NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 26 draft remits and draft scopes and Summary of comments and discussions at scoping workshops

	Batch 26 topics
5.1	Lung cancer (non-small cell, EGFR mutation positive, locally advanced or metastatic) – afatinib
5.2	Macular oedema (central retinal vein occlusion) – aflibercept solution for injection
5.3	Multiple sclerosis (relapsing-remitting) – alemtuzumab, dimethyl fumarate, laquinimod and terilunomide
5.4	Melanoma (unresectable, advanced or metastatic BRAF V600 mutation-positive) – dabrafenib
5.5	Melanoma (unresectable, advanced or metastatic BRAF V600 mutation-positive) – trametinib
5.6	Bone metastases in prostate cancer (castration resistant) – radium-223 chloride
5.7	Prostate cancer (metastatic, castration-resistant) – sipuleucel-T
5.8	Psoriatic arthritis (active and progressive) – ustekinumab

Provisional Title	Afatinib for the treatment of epidermal growth factor receptor mutation positive locally advanced or metastatic non-small cell lung cancer.
Topic Selection ID Number	4936
Wave/Round	R16
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of afatinib for the treatment of epidermal growth factor receptor mutation positive 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 afatinib for the treatment of epidermal growth factor receptor (EGFR) mutation positive locally advanced or metastatic non-small cell lung cancer is appropriate. The position of afatinib in the treatment pathway is not yet clear, therefore the scope includes comparators for first, second and subsequent lines of treatment. There was a consensus among consultees that an STA would be appropriate to ensure issue of timely guidance. Approximately 75% of newly diagnosed NSCLC patients have advanced (stage III or IV) disease in England and Wales (approximately 21,000 patients) which has a five-year survival rate of less than 1%. Overexpression of EGFR has been detected in around 10% of NSCLC (2,100 patients).
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	Afatinib has a potential patient population of around 430 patients. These patients are those with locally advanced or metastatic disease with EGFR mutation. At present the cost of the drug is unknown, however there may be offsetting costs as the drug is intended to be used as a substitute for other currently approved therapies. There may be some offsetting savings, where afatinib replaces existing treatments for this patient group.
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	Aflibercept solution for injection for the treatment of macular oedema caused by central retinal vein occlusion.
Topic Selection ID Number	5463
Wave/Round	R16
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of aflibercept within its licensed indication for the treatment of macular oedema caused by central retinal vein occlusion.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of aflibercept solution for injection for the treatment of macular oedema caused by central retinal vein occlusion is appropriate. The proposed remit should be changed to reflect standard clinical terminology: '...the treatment of **visual impairment due to** macular oedema caused by central retinal vein occlusion.' The manufacturer and comparator manufacturers indicated that bevacizumab cannot be considered routine and best practice in the NHS, mainly due to absence of national guidance or guidelines and safety concerns. NICE considers it reasonable to include bevacizumab as a comparator in the scope of this appraisal as it has been identified as being in use for the treatment of patients with macular oedema caused by central retinal vein occlusion. It will be up to the Appraisal Committee, on the basis of the evidence provided to it, to decide whether it indeed is an appropriate comparator for decision making. In doing so the Appraisal Committee will take into consideration clinical practice in the NHS as it finds it, the extent to which bevacizumab is in actual use in the NHS for the indication specified in this appraisal, and will have due regard to the extent and quality of the evidence, particularly for safety and efficacy for technologies for which use is considered to be 'unlicensed'. It is estimated that for every 100,000 population, 17 people aged 40 years or over will require treatment for macular oedema caused by CRVO annually.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of aflibercept within its licensed indication for the treatment of **visual impairment due to** macular oedema caused by central retinal vein occlusion.'
Costing	No changes to the costing comments are required

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.

Provisional Title	Alemtuzumab, dimethyl fumarate, laquinimod and terilunomide for the treatment of relapsing-remitting multiple sclerosis.
Topic Selection ID Number	5235/5988/5447/5493
Wave/Round	R19/R22/W28/R19
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of alemtuzumab, dimethyl fumarate, laquinimod and teriflunomide within their licensed indications for the treatment of relapsing forms of multiple sclerosis.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that a multiple technology appraisal of alemtuzumab, dimethyl fumarate, laquinimod and teriflunomide for the treatment of relapsing forms of multiple sclerosis is not appropriate. In order to ensure timely appraisals, the technologies should be appraised separately as single technology appraisals (STAs). Consultees agreed the population should reflect the different population for alemtuzumab compared with the other three technologies: • Dimethyl fumarate, laquinimod and teriflunomide: People with previously untreated relapsing-remitting multiple sclerosis and people with relapsing-remitting multiple sclerosis who experience a lack of tolerability on another disease modifying therapy. • Alemtuzumab: people with rapidly evolving severe multiple sclerosis and people who continue to experience relapses on another disease modifying therapy. • Additionally, there is a smaller population of people with secondary progressive MS (SPMS) for which teriflunomide is expected to be licensed. The manufacturer of lanquinimod confirmed that their application to EMA is about 6 months behind the other technologies in the regulatory process. It was also noted that alemtuzumab will probably be used in a different population to the other drugs and so could be considered separately as an STA particularly if timeliness was an issue. During the consultation most consultees suggested that an STA process is more appropriate because of the need for timely guidance to allow patients to access these therapies. The institute therefore proposes that the technologies be appraised as separate STAs.

