ITEM 5

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 19 draft remits and draft scopes

Summary of comments and discussions at scoping workshops

	Batch 19 topics
5.1	Vemurafenib for the treatment of unresectable locally advanced or metastatic BRAFV600 mutation-positive malignant melanoma
5.2	Ivabradine for the treatment of chronic heart failure
5.3	Bevacizumab for the treatment of platinum-sensitive or partially platinum-sensitive recurrent advanced ovarian cancer (including fallopian tube and primary peritoneal cancer)
5.4	Bevacizumab in combination with chemotherapy for the second line treatment of human epidermal growth factor 2 (HER2) negative metastatic breast cancer
5.5	Ridaforolimus for the maintenance treatment of metastatic soft tissue or bone sarcoma

Provisional Title	Vemurafenib for the treatment of unresectable locally advanced or metastatic $BRAF^{V600}$ mutation-positive malignant melanoma
Topic Selection ID Number	4958
Wave	27
Anticipated licensing information	CONFIDENTIAL
Draft remit	To appraise the clinical and cost effectiveness of vemurafenib within its licensed indication for the treatment of locally advanced or metastatic $BRAF^{V600E}$ mutation-positive malignant melanoma.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of vemurafenib for the treatment of locally advanced or metastatic $BRAF^{V600E}$ mutation-positive malignant melanoma is appropriate. The appraisal will cover the use of vemurafenib in both previously treated and previously untreated patients (that is, marketing authorisation will cover all lines of treatment). The proposed remit and population are not appropriate and should be changed in line with the anticipated marketing authorisation and terminology routinely used in clinical practice to describe patients with this type of melanoma, that is adults with unresectable locally advanced or metastatic $BRAF^{V600}$ mutation-positive malignant melanoma. The manufacturer expects vemurafenib to be licensed for patients with a $BRAF^{V600}$ mutation. The majority of $BRAF^{V600}$ mutations are $BRAF^{V600E}$, however around 10-15% are $BRAF^{V600K}$. Both mutations appear to have been detected by the manufacturer's cobas 4800 $BRAF^{V600}$ test in patients enrolled in the pivotal clinical trials. The change in the wording of the remit and population is not expected to significantly increase the population size.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of vemurafenib within its licensed indication for the treatment of **unresectable** locally advanced or metastatic **$BRAF^{V600}$** mutation-positive malignant melanoma.
Costing implications of remit change	The change in remit affects the eligible population slightly. It is now estimated to be around 1000 people who would be eligible. The cost of the technology is not known however there would be some modest offsetting savings from current treatments avoided. The topic would be high cost if the annual cost of treatment per patient was around £16,000. It is considered that there is potential for the technology to be low cost.
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	Ivabradine for the treatment of chronic heart failure
Topic Selection ID Number	4714
Wave	26
Anticipated licensing information	CONFIDENTIAL
Draft remit	To appraise the clinical and cost effectiveness of ivabradine within its licensed indication for the treatment of chronic heart failure.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ivabradine for the treatment of chronic heart failure is appropriate. The proposed remit is appropriate. Ivabradine is being considered as an add-on treatment for adults with symptomatic chronic heart failure in sinus rhythm due to left ventricular systolic dysfunction of ischaemic or non-ischaemic origin who have been prescribed standard optimal heart failure therapy. The exact wording of the marketing authorisation is still uncertain, however any changes to the population in the scope as a result of the final marketing authorisation, will not affect the remit. The scoping workshop attendees discussed whether an MTA should be conducted with eplerenone. It was noted that the relevant extension to the indication for eplerenone was not included in clinical guideline 108 (Chronic heart failure: management of chronic heart failure in adults in primary and secondary care) due to regulatory timings (extension anticipated 2012). It was also noted that Topic Selection did not filter this topic to the appraisal programme under the assumption that it was going to be included in clinical guideline 108. The wording of clinical guideline 108 is broad enough to cover the use of eplerenone under its extended indication and clinical specialists have confirmed that it is already being used in clinical practice in line with this extension, therefore additional guidance is not required. Attendees acknowledged that an STA would be the most appropriate process to ensure timely guidance for ivabradine.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	No change to cost impact

