ITEM 5

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 28 draft remits and draft scopes and Summary of comments and discussions at scoping workshops

5.1	Nimotuzumab for the first-line treatment of locally advanced and/or metastatic pancreatic cancer
5.2	Masitinib for the treatment of unresectable or metastatic gastrointestinal stromal tumours after treatment with imatinib
5.3	Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism
5.4	Regorafenib for the treatment of metastatic colorectal cancer following prior treatment for metastatic disease

Provisional Title	Nimotuzumab for the first-line treatment of locally advanced and/or metastatic pancreatic cancer		
Topic Selection ID Number	5201	**Wave/Round**	W28
TA ID Number	513		
Manufacturer	Oncoscience AG		
Anticipated licensing information	**CONFIDENTIAL**		
Draft remit	To appraise the clinical and cost effectiveness of nimotuzumab within its licensed indication for the first-line treatment of locally advanced and/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 nimotuzumab for the first-line treatment of locally advanced or metastatic pancreatic cancer is appropriate. Locally advanced and metastatic pancreatic cancers are mutually exclusive disease stages, they do not overlap, therefore the remit should reflect this. In accordance with the recommended wording changes to the proposed remit, the population should be "Adults with locally advanced or metastatic pancreatic cancer not previously treated with chemotherapy.		
Population size	The estimated incident population is over 8,000 people. 95% will be adenocarcinomas, and only 10-20% will be suitable for surgery at diagnosis (current NICE guidance for gemcitabine states that gemcitabine is not recommended for patients who are suitable for potentially curative surgery; the clinical trial for nimotuzumab excludes those whose cancers were not amenable to curative radiotherapy or surgery). This gives a potential population size of between 6000 and 7000. **CONFIDENTIAL**		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of nimotuzumab within its licensed indication for the first-line treatment of locally advanced **or** metastatic pancreatic cancer		
Costing implications of remit change	No change to costing comments. Note: The costing comments estimate the population as around 5400 people. The 'population size' field above includes population data but doesn't give a final estimate of eligible population. It looks like it may be fewer than 5400 though and could therefore be contradictory.		
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 unresectable or metastatic gastrointestinal stromal tumours after treatment with imatinib		
Topic Selection ID Number	6166	**Wave/Round**	R31
TA ID Number	622		
Manufacturer	AB Science		
Licensing information	**CONFIDENTIAL**		
Draft remit	To appraise the clinical and cost effectiveness of masitinib within its licensed indication for the treatment of unresectable or metastatic gastrointestinal stromal tumours after progression with imatinib.		
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 unresectable or metastatic gastrointestinal stromal tumours after treatment with imatinib is appropriate. The scoping workshop attendees discussed whether sunitinib was an appropriate comparator and if any additional comparators had been identified. A consensus was reached that sunitinib is the sole appropriate comparator. Consultees suggested that time to treatment failure could be considered a 'harder' endpoint than progression-free survival because progression-free survival is difficult to define. It was agreed that time to treatment failure should be considered as an additional outcome. The attendees noted the strong evidence linking to tumour mutational status with responsiveness to tyrosine kinase inhibitors for genes such as PDGF-alpha and c-Kit (exons 11, 9 and others). The manufacturer confirmed that they would be conducting retrospective analyses for c-Kit exons 9 and 11, and other mutations. The draft scope has been amended to include subgroups according to the genetic mutational status of the tumour (such as exon 11 and exon 9 c-Kit mutations).		
Population size	Around 750–800 people in England and Wales are diagnosed with GIST each year, with an estimated 500 people in the UK experiencing recurrence annually (based on clinical specialist opinion at the scoping workshop). Virtually all people with unresectable or metastatic disease will experience disease progression following first-line treatment with a tyrosine kinase inhibitor. The population is relatively small, but is the same population as that for the published NICE technology appraisal TA179 'Sunitinib for the treatment of gastrointestinal stromal tumours'		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	n/a		
Costing	Due to a change to the draft scope to include genetic		