	NICE intends to initiate a review proposal for technology appraisal guidance 32 on Beta interferon and glatirameracetate for the treatment of multiple sclerosis, subject to approval by it Guidance Executive, expecting to consult on a review proposal in month/year.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	**To appraise the clinical and cost effectiveness of alemtuzumab within its licensed indication for the treatment of relapsing-remitting multiple sclerosis.** **To appraise the clinical and cost effectiveness of dimethyl fumarate within its licensed indication for the treatment of relapsing-remitting multiple sclerosis.** **To appraise the clinical and cost effectiveness of laquinimod within its licensed indication for the treatment of relapsing-remitting multiple sclerosis.** **To appraise the clinical and cost effectiveness of teriflunomide within its licensed indication for the treatment of relapsing forms of multiple sclerosis.**
Costing implications of remit change	It is assumed that alemtuzumab, dimethyl fumarate and laquinimod would each be appraised independently as a STA topic and they are for people with relapsing-remitting multiple sclerosis (RRMS). It is estimated that around 80% (45,000) people have this presentation of the condition. If the drugs are for those people who experience a lack of tolerability of other disease modifying therapies, the eligible population will be less than 45,000. As these drugs represent another treatment option, it is currently unknown what proportion may switch. It is assumed that teriflunomide would be appraised as an STA topic with an eligible population being those people who have a secondary progressive presentation of the condition. It is estimated that this group is a subset of the RRMS population and is around 65% (29,000) people. The cost impact cannot be estimated at this time from the information available.
Timeliness statement	Assuming that these anticipated dates of the marketing authorisations are the latest dates that we are aware of and the expected referral date of these topics, issuing timely guidance for these technologies will be possible.

Provisional Title	Dabrafenib for the treatment of unresectable, advanced or metastatic BRAF ^{V600} mutation-positive melanoma.
Topic Selection ID Number	5627
Wave/Round	R19
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of dabrafenib within its licensed indication for the treatment of unresectable, advanced or metastatic BRAF^{V600} mutation-positive melanoma.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of dabrafenib for the treatment of unresectable, advanced or metastatic BRAF^{V600} mutation-positive melanoma is appropriate. Stakeholders considered the draft remit to be appropriate, however the manufacturer expects that the licence will not specifically mention first-line use, and apply to first and second line treatment, similar to the marketing authorisation of vemurafenib for the same indication. A diagnostic test for the BRAF^{V600} mutation is required, however the manufacturer expects that a Cobas test, generic PCR sequencing tests or other validated BRAF mutation tests could be used. ***Confidential information removed *** According to clinicians who were consulted in the appraisal for vemurafenib, which has the same population, less than 1,000 people each year in England and Wales would be eligible for treatment.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	The original costing comments were produced using the National Horizon Scanning Centre briefing note. The briefing note defined the condition to be treated to be people with a BRAF^{V600E} mutation and identified a population of around 600 people. This remit identifies people with a BRAF V600 mutation, not the 'E' variant. With this revised information, the eligible population is considered to be slightly larger than first estimated. Revised costing comments would indicate that in 2009 around 9700 people were diagnosed with malignant melanoma in England, of whom around 16% were stage III or IV. It is estimated that around 50% patients have a BRAF mutation.

