selection ID Number	7075	**Wave / Round**	R86
TA ID Number	739		
Company	Celgene		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of lenalidomide within its licensed indication for treating relapsed or refractory mantle cell lymphoma		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of lenalidomide for treating relapsed or refractory mantle cell lymphoma is appropriate The proposed remit is appropriate. No changes are required. <u>Comparators</u> Updated to include gemcitabine • The company noted that in the Sprint trial 20% of clinicians chose to use single-agent gemcitabine (including the 2 UK centres). The clinical experts confirmed that gemcitabine is sometimes used to treat lymphomas in practice.		
Population size	The number of people diagnosed with mantle cell lymphoma is approximately 500 per year. The proportion receiving treatment for relapsed and refractory disease will be less than this.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of lenalidomide within its **marketing authorisation** for treating relapsed or refractory mantle cell lymphoma.		
Costing implications of remit change	Lenalidomide is intended to be used as therapy for relapsed or refractory mantle cell lymphoma. In 2011 10,789 people in England were diagnosed with Non - Hodgkin's Lymphoma. It is estimated that approximately 500 of these people have mantle cell lymphoma but not all of these people will be eligible for treatment with lenalidomide for relapsed and refractory disease. The cost of treatment for mantle cell lymphoma with lenalidomide has not been confirmed, however based on the cost for the treatment of multiple myeloma which lenaliomide currently has marketing authorisation for, the cost per 28 day cycle is around £4400. There are a wide range of current treatments that could be replaced. This could include reduced administration costs as lenalidomide is delivered orally.		
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	**Carfilzomib for treating multiple myeloma in people who have received at least 1 prior therapy**		
Topic Selection ID Number	7227	**Wave / Round**	R45/86
TA ID Number	677		
Manufacturer	Amgen		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of carfilzomib in combination with lenalidomide and dexamethasone within its marketing authorisation for treating multiple myeloma in people who have received at least 1 prior therapy		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of carfilzomib in combination with lenalidomide and dexamethasone for treating multiple myeloma in people who have received at least 1 prior therapy is appropriate. The proposed remit is appropriate. No changes are required. A number of changes to the comparators are proposed: • Stakeholders advised that bortezomib is an appropriate comparator but that monotherapy is rarely used in clinical practice, and that bortezomib is also used in combination with treatments other than dexamethasone. Consultees advised that it was appropriate to reword this comparator to: "bortezomib containing regimens". • Thalidomide was not considered an appropriate comparator because it is a first line therapy, and would be positioned before carfilzomib in the treatment pathway. • Chemotherapy was not considered an appropriate comparator because it is not used from 2nd line onwards. • Lenalidomide in combination with dexamethasone was considered to be an appropriate comparator • Pomalidomide in combination with dexamethasone was considered to be an appropriate comparator. Stakeholders advised that pomalidomide would often be given as a later line of therapy after carfilzomib but that patients are increasingly receiving bortezomib as their first line treatment, leading to eligibility for lenalidomide 2nd line (via the Cancer Drugs Fund) and then pomalidomide 3rd line. Stakeholders felt it was pragmatic to include comparators which could be used as later line therapies, given that the carfilzomib trial population included people who have received 1-3 prior therapies, and that the anticipated marketing authorisation for carfilzomib is broad, that is, following at least 1 prior therapy.		

	• Bendamustine was considered an appropriate comparator given the trial population and the expected marketing authorisation for carfilzomib. One change to the outcomes is proposed. Stakeholders advised that complete response is a particularly important outcome, as it has a strong correlation with length of survival, whereas other types of response do not, and would be achieved in around 1/3 of the population being treated. Consultees considered therefore that complete response should be given as an example in brackets under the outcome 'response rates'. Stakeholders considered carfilzomib to be a genuine step change in treatment because of the reduction in peripheral neuropathy, for example they advised that one clinical trial demonstrated a novel peripheral neuropathy rate of around 1%.
Population size	In 2011, 4039 people were diagnosed with multiple myeloma in England. Of these, around 85% would not be eligible for stem cell transplantation and would move onto 1st line treatment either with thalidomide or bortezomib (TA228), followed by bortezomib 2nd line (TA129) and lenalidomide 3rd line (TA171).
