ITEM 5

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 23 draft remits and draft scopes and summary of comments and discussions at scoping workshops

	Batch 23 topics
5.1	Mirabegron for the treatment of symptoms associated with overactive bladder
5.2	Pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer
5.3	Everolimus for the treatment of advanced or metastatic HER2 negative, oestrogen receptor positive breast cancer
5.4	Phentermine with topiramate for the treatment of obesity and overweight
5.5	Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia

Provisional Title	Mirabegron for the treatment of symptoms associated with overactive bladder
Topic Selection ID Number	5128
Wave	28
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of mirabegron within its licensed indication for the treatment of overactive bladder.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of mirabegron for the treatment of overactive bladder is appropriate. The proposed remit is appropriate but should be amended to specify that mirabegron will be a symptomatic treatment. Although the marketing authorisation for mirabegron is unlikely to specify where it should be used in the treatment pathway, attendees and the manufacturer considered that it would most likely be used after previous treatment with one or two different antimuscarinic agents (some of which are now generic). The scope has been updated to include 'previously untreated and previously treated overactive bladder' as potential subgroups for consideration if the evidence allows.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of mirabegron within its licensed indication for the treatment of **symptoms associated with** overactive bladder.
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	Pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer
Topic Selection ID Number	5139
Wave	28
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost-effectiveness of pertuzumab in combination with trastuzumab and a taxane within its licensed indication for the treatment of human epidermal growth factor receptor 2 (HER2) positive 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 pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer is appropriate. The proposed remit and title should be changed to reflect the wording of proposed marketing authorisation and also include patients with locally recurrent unresectable breast cancer. Clinical specialists at the scoping workshop agreed that broadening the remit to include people with locally recurrent, unresectable breast cancer will not significantly affect the population size because it constitutes a small minority of patients encountered in clinical practice. The proposed marketing authorisation does not preclude use in men although the trial population in the pivotal study only included female patients. Breast cancer in men is very rare, therefore, including men as part of the patient population is not expected to significantly impact on the population size eligible for treatment. The intervention should be changed in line with the proposed marketing authorisation to 'pertuzumab in combination with trastuzumab and docetaxel'.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost-effectiveness of pertuzumab in combination with trastuzumab and **docetaxel** within its licensed indication for the treatment of human epidermal growth factor receptor 2 (HER2) positive metastatic **or locally recurrent unresectable** breast cancer, **which has not been previously treated, or has relapsed after adjuvant therapy.**

Costing implications of remit change	The proposed change to the remit to include locally recurrent unresectable breast cancer slightly increases the eligible population. Revised costing comments are: In 2009 approximately 5500 women were diagnosed with metastatic HER2-positive breast cancer and may be eligible for treatment with pertuzumab. Further to this are women who have HER2 positive locally recurrent breast cancer. This number is currently unknown but not it is not anticipated that it is big. Pertuzumab is administered in combination with trastuzumab and docetaxel and it is assumed that the cost of pertuzumab will be incremental to current practice. As trastuzumab is administered by IV it is assumed that there will not be any incremental administration costs. The cost of pertuzumab is not yet known. As pertuzumab would be one of several treatment options the incremental cost will depend on the number of patients who receive the treatment and the cost; at this stage it is not possible to judge whether it would be low or high 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	Everolimus for the treatment of advanced or metastatic HER2 negative, oestrogen receptor positive breast cancer
Topic Selection ID Number	5446
Wave	29
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of everolimus in combination with exemestane within its licensed indication for the treatment of human epidermal growth factor 2 (HER2) negative, oestrogen receptor positive locally advanced or metastatic breast cancer after prior endocrine therapy.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of everolimus for the treatment of advanced or metastatic HER2 negative, oestrogen receptor positive breast cancer is appropriate. Everolimus is likely to be used in a number of positions in the clinical pathway. These include second-line after failure of anastrozole or letrozole, or subsequent to this after the failure of both anastrozole or letrozole and tamoxifen. Some people in the everolimus trial had already received chemotherapy for metastatic disease, therefore for these people everolimus could also be a treatment subsequent to chemotherapy. The pivotal trial considered everolimus in combination with exemestane and is therefore likely to reflect the marketing authorisation. However, everolimus has also been studied in combination with other agents (tamoxifen) in this indication. There is uncertainty over the exact wording of the marketing authorisation for this indication; therefore attendees at the scoping workshop considered that the remit should be broadened to allow for potential use in combination with other treatments. In light of these comments, the proposed remit is <u>not</u> appropriate and should be amended to specify that everolimus will be used in combination with an aromatase inhibitor rather than exemestane. In light of the proposed changes to the remit, the intervention should be amended to 'everolimus in combination with an aromatase inhibitor'. The population in the scope should be amended to 'post-menopausal women with HER2-negative, oestrogen receptor-positive locally advanced or metastatic breast cancer whose disease has recurred or progressed after prior therapy which has included a non-steroidal aromatase inhibitor' in line with the population in the pivotal trials.
Process (MTA/STA)	STA

Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of everolimus in combination with ~~exemestane~~ **an aromatase inhibitor** within its licensed indication for the treatment of human epidermal growth factor 2 (HER2) negative, oestrogen receptor positive locally advanced or metastatic breast cancer after prior endocrine therapy".
Costing implications of remit change	The changes discussed at the scoping workshop around the number of positions in the clinical pathway that the technology may be used at, the uncertainty of wording in the marketing authorisation and the widening of the remit necessitates changes to the costing comments. Revised costing comments are: It is estimated that there are approximately 16,000 post menopausal women each year with locally advanced or metastatic, HER2-negative, ER-positive breast cancer. It is not known how many of these women have received prior endocrine therapy. Assuming that anastrozole and letrozole are the main comparators, all three treatments involve oral administration therefore administration costs are assumed to be equal. The cost is around £27,000 per patient. Considering the assumption around comparators, only 4% of these women would need to switch to everolimus in combination with endocrine therapy for this topic to be high cost. This topic has potential to be high 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	Phentermine with topiramate for the treatment of obesity and overweight
Topic Selection ID Number	5400
Wave	29
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of phentermine with topiramate within its licensed indication for the treatment of adults who are obese or who are overweight and have weight-related co-morbidities.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of phentermine with topiramate for the treatment of obesity and overweight is appropriate. The proposed remit is appropriate. No changes are required. The manufacturer anticipates that specific BMI ranges are likely to be included in the marketing authorisation, however these BMI cut off values are unknown at present. Current NICE clinical guideline 87 for type 2 diabetes recommends adjusting BMI ranges for people from certain ethnic backgrounds, including people of South Asian family origin. Adjusted BMI ranges for these populations will also be considered in this appraisal. Consultees considered whether the STA process was appropriate for this topic or whether phentermine with topiramate should be considered with lorcaserin (which has already been referred as an STA but an appraisal is not due to begin until 2013 based on regulatory timelines) as an MTA. It was noted that the regulatory timelines for lorcaserin are uncertain and there would be a risk of a delay to guidance on the use of phentermine with topiramate if an MTA was considered.
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	Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia
Topic Selection ID Number	5114
Wave	28
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of tadalafil within its licensed indication for the treatment of benign prostatic hyperplasia.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of tadalafil for the treatment of benign prostatic hyperplasia (BPH) is appropriate. The manufacturer indicated that the prescription of tadalafil for erectile dysfunction is already strictly regulated (as a Schedule II drug). Because the licence extension for tadalafil will be for the treatment of BPH in men with and without erectile dysfunction, the manufacturer considered that the restrictions in Schedule II will prevent tadalafil being prescribed through the NHS for men with BPH and erectile dysfunction unless they also have one of the risk factors listed in the Schedule II. Therefore, the manufacturer emphasised that they were unwilling to pursue an appraisal for tadalafil for the treatment of BPH because of concerns over reimbursement for this indication. The Department of Health has confirmed that the existing restrictions on the use of tadalafil for erectile dysfunction (under Schedule II) will not apply to the licence extension for benign prostatic hyperplasia. Although there is a risk that tadalafil may be used for erectile dysfunction, even if it is prescribed for benign prostatic hyperplasia, this is a risk which would occur regardless of whether or not an appraisal is undertaken. Consultees considered that the current prescribing regulations for tadalafil should not preclude this topic from being considered for appraisal. Consultees suggested that once recommendations on the use of tadalafil for BPH are issued by NICE, the manufacturer should discuss with the Department of Health how the Schedule II restrictions for tadalafil (for erectile dysfunction) can be amended to take account of the BPH recommendations. The proposed remit should be changed for greater clinical accuracy to: “To appraise the clinical and cost effectiveness of tadalafil within its licensed indication for the treatment of symptoms associated with benign prostatic hyperplasia”.

	Similarly, the title of the appraisal and scope should be changed to: "Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia".
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of tadalafil within its licensed indication for the treatment of **symptoms associated with** benign prostatic hyperplasia.
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.