	This gives an eligible population for the technology of around 750 people. The cost of the technology is not yet known. Due to the number of people who may switch and the cost of comparators being unknown, the cost impact cannot be estimated from the information currently available.
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	Trametinib for the treatment of unresectable, advanced or metastatic BRAF V600 mutation-positive melanoma.
Topic Selection ID Number	5628
Wave/Round	R20
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of trametinib within its licensed indication for the treatment of unresectable, advanced or metastatic $BRAF^{V600}$ mutation-positive melanoma.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of trametinib for the treatment of unresectable, advanced or metastatic $BRAF^{V600}$ mutation-positive melanoma is not appropriate. ***Confidential information removed ***
Process (MTA/STA)	N/A – referral not sought
Proposed changes to remit (in bold)	N/A – referral not sought
Costing implications of remit change	N/A – referral not sought
Timeliness statement	N/A – referral not sought

Provisional Title	Radium-223 chloride for the treatment of bone metastases in castrate resistant prostate cancer.
Topic Selection ID Number	5030
Wave/Round	R16
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of radium-223 chloride within its licensed indication for the treatment of bone metastases in castrate resistant prostate cancer
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of radium-223 dichloride for the treatment of castration resistant prostate cancer with bone metastases is appropriate. Consultees agreed the remit should be changed to reflect the expected licence and that radium-223 dichloride would be a treatment for castration-resistant prostate cancer with bone metastases rather than a treatment of bone metastases. The key trials included people with multiple, painful bone metastases, and therefore the population was narrowed to 'adults with castration resistant prostate cancer with **symptomatic** bone metastases' During consultation, patient groups indicated that the term 'castration resistant' was unhelpful and insensitive to patients. However, the Institute acknowledges that there is no consensus within the clinical community regarding an alternative wording. Additionally, marketing authorisation is expected to contain this terminology. NICE will write to the clinical societies and royal colleges to advise them to work with patient groups to develop a terminology that is acceptable to patients.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of radium-223 **di**chloride within its licensed indication for the treatment **castration-resistant prostate cancer with bone metastases.**
Costing implications of remit change	No changes to the costing comments are required
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	Sipuleucel-T for the treatment of metastatic castrate-resistant prostate cancer
Topic Selection ID Number	5455
Wave/Round	R15
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of sipuleucel-T within its licensed indication for the treatment of metastatic castrate-resistant prostate cancer.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of sipuleucel-T for the treatment of metastatic castration-resistant prostate cancer is appropriate. Consultees indicated that it was unlikely that people with moderate or severe symptoms of metastatic castration-resistant prostate cancer would be considered eligible for treatment with sipuleucel-T (that is, those who require opioid treatment to control their pain) and that that the UK marketing authorisation would likely specify that patients should be asymptomatic or minimally symptomatic. Therefore the remit has been amended to reflect this. It was agreed that abiraterone should be added as a comparator for people with metastatic castration-resistant prostate cancer who had not previously received chemotherapy, subject to its recommendation in NICE technology appraisal guidance in the first-line setting. Consultees considered that the MTA process with other treatments (abiraterone and enzalutamide) could provide useful information on treatment sequencing, however an STA would likely provide a more timely option.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of sipuleucel-T within its licensed indication for the treatment of **asymptomatic or minimally symptomatic** metastatic castrat**ion**-resistant prostate cancer.
Costing implications of remit change	The changes to the remit define a population who are asymptomatic or minimally symptomatic. This reduces the eligible population. Revised costing comments are provided. It is estimated that around 32,000 men are diagnosed with prostate cancer each year and that around 25% (8000) of these are metastatic. The drug is to be appraised for people who are asymptomatic or minimally asymptomatic. It is not known what portion of people have these types of presentation of disease. Sipuleucel-T is a new first line treatment option. The briefing note states that there is the potential for sipuleucel-T to decrease the length of hospital stay for patients however it is unclear why and so this cannot be verified or quantified at this

	stage.. The cost of sipuleucel-T is not currently known. As the number of people who would switch is not known, offsetting savings are unclear and the cost is unknown, the cost impact cannot currently be estimated.
Timeliness statement	Assuming that the anticipated date of the marketing authorisation and launch 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	Ustekinumab for the treatment of active and progressive psoriatic arthritis
Topic Selection ID Number	4561
Wave/Round	W25
Anticipated licensing information	***Confidential information removed ***
Draft remit	To appraise the clinical and cost effectiveness of ustekinumab within its licensed indication for the treatment of active and progressive psoriatic arthritis.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ustekinumab for the treatment of active and progressive psoriatic arthritis is appropriate. Consultees suggested that, although one of the two ongoing phase III trials included patients who may have been previously treated with TNF-α inhibitors, the evidence base for sequencing of biologic treatments is limited. Accordingly, the consideration that states: "Sequencing of different drugs should be considered" should be replaced by "Subgroup analysis should be carried out according to previous treatment, including previous treatment with TNF-α inhibitors". It was considered that because of its alternative mechanism of action, it might have a specific role for patients whose disease has not responded to a TNF inhibitor. Consultees also noted that the less frequent dosing schedule might also be an advantage of ustekinumab. ***Confidential information removed ***
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	No changes to the costing comments are required
Timeliness statement	***Confidential information removed ***