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	No change
Costing implications of remit change	Carfilzomib is intended to be used as second or subsequent line therapy for the treatment of multiple myeloma. In 2011 4039 people were diagnosed with multiple myeloma in England. Using data for the costing template TA228 (Multiple myeloma (first line) - bortezomib and thalidomide) it is assumed 86.4% (approximately 3500) will not be eligible for high-dose chemotherapy with stem cell transplantation and will therefore have first line treatment using thalidomide or bortezomib based regimens. It is also assumed 38% (approximately 1300) will be eligible for second line treatment. The cost of carfilzomib in the UK is unknown, however carfilzomib costs $1658 in the USA (approximately £1039) for a 60mg vial and each cycle will need 6 vials (assuming no vial sharing) costing approximately £6200. This is an incremental cost of between £1900 and £3200 compared to existing treatments. The average number of cycles needed is unknown as it will be patient specific and depend on age.
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	**Talimogene laherparepvec for treating metastatic melanoma**		
Topic Selection ID Number	4942	**Wave / Round**	W27
TA ID Number	508		
Manufacturer	Amgen		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of talimogene laherparepvec (T-VEC) within its marketing authorisation for treating metastatic melanoma.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of talimogene laherparepvec for treating metastatic melanoma is appropriate. The proposed remit is appropriate. No changes are required. Stakeholders considered that the population was appropriate, noting that people who would benefit most from treatment would be those with good prognosis, small volume and slow progressing disease (approximately a third of all patients with metastatic melanoma). They also noted that T-VEC will most likely be used as a first line treatment for stage IIIb – IV melanoma. Therefore best supportive care was not considered an appropriate comparator. Stakeholders considered that dacarbazine should be removed from the list of comparators because it is not commonly used. Clinical experts advised that the main comparator for T-VEC is ipilimumab which also produces an immuno-systemic effect and is normally used in people with slow progressing, small volume disease. They also advised that vemurafenib and dabrafenib, used in people with BRAF V600 mutation positive disease, were appropriate comparators. Stakeholders discussed that T-VEC is under investigation in combination with ipilimumab compared with ipilimumab alone (estimated study completion date July 2017). Clinical experts considered that the combination therapy is potentially more clinically relevant than the monotherapy approach because it provides the option of targeting the more clinically relevant lesions directly and still getting the systemic effect from ipilimumab. However they also highlighted that the side effect profile is expected to be better with T-VEC than with ipilimumab and therefore that T-VEC monotherapy can provide additional benefits to patients with metastatic melanoma. Stakeholders highlighted that the comparator of T-VEC in the main OPTiM trial was subcutaneous GM-CSF which is not established clinical practice in the NHS. Therefore, forming an evidence network to allow a comparison of the clinical and cost effectiveness of T-VEC with ipilimumab, vemurafenib or dabrafenib will be challenging and potentially subject to a high		

	degree of uncertainty. Stakeholders considered that the following outcomes should be added: time to treatment failure, durable response rate and duration of response. They also considered that response to treatment could differ according to volume of disease and distribution of disease and recommended that these be included as subgroups. Stakeholders noted the novel approach of T-VEC because it offers the possibility of targeting tumours/lesions directly. However, they advised that T-VEC could potentially impact on health service resources because of the need for hospital visits every 2 weeks, the need to control for potential infection and guidance development for injection.
Population size	Incidence of melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 11,121 people diagnosed with melanoma and 1871 related deaths in England in 2011.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	No change
Costing implications of remit change	There are around 11,000 cases of melanoma each year and estimates suggest around 10% of these cases have unresectable metastatic disease. Though a US study found that 55% of new cases were invasive at presentation. The cost of talimogene laherparepvec (T-VEC) is currently unknown, in addition to the cost of T-VEC there will be frequent outpatient visits for intratumoural injections, costing in the region of £80 per visit.