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	Bevacizumab for the treatment of recurrent advanced ovarian cancer
Topic Selection ID Number	5138
Wave	28
Anticipated licensing information	CONFIDENTIAL
Draft remit	To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication for the treatment of platinum-sensitive or partially platinum-sensitive recurrent or relapsed advanced ovarian 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 the treatment of recurrent or relapsed advanced ovarian cancer is appropriate. The proposed remit is not appropriate and should be amended to reflect the anticipated marketing authorisation, which also includes fallopian tube cancer and primary peritoneal cancer. In addition, only the term 'recurrent' should be used (not relapsed) to describe a patient's cancer. Consultees highlighted that the pivotal trials for bevacizumab also included patients with fallopian tube cancer or primary peritoneal cancer and the anticipated marketing authorisation will include these patients as well. Clinical specialists at the scoping workshop confirmed that fallopian tube cancer, primary peritoneal cancer and epithelial ovarian cancer are all treated in the same manner in UK clinical practice and that all of these groups can be classified together as ovarian cancer, rather than as individual subgroups. The manufacturer of bevacizumab confirmed at the scoping workshop that the clinical trials for bevacizumab showed that the study participants had similar outcomes after treatment regardless of their type of ovarian cancer. Attendees at the Scoping Workshop noted that bevacizumab in combination with paclitaxel and carboplatin for the first-line treatment of advanced and/or metastatic ovarian cancer was scheduled to be appraised by NICE with guidance likely in July 2012. Consultees questioned the impact of the recommendations from the ongoing appraisal on this proposed topic. In particular, clinicians were concerned that if patients can only receive 2nd or subsequent-line treatment with bevacizumab if they are bevacizumab-naïve, then clinicians may be reluctant to use it 1st-line (even if it is recommended by NICE) and wait until their patient's disease has recurred. However, it was noted that this concern was beyond the remit of Technology Appraisals and would be best addressed as part of a Clinical Guideline which would outline the optimal treatment pathway.

	The clinical specialists noted that TA 91 (Ovarian cancer (advanced) - paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan) was out of date. It is scheduled to be reviewed in November 2012 once ongoing research (CALYPSO trial) is completed and will also include trabectedin and gemcitabine subject to approval of the Department of Health. The clinical specialists emphasised that a short clinical guideline on the use of chemotherapy in ovarian cancer is needed.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication for the treatment of platinum-sensitive or partially platinum-sensitive recurrent advanced ovarian cancer **(including fallopian tube and primary peritoneal cancer).**
Costing implications of remit change	No change to cost impact
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	Bevacizumab in combination with standard chemotherapy for the second line treatment of HER2 negative metastatic breast cancer
Topic Selection ID Number	5101
Wave	27
Anticipated licensing information	CONFIDENTIAL
Draft remit	To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication in combination with chemotherapy for the second line treatment of human epidermal growth factor 2 (HER2) negative metastatic breast cancer.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of bevacizumab in combination with standard chemotherapy for the second line treatment of HER2 negative metastatic breast cancer is appropriate. ****Confidential ***
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	No change to cost impact
Timeliness statement	Assuming that the intended marketing authorisation submission date is the latest that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.

Provisional Title	Ridaforolimus for the maintenance treatment of soft tissue or bone sarcoma
Topic Selection ID Number	4610
Wave	25
Anticipated licensing information	CONFIDENTIAL
Draft remit	To appraise the clinical and cost effectiveness of ridaforolimus within its licensed indication for the first-line maintenance treatment of metastatic soft tissue or bone sarcoma.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ridaforolimus for the maintenance treatment of metastatic soft tissue or bone sarcoma is appropriate. This appraisal will consider the use of ridaforolimus maintenance treatment for people aged 13 years and older with metastatic soft tissue or bone sarcoma who have achieved a complete response, partial response, or stable disease following treatment with first line, second line or third line chemotherapy (in line with the proposed marketing authorisation). Therefore, the proposed remit is not appropriate and should be amended in line with the marketing authorisation to specify that ridaforolimus will be considered in the metastatic setting for all lines of maintenance treatment, not just as first-line maintenance.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of ridaforolimus within its licensed indication for the **maintenance** treatment of metastatic soft tissue or bone sarcoma.
Costing implications of remit change	No change to cost impact
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.