NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 27 draft remits and draft scopes and summary of comments and discussions at scoping workshops

5.1	Canagliflozin for the treatment of type 2 diabetes
5.2	Degarelix for the treatment of advanced hormone-dependent prostate cancer
5.3	Enzalutamide for the treatment of metastatic hormone relapsed prostate cancer previously treated with a docetaxel-containing regimen
5.4	INTRABEAM Photon Radiosurgery System for the adjuvant treatment of early or locally advanced breast cancer
5.5	Trastuzumab emtansine for the treatment of locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane
5.6	Vortioxetine for the treatment of moderate to severe major depressive disorder

Provisional Title	Canagliflozin for the treatment of type 2 diabetes		
Topic Selection ID Number	5425	**Wave/Round**	R16
TA ID Number	554		
Manufacturer	Janssen		
Anticipated licensing information	***Confidential information removed ***		
Draft remit	To appraise the clinical and cost effectiveness of canagliflozin within its licensed indication for the treatment of type 2 diabetes		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of canagliflozin for the treatment of type 2 diabetes is appropriate. The draft remit is considered appropriate. The draft scope included canagliflozin monotherapy as an intervention and its use was discussed at the scoping workshop. The manufacturer confirmed that it was seeking a monotherapy licence, but that this would be limited to people for whom metformin was considered inappropriate. Clinicians at the workshop did not consider that canagliflozin would be used as a monotherapy given the current treatment options available, and recommended that the appraisal need not consider canagliflozin as a monotherapy treatment.		
Population size	In the appraisal of dapagliflozin for the same indication it was estimated that approximately 2 million people with type 2 diabetes are suitable for oral anti-diabetic drugs.		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	No changes proposed		
Costing implications of remit change	The briefing note for this topic stated that the use of this technology was as mono-therapy, dual-therapy and triple-therapy. It is assumed following the consultation and the workshop that it is now just dual and triple-therapy. The original population identified was between 2 and 2.3 million people. If the eligible population does now not include mono-therapy people, it is reduced slightly but is more likely to be around 2 million people. Without knowing what offsetting savings would be achieved, it is estimated that this topic would be high cost if the incremental cost per person was around £7.50 per person and all eligible people chose the new technology. As the population is potentially large, it is considered that there is potential for this topic to be high cost.		
Timeliness	Assuming that the anticipated date of the marketing		

statement	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	Degarelix for the treatment of advanced hormone-dependent prostate cancer		
Topic Selection ID Number	2613	**Wave/Round**	R23
TA ID Number	590		
Manufacturer	Ferring Pharmaceuticals		
Licensing information	Marketing Authorisation: Degarelix has a UK marketing authorisation for the treatment of adult male patients with advanced hormone-dependent prostate cancer Marketing Authorisation was received in February 2009		
Draft remit	To appraise the clinical and cost effectiveness of degarelix within its licensed indication for the treatment of advanced hormone-dependent prostate cancer.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of degarelix within its licensed indication for the treatment of advanced hormone-dependent prostate cancer is appropriate. The draft remit is considered appropriate. Attendees at the scoping workshops considered that the population in the appraisal should be adults with advanced hormone-dependent prostate cancer in whom orchidectomy is not preferred. This is to clarify that a person with prostate cancer would initially need to take a decision about whether to proceed with a surgical or non-surgical intervention. If they decided to proceed with pharmacological treatment then there would be a second decision about which drug to take. On this basis workshop attendees considered that bilateral orchidectomy was not a suitable comparator for degarelix. Degarelix is not associated with a temporary rise in testosterone levels. Attendees suggested that there were several subgroups that could particularly benefit from the rapid reduction in testosterone associated with degarelix. These comprised: high-risk patients with PSA >20 ng/mL; patients with spinal metastases with impending or actual spinal cord compression; patients with high tumour volume with impending or actual urinary outflow obstruction: patients with bony metastases associated with intractable pain. Other potential subgroups were patients for whom standard anti-androgen treatment is contraindicated and patients at risk of evolving cardiovascular comorbidity.		
Population size	There are approximately 37,000 diagnoses of prostate cancer in England and Wales each year. Approximately thirty percent of new diagnoses are expected to have locally advanced or metastatic prostate cancer on presentation (approximately 11,000 people). It is estimated that between 3000 and 8000 people could be suitable for degarelix.		
Process (MTA/STA)	STA		
Proposed changes to remit	No changes proposed		

(in bold)	
Costing implications of remit change	The original costing comments identified that around 24,000 men in England per year may be eligible for this treatment. The scoping workshop change to the scope indicates that the eligible population is now those for whom orchidectomy is not preferred. It is estimated that around 37,000 men are diagnosed with prostate cancer in England and Wales each year and that there are around 30% (11,000) who are locally advanced or metastatic. The proportion who choose orchidectomy is not known and there is a range of estimates based on medical and surgical opinion. It is estimated that the range may be between 3000 and 8000 men who would be eligible for using degarelix. Based on the potential range of populations, the cost impact could be between £4 million and £13 million. The population needs verification, but it is considered that the topic has potential to be low cost.
Timeliness statement	Given that degarelix achieved UK marketing authorisation in February 2009 for this indication issuing timely guidance for this technology will not be possible.