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	**Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia**		
Topic Selection ID Number	6841	**Wave / Round**	R52
TA ID Number	779		
Manufacturer	Sanofi		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of alirocumab within its marketing authorisation for treating primary hypercholesterolaemia (heterozygous familial and non-familiar) and mixed dyslipidaemia.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia appraisal is appropriate. The proposed remit is appropriate. No changes are required. <u>Intervention</u> It was agreed that alirocumab was likely to be positioned as an alternative to ezetimibe or as an add-on to ezetimibe. This means it is likely to be used as dual therapy in combination with statins or as triple therapy as an add-on to statins and ezetimibe. In people who cannot take statins, alirocumab could also be used as monotherapy or dual therapy in combination with ezetimibe. It was agreed at the Decision Point 4 meeting that the intervention should be changed to: • Alirocumab alone or in combination with a statin with or without ezetimibe, or in combination with ezetimibe <u>Comparators</u> Stakeholders suggested other emerging technologies that could be included as relevant comparators. Attendees discussed the timelines for these treatments. As evolocumab already has a marketing authorisation and is currently going through the appraisal process at NICE, it was agreed that if it is recommended by NICE, evolocumab would be a relevant comparator for alirocumab as it is likely to be used in the same population as alirocumab. The comparators should be amended to: • When optimised statin therapy does not appropriately control LDL-C: o Ezetimibe in combination with a statin o Evolocumab in combination with a statin (subject to NICE guidance) • When LDL-C is not adequately controlled with optimised statin therapy in combination with ezetimibe: o Evolocumab in combination with ezetimibe and a statin (subject to NICE guidance) • When statins are contraindicated or not tolerated: o Ezetimibe		

	o Evolocumab (subject to NICE guidance) o Evolocumab in combination with ezetimibe (subject to NICE guidance) <u>Outcomes</u> It was stated that apolipoprotein B and lipoprotein a are used to assess risk for cardiovascular disease and adjust treatment accordingly. It was agreed to include apolipoprotein B and lipoprotein a as examples of plasma lipid and lipoprotein levels in the list of outcomes in the scope.
Population size	The estimated population currently diagnosed and receiving treatment is 450,000 for non-familial hypercholesterolaemia and around 18,000 for heterozygous-familial hypercholesterolaemia.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	No change
Costing implications of remit change	It is estimated that around 470,000 people are eligible for treatment in England. Of these, around 148,000 cannot tolerate statins, have an inadequate response or have adverse events. This group would be eligible to use alirocumab. However, it is believed that there are many people with hypercholesterolaemia who are not diagnosed. Future focus on diagnosis of this condition and publication of the Quality Standard 41 Familial hypercholesterolaemia in August 2013 may increase the number of people using statins and consequently the number of people eligible for this technology. The cost of alirocumab isn't known. The cost of the comparator ezetimibe is around £300 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	**Dinutuximab for treating high-risk neuroblastoma**		
Topic Selection ID Number	7370	**Wave / Round**	R110
TA ID Number	799		
Manufacturer	United Therapeutics		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of dinutuximab within its marketing authorisation for treating high-risk neuroblastoma following myeloablative therapy and autologous stem cell transplant.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of dinutuximab for treating high-risk neuroblastoma is appropriate. At the Decision Point 4 meeting it was agreed that the proposed remit should be amended to include the combination therapy. <u>Intervention</u> At the Decision Point 4 meeting it was agreed that the intervention should be amended to include only the British Approved Names for the combination therapy. • Dinutuximab in combination with sargramostim, aldesleukin, and isotretinoin <u>Outcomes</u> Response rate is not an appropriate outcome because patients with high-risk neuroblastoma receiving maintenance therapy typically do not have measurable disease since maintenance therapy is designed to target minimal residual disease and to prevent relapse therefore should be removed from the scope. It was noted that health-related quality of life was not assessed in the pivotal trials because most children treated were too young to collect data on health-related quality of life from them. Given the potential benefit of this treatment is on survival, overall survival would be the primary outcome of interest in treating children with high-risk neuroblastoma. <u>Subgroups</u> It was stated that children whose disease relapses may be offered immunotherapy as part of their relapse therapy if they have not received it before. The clinical experts indicated that the response rate with immunotherapy in patients with relapsed/refractory disease is around 30%. It was also noted that dinutuximab has been studied in this population in a phase II study. It was agreed to include people with relapsed disease and people with refractory disease as subgroups in the scope. It was noted however that there may not be any evidence available for these subgroups. It was considered that if this was the case this should be stated, and the Appraisal Committee should then decide if the available evidence could be extrapolated to people with relapsed or refractory disease.		

