ITEM 5

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 24 and Batch 25 draft remits and draft scopes and Summary of comments and discussions at scoping workshops

	Batch 24 topics
5.1	Ocriplasmin for first line treatment of symptomatic vitreomacular adhesion
	Batch 25 topics
5.2	Vintafolide in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate- receptor-positive, platinum-resistant ovarian cancer
5.3	Rituximab in combination with corticosteroids for the treatment of anti-neutrophil cytoplasmic antibody-associated vasculitis
5.4	Ranibizumab for the treatment of choroidal neovascularisation associated with pathological myopia
5.5	Everolimus for the prevention of organ rejection in allogeneic liver transplantation
5.6	Masitinib for the treatment of advanced or metastatic pancreatic cancer

Provisional Title	Ocriplasmin for first line treatment of symptomatic vitreomacular adhesion
Topic Selection ID Number	4715
TA ID Number	544
Wave/Round	R21
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of ocriplasmin within its licensed indication for the first-line treatment of symptomatic vitreomacular adhesion.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ocriplasmin for first line treatment of symptomatic vitreomacular adhesion is appropriate. The proposed remit should be amended to include the specification of stage I or II macular holes with a diameter ≤400µm, in line with the proposed marketing authorisation as suggested by scoping workshop attendees. In addition, attendees agreed to remove 'first-line' from the scope to ensure that ocriplasmin was appraised at any stage deemed clinically appropriate consistent with its marketing authoraisation. However, ahead of the DP4 meeting, the manufacture informed NICE of the change in the proposed licensed indication with symptomatic vitreomacular adhesion (sVMA) being replaced by vitreomacular traction (VMT) as above, and so references to sVMA should be amended to VMT.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of ocriplasmin within its licensed indication for the **~~first-line~~** treatment of **~~symptomatic~~** vitreomacular **~~adhesion~~ traction including stage I or II macular holes with a diameter ≤400µm**.
Costing implications of remit change	The changes in remit concerning the stage and diameter of macular holes requires a change in the costing comments. Revised comments are seen below: ——————————————— The incidence of sVMA in England is not known. The main comparator is vitrectomy surgery; there were 16400 vitrectomies in 2009-10 which cost in the region of £1,600 to

	£2,200 (PbR tariff for cat 3 and 4 Vitreous Retinal Procedures). Only a portion of these will be for people with macular holes with a diameter ≤400µm or with epiretinal membrane (ERM), however this proportion cannot currently be estimated, and not all these people would necessarily have vitrectomy as a treatment option. As a less invasive treatment than surgery, ocriplasmin may be used for patients for whom surgery is not an option or earlier before the disease progresses to the stage where surgery is normally considered. The forecast number of people receiving the technology cannot be estimated from data currently available. The cost of ocriplasmin for this indication is not known. It is to be administered by intravitreal injection and so there could be associated administration costs. Where it replaces surgery then there will be offsetting savings.
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 not be possible.

Provisional Title	Vintafolide in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate- receptor-positive, platinum-resistant ovarian cancer
Topic Selection ID Number	5957
Wave/Round	Round 22
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of EC145 within its licensed indication in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate-receptor-positive, platinum-resistant ovarian cancer.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of vintafolide for the treatment of folate receptor positive, platinum resistant ovarian cancer is appropriate. No changes to the draft remit have been proposed, except to change the technology name to vintafolide. The title of the appraisal has also been updated with the correct technology name. Vintafolide has a companion diagnostic (EC20) that is required to establish folate receptor status. The companion diagnostic includes an IV folic acid infusion and a SPECT scan. EC20 cannot distinguish between different types of folate receptors. The manufacturer has confirmed that it is likely the use of the EC20 companion diagnostic will be stipulated in the marketing authorisation for vintafolide. A regulatory application for this diagnostic test is pending. Clinicians confirmed that although SPECT imaging is not currently used in the treatment of ovarian cancer, it should be feasible to implement folate receptor testing using EC20 and SPECT imaging in the NHS. *CONFIDENTIAL* (information removed) In 2008, approximately 6,000 women were diagnosed with ovarian cancer in England and Wales and of these, 4,500 were in the advanced stage. There is a shortage of pegylated liposomal doxorubicin hydrochloride (PLDH) in the NHS due to manufacturing issues. This supply shortage has also affected the timeliness of the ongoing phase III trials for vintafolide. The MHRA have written to clinicians suggesting that no new patients should be started on PLDH until the manufacturing issues are resolved (noting that this issue is unlikely to be resolved this year). As a temporary measure, some patients are receiving LDH (unpegylated formulation) but clinicians at the workshop have confirmed that patients will be switched to PLDH when supplies increase again.
Process (MTA/STA)	STA

Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of **vintafolide** within its licensed indication in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate-receptor-positive, platinum-resistant ovarian cancer.
Costing implications of remit change	No changes to the costing comments are required other than to change the name of the technology. Updated comments reflecting this name change are seen below. _____ In 2009 around 5514 people were diagnosed with ovarian cancer in England, of whom around 85% (4700) overexpress the folate receptor (positive). Of these approximately 70% (3300) do not respond to initial treatment. The cost of vintafolide will be incremental as it is an add-on therapy. The briefing note states that a companion diagnostic (EC20) has also been developed and will be performed together with administration of the drug. Neither the cost for this indication nor diagnostic test is known. All the cost will be incremental as it is an add-on therapy. The topic would be high cost if the incremental cost per person is around £4500. It is considered that this topic may 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	Rituximab in combination with corticosteroids for the treatment of anti-neutrophil cytoplasmic antibody-associated vasculitis
Topic Selection ID Number	5921
Wave/Round	Round 22
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of rituximab in combination with corticosteroids within its licensed indication for the treatment of anti-neutrophil cytoplasmic antibody-associated vasculitis.
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of rituximab in combination with corticosteroids for the treatment of anti-neutrophil cytoplasmic antibody-associated vasculitis is appropriate. Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is an umbrella term for several related conditions, including microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA; Wegener's granulomatosis). The annual incidence of MPA and GPA is estimated to range from 600-1200 patients in England and Wales. The clinical trials were not restricted to adults (participants were aged 15 years and over); therefore the population in the scope has been amended to include 'people' rather than 'adults'. The position of rituximab in the treatment pathway is unlikely to be specified in the marketing authorisation. The treatment pathway for ANCA-associated vasculitis is complex, with the core three stages being induction of remission, maintenance therapy, and treatment of relapse. The evidence for rituximab is strongest in the induction phase, although there is an ongoing trial examining rituximab for maintenance therapy.
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 an anticipated date of the marketing authorisation of *CONFIDENTIAL* is the latest date and the expected referral date of this topic, issuing timely guidance for this technology will be possible. If marketing authorisation is granted in *CONFIDENTIAL*, issuing timely guidance for this topic will not be possible.

Provisional Title	Ranibizumab for the treatment of choroidal neovascularisation associated with pathological myopia
Topic Selection ID Number	5510
Wave/Round	Round 19
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of ranibizumab within its licensed indication for the treatment of choroidal neovascularisation associated with pathological myopia
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of ranibizumab for the treatment of choroidal neovascularisation associated with pathological myopia is appropriate. No changes to the draft remit or scope were proposed. Approximately 200,000 people have pathological myopia in the UK. The prevalence of choroidal neovascularisation (CNV) in people with pathological myopia is likely to be less than 10% (data are lacking). Bevacizumab is included as a comparator in the scope because consultees confirmed that it is used in some centres in the UK.
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	Everolimus for the prevention of organ rejection in allogeneic liver transplantation
Topic Selection ID Number	4947
Wave/Round	Wave 27
Anticipated licensing information	*CONFIDENTIAL*
Draft remit	To appraise the clinical and cost effectiveness of everolimus within its licensed indication for the prevention of organ rejection in allogeneic liver transplantation.
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 prevention of organ rejection in allogeneic liver transplantation is appropriate. The draft remit is appropriate and is in line with the anticipated marketing authorisation. Stakeholders considered that an appraisal of everolimus would be worthwhile given the complexity surrounding the available treatment protocols for the prevention of organ rejection in allogeneic liver transplantation and the paucity of NICE guidance in this area. Stakeholders anticipate that everolimus will be licensed for use as a triple therapy and will be used in clinical practice initially after transplant and in the longer term as a maintenance treatment. They emphasised that everolimus would be most useful in helping patients switch to a calcineurin inhibitor (CNI)-free regimen (to reduce treatment-related adverse events associated with CNIs such as nephrotoxicity and preserve renal function). There are approximately 600 liver transplant recipients annually in the UK.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	No changes to the costing comments are required. The inclusion of 'locally advanced' does not affect the costing comments as they already included this population. _____ 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	Masitinib for the treatment of advanced or metastatic pancreatic cancer
Topic Selection ID Number	5952
Wave/Round	Round 22
Anticipated licensing information	Expected marketing authorisation wording: The manufacturer has not yet provided the anticipated wording of the UK marketing authorisation. Based on clinical trial design, the anticipated indication is likely to be for the treatment of patients with locally advanced or metastatic adenocarcinoma of the pancreas that has not previously been treated with chemotherapy. *CONFIDENTIAL* (information removed)
Draft remit	To appraise the clinical and cost effectiveness of masitinib within its licensed indication for the treatment of advanced or metastatic pancreatic cancer
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of masitinib for the treatment of advanced or metastatic pancreatic cancer is appropriate. The proposed remit should be changed for greater clinical accuracy to: "To appraise the clinical and cost effectiveness of masitinib within its licensed indication for the treatment of locally advanced or metastatic pancreatic cancer". Because masitinib has been developed to treat adenocarcinoma of the pancreas, consultees considered that the population should be amended to reflect this, rather than using the broader term 'pancreatic cancer', which would include tumours of other pathologies. The population in the scope has been amended to "adults with locally advanced or metastatic adenocarcinoma of the pancreas that has not been previously treated with chemotherapy". Another drug, nimotuzumab (Theraloc, Oncoscience AG), is being developed for the first-line treatment of locally advanced or metastatic pancreatic cancer that is also in the scoping process (Batch 27). Given the current uncertainty around regulatory timings for the two technologies, consultees considered that the STA process would be preferable to ensure the timely appraisal of masitinib.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of masitinib within its licensed indication for the treatment of **locally** advanced or metastatic pancreatic cancer.

Costing implications of remit change	A change is required to the costing comments to reflect a potential change to the population. Updated comments are seen below. In 2009 around 6800 people were diagnosed with pancreatic cancer in England, of whom around 85% (5800) had locally advanced or metastatic stage disease. This group would be eligible to receive masitinib. The block scoping stage has highlighted that the manufacturer has identified a 'genetic fingerprint' that would indicate those people who would respond to the technology. If this is stipulated in the marketing authorization, the eligible population will be lower. Masitinib is a treatment option and is administered orally in combination with gemcitabine intravenous infusion which is an existing therapy for the condition. The cost of masitinib is unknown but if the incremental cost of the treatment exceeds £2,600 per patient then this topic has the potential to be high cost. There may be some offsetting costs from drug administration costs as other combination therapies are given via an injection or infusion. As there are several unknowns at this stage, the cost impact cannot be estimated however, it is considered that this topic may 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 as an STA will be possible. Issuing timely guidance for this technology as an MTA will not be possible