Provisional Title	Enzalutamide for the treatment of metastatic hormone relapsed prostate cancer previously treated with a docetaxel-containing regimen.		
Topic Selection ID Number	5992	**Wave/Round**	R25
TA ID Number	600		
Manufacturer	Astellas Pharma		
Anticipated licensing information	***Confidential information removed ***		
Draft remit	To appraise the clinical and cost effectiveness of enzalutamide within its licensed indication for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of enzalutamide for the treatment of metastatic hormone relapsed prostate cancer previously treated with a docetaxel-containing regimen is appropriate. The proposed remit is not appropriate. The remit has been amended to replace the term castration-resistant with the term hormone relapsed prostate cancer which is considered to be more acceptable by patients. Attendees noted that although not recommended by NICE, cabazitaxel may be provided though the cancer drugs fund. However, this was not added as a comparator to the scope because of the negative NICE recommendation.		
Process (MTA/STA)	STA		
Population size	There are approximately 37,000 diagnoses of prostate cancer in England and Wales each year. Approximately thirty percent of new diagnoses are expected to have locally advanced or metastatic prostate cancer on presentation (approximately 11,000 people). Eighty percent initially respond to hormone treatment, meaning that approximately 1500 to 2000 people may be expected to present with metastatic hormone relapsed prostate cancer.		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of enzalutamide within its licensed indication for the treatment of metastatic **hormone relapsed** prostate cancer previously treated with a docetaxel-containing regimen.		
Costing implications of remit change	No change to cost implications.		
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	INTRABEAM Photon Radiosurgery System for the adjuvant treatment of early or locally advanced breast cancer		
Topic Selection ID Number	n/a	**Wave/Round**	n/a
TA ID Number	618		
Manufacturer	CarlZeiss		
Anticipated licensing information	INTRABEAM Photon Radiosurgery System received a CE mark in 1999 for radiosurgery treatment		
Draft remit	To appraise the clinical and cost effectiveness of INTRABEAM Radiosurgery System for the adjuvant treatment of early or locally advanced breast cancer during surgical removal of the tumour.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of INTRABEAM Radiosurgery System for the adjuvant treatment of early or locally advanced breast cancer during surgical removal of the tumour is appropriate. The draft remit should be amended to remove locally advanced disease. The main source of evidence for the use of INTRABEAM comes from the TARGIT-A trial. Participants at the workshop noted that TARGIT-A recruited people with early breast cancer therefore the evidence for INTRABEAM in people with locally advanced disease is currently limited. Participants noted that there were perceived benefits of INTRABEAM particularly for those people currently considered unsuitable for external beam radiotherapy, and more generally because for the majority of people with early breast cancer INTRABEAM may be used as a single intervention during surgery. This provides greater convenience for patients and has the potential to free up existing radiotherapy capacity. A number of other intra-operative techniques are being developed. However, currently high levels of evidence for these do not exist. Attendees at the workshop did not consider that the evidence available for these other techniques meant that their inclusion in an appraisal of INTRABEAM was appropriate. Radiotherapy is an established intervention, but attendees noted that there are concerns within the clinical community that some women with 'low risk' early breast cancer are currently being over treated. Local radiotherapy practice may change in the future because there are ongoing studies comparing 3 weeks of therapy (15 fractions) to 1 week of therapy (5 fractions). Intensity modulated radiotherapy is also likely to become more widely used in the NHS. Therefore, in the future the specific target population for radiotherapy may change as well as the administration schedule for external beam radiotherapy, the comparator in the appraisal. Attendees at the workshop did not consider that follow up data		