	STA/MTA There are 2 forms of anti-GD2 agents that have been widely used for high-risk neuroblastoma; dinutuximab and another agent that is being developed by Apeiron Biologics (the former is being used in US trials and the latter in European trials, all children with neuroblastoma have been part of the European trials). The 2 agents are from the same original hybridoma clone, and have identical amino acid sequences, but have been grown in different producer cell lines. Because of this, they are likely to have different glycosylation patterns, which might affect effector function. In view of the potential functional differences between the 2 agents, it has been recommended during consultation that both technologies be appraised at the same time in a MTA. *****CONFIDENTIAL INFORMATION REMOVED***** Given the potential difference in timings of both products an MTA would mean guidance on dinutuximab would **not** be timely.
Population size	1-year incidence: approximately 30 children
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of dinutuximab **in combination with sargramostim, aldesleukin and isotretinoin** within its marketing authorisation for treating high-risk neuroblastoma following myeloablative therapy and autologous stem cell transplant.
Costing implications of remit change	It is estimated that around 30 people in England may be eligible for treatment with dinuntuximab each year. The unit cost is not yet known however any costs would be additional for the NHS as this treatment represents an alternative maintenance therapy for people with high risk neuroblastoma whose condition has not responded to other available 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	**Lesinurad in combination with a xanthine oxidase inhibitor for treating gout.**		
Topic Selection ID Number	6519	**Wave / Round**	R54
TA ID Number	761		
Manufacturer	AstraZeneca		
Anticipated licensing information	*****CONFIDENTIAL INFORMATION REMOVED*****		
Draft remit	To appraise the clinical and cost effectiveness of lesinurad in combination with a xanthine oxidase inhibitor within its marketing authorisation for previously treated chronic hyperuricaemia in people with gout.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of lesinurad in combination with a xanthine oxidase inhibitor for previously treated chronic hyperuricaemia in gout is appropriate. The proposed remit is <u>not</u> appropriate. As lesinurad is an add-on treatment to xanthine oxidase inhibitors, the remit would be clearer if it did not include the words “previously treated”. The inclusion of these words imply that the person was treated, and is no longer receiving that treatment because it was unsuccessful. Rather, if a person’s hyperuricaemia persisted despite receiving an optimal dose of the treatment, then lesinurad would be added to the person’s treatment regimen. <u>Population</u> Scoping workshop attendees agreed that it was appropriate to change the population in the draft scope to: People with chronic hyperuricaemia in gout treated with a xanthine oxidase inhibitor whose disease had an inadequate response or in people who continue to have urate crystals in and around joints and skin. <u>Comparators</u> The attendees agreed that the 2 comparators for this appraisal should be allopurinol, and febuxostat for people who are intolerant or contraindicated to allopurinol. <u>Outcomes</u> Pain and tender and swollen joints would be captured within the outcome measure for gout flares and reduction in tophus. Physical function would be captured within health-related quality of life as it is a dimension of the EQ-5D. Therefore pain, tender and swollen joints and physical function could be removed from the list of outcome measures to be included in the scope. <u>Subgroups</u> The company stated that it had prespecified subgroups in the pivotal studies in which there may be evidence of greater clinical effectiveness or higher baseline risk. These include people taking thiazide diuretics, people with renal function impairment and other comorbidities. The attendees agreed that a statement similar to the one included in the febuxostat scope		

	should be included in this scope: *If the evidence allows, the appraisal will consider subgroups of patients for whom the technology is particularly appropriate due to greater clinical effectiveness or higher baseline risk (for example subgroups related to risk factors, co-morbidities or clinical features).*
Population size	It is estimated that the prevalence of gout is around 1.5% and therefore around 774,000 people in England have gout. Around 61% (472,000) are eligible to receive urate-lowering therapy as per TA164 (febuxostat for the management of hyperuricaemia in people with gout). According to Arthritis Research UK, between 8-25% of these people will have their xanthine oxidase treatments optimised, but will still be unable to reach the appropriate serum uric acid levels.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of lesinurad in combination with a xanthine oxidase inhibitor within its marketing authorisation for ~~**previously treated**~~ chronic hyperuricaemia in people with gout.
Costing implications of remit change	It is estimated that the prevalence of gout is around 1.5% and therefore around 774,000 people in England have gout. Around 61% (472,000) are eligible to receive urate-lowering therapy as per TA164 (febuxostat for the management of hyperuricaemia in people with gout), and that around 5% are contraindicated or intolerant of the first line drug option allopurinol. The number of people who would be likely to receive treatment with lesinurad is not known. The cost of lesinurad is unknown. The average annual cost of current treatments ranges from £15 to £293 (average £141).
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.