	are sufficiently mature to conclusively show the relative efficacy compared to external beam radiotherapy. Five year follow up data from the TARGIT-A trial suggests an ipsilateral recurrence rate of 1.3% in the external beam radiotherapy group and 3.3% in the INTRABEAM group. Uncertainty in efficacy may affect the uptake of INTRABEAM which will affect the amount of capacity that could be freed from existing radiotherapy units. Radiotherapy services are currently switching to national specialised commissioning. This will include standardisation of tariffs for radiotherapy, but could also include recommendations on the investment of equipment. In addition to issues described above, the health economic issues in an appraisal are likely to be complex with the need to account for on the one hand an existing service where there has already been investment in equipment, and on the other hand a new service where there is currently limited investment. For these reason a multiple technology appraisal is considered the most appropriate process to appraise this topic.
Population size	There were 43,183 diagnoses of breast cancer in England and Wales with approximately 95% of these being for early disease. Women who have had breast conserving surgery will usually receive radiotherapy as part of adjuvant treatment. Breast cancer makes up 30% of the radiotherapy caseload.
Process (MTA/STA)	MTA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of INTRABEAM Radiosurgery System for the adjuvant treatment of early breast cancer during surgical removal of the tumour. **(removal of the words locally advanced)**
Costing implications of remit change	No change to MTG costing comments.
Timeliness statement	Given that INTRABEAM Photon Radiosurgery System received a CE mark in 1999, issuing timely guidance for this technology will not be possible.

Provisional Title	Trastuzumab emtansine for the treatment of locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane		
Topic Selection ID Number	5206	**Wave/Round**	R17
TA ID Number	603		
Manufacturer	Roche Products		
Anticipated licensing information	***Confidential information removed ***		
Draft remit	To appraise the clinical and cost effectiveness of trastuzumab emtansine within its licensed indication for the treatment of locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of trastuzumab emtansine for the treatment of locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane is appropriate. It is recommended that the draft remit is amended to reflect the proposed marketing authorisation. Scoping workshop attendees considered that lapatinib in combination with capecitabine was the most widely used treatment at this point in the treatment pathway, but that capcitabine monotherapy and vinorelbine monotherapy were also relevant. Continued trastuzumab in combination with chemotherapy (either capecitabine or vinorelbine) were also added as appropriate comparators during the scoping workshop. Therefore the comparators specified for this appraisal relate to the interventions included in currently suspended technology appraisals of lapatinib and trastuzumab.		
Population size	In the appraisal of lapatinib in combination with capecitabine, it was estimated that approximately 2000 people would be suitable for treatment.		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of trastuzumab emtansine within its licensed indication for the treatment of **unresectable** locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane.		
Costing implications of remit change	The original costing comments identified that around 5000 women per year would have HER-2 positive locally advanced or metastatic breast cancer. It was assumed that most would not have a full response to HER-2 targeted pharmacological therapies and so be eligible for Trastuzumab emtansine. The scoping workshop change to the scope indicates that the eligible population is now those who are unresectable. It is estimated from the appraisal of lapatinib in combination with capecitabine that around 2000 people would be suitable for		

	treatment. The cost of the drug per person isn't known. From the information available, the cost impact can't 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	Vortioxetine for the treatment of moderate to severe major depressive disorder		
Topic Selection ID Number	5692	**Wave/Round**	R21
TA ID Number	583		
Manufacturer	Lundbeck and Takeda		
Anticipated licensing information	***Confidential information removed ***		
Draft remit	To appraise the clinical and cost effectiveness of vortioxetine within its licensed indication for the treatment of major depressive disorder.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of vortioxetine for the treatment of major depressive disorder is appropriate. The draft remit is considered appropriate. During the scoping workshop consultees discussed the differences between major depressive disorder and major depressive episodes. Attendees noted that, in clinical practice, people with major depressive episodes would be formally diagnosed with major depressive disorder using a validated classification system such as the DSM-IV-TR criteria. Trials included in the regulatory submission are unlikely to be sufficient to support a submission to NICE, in which vortioxetine would be appraised in the context of the treatment pathway described in NICE Clinical guideline no. 90. There are 5 on-going phase IIIb clinical trials ***Confidential information removed *** which will provide further evidence about the clinical effectiveness of vortioxetine in the context of European clinical guidelines on depression. At this point more detailed information on the likely positioning of vortioxetine will be available. However, attendees agreed that vortioxetine is unlikely to be used as a first-line treatment for major depressive disorder, because Clinical guideline no. 90 recommends selective serotonin reuptake inhibitors as the antidepressants of choice for initiating therapy.		
Population size	Depression affects 10% of the population in Britain at any one time.		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	No changes proposed		
Costing implications of remit change	The original costing comments identified that around 850,000 people have moderate to severe major depressive disorder and would be eligible for vortioxetine as a first line treatment. The scoping workshop has identified that the topic would be		

	appraised in the context of the treatment pathway in NICE Clinical guideline 90 and that it is unlikely that this technology would be used as a first line treatment. The population is unknown at this stage, but would be less than the 850,000 first identified. From the information currently available, the cost impact cannot accurately be estimated but as there is a potential large population, there is potential for the topic 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.