implications of remit change	subgroups, the costing comments are revised. "Approximately 800 people are diagnosed with gastrointestinal stromal tumours (GISTs) each year in England. Approximately 300 people per year have metastatic and/or unresectable GISTs. It is estimated that around two thirds (200) develop resistance to imatinib or progress following treatment. The scope may include subgroups according to genetic mutational status. It is not known what proportion of people this would be and would therefore be eligible for second line treatment with masitinib. Masitinib is an additional treatment option alongside other drugs and its cost is not yet known. It would represent an incremental cost only if the treatment costs exceed that of sunitinib it is intended to replace. Because of the small size of the eligible population and that the technology is an option, it is anticipated that this topic may be low cost". *Note:* *The costing comments estimate the population as around 200 people that is then reduced due to the genetic mutational status. The 200 figure is contrary to the 'population size' field above.*
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	Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism		
Topic Selection ID Number	4646	**Wave/Round**	W26
TA ID Number	483		
Manufacturer	Boehringer Ingelheim		
Anticipated licensing information	**CONFIDENTIAL**		
Draft remit	To appraise the clinical and cost effectiveness of dabigatran etexilate within its licensed indication for the treatment and secondary prevention of symptomatic venous thromboembolism.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of dabigatran etexilate for venous thromboembolism (VTE) is appropriate. It was agreed that the word symptomatic should be removed from the remit in order to reflect the potential marketing authorisation for the licence extension. It was agreed that the suggested wording of treatment and secondary prevention of DVT and/or PE was clearer and would be in line with the anticipated marketing authorisation. Comparators: Despite a suggestion to separate the comparators for the treatment of VTE (DVT or PE) and for secondary prevention of VTE (DVT or PE) this would not reflect clinical practice. Consultees suggested that it was appropriate to list fondaparinux alongside initial treatment with low molecular weight heparin rather than as a separate comparator. Outcomes: Consultees agreed that it is important to specify two adverse events within the outcomes, considering the impact that these have on mortality, morbidity as well as the potential impact on the cost effectiveness of dabigatran. These are intracranial bleeding and gastrointestinal bleeding. Subgroups: The Consultees noted that people with DVT and PE have very different prognoses. The manufacturer explained that the trials included people with DVT and/or PE and it would be possible to stratify the results to show differences between the two populations.		
Process (MTA/STA)	STA A question was asked at consultation of whether the combination of acute treatment of VTE and secondary prevention should be considered as a single STA, as an MTA, or be split into two separate STAs. The manufacturer confirmed that there would be one economic model which would separate out the treatment and secondary prevention of VTE and that it planned on making one submission to NICE for both indications (treatment and secondary prevention).		

Population size	Population for TA261 (Rivaroxaban for treatment of DVT and prevention of recurrent DVT and PE in adults) calculated to be 100,000. The licence extension for treatment of PE is currently under appraisal.
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of dabigatran etexilate within its licensed indication for the treatment and secondary prevention of **deep vein thrombosis and/or pulmonary embolism**. Remove the word '**symptomatic**' from the remit
Costing implications of remit change	Changes to drug costs since original costing comments were drafted result in new comments being necessary. "It is estimated that annual cost of dabigatran etexilate is around £1800 per person per year based on list price. The incremental cost of the drug over that of a vitamin K antagonist is around £1400 per person per year. Recurrence of VTE occurs in around 25,000 people each year. If around 40% of people switched, this topic may be high cost. However, there may be local procurement discounts on the drug price that would increase the number who switch 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.

Provisional Title	Regorafenib for the treatment of metastatic colorectal cancer following prior treatment for metastatic disease		
Topic Selection ID Number	5464	**Wave/Round**	R20
TA ID Number	593		
Manufacturer	Bayer		
Anticipated licensing information	**CONFIDENTIAL**		
Draft remit	To appraise the clinical and cost effectiveness of regorafenib within its licensed indication for the treatment of metastatic colorectal cancer that has progressed following prior treatment for metastatic disease.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of regorafenib for the treatment of metastatic colorectal cancer following prior treatment for metastatic disease is appropriate. The marketing authorisation wording may define the population more narrowly than is currently the case in the PICO table. However, the uncertainty regarding the final wording of the MA was noted, and it was decided to keep the population, and the remit, broad at this stage. Attendees at the scoping workshop discussed the innovative nature of regorafenib. Patient representatives considered that regorafenib constitutes a step-change in the management of the condition given the high value patients place on life extension at this stage in therapy and the potential survival benefit that regorafenib could bring about. Clinicians also agreed with the patient representative that regorafenib is a promising drug for a group of patients who currently have limited treatment options.		
Population size	There are around 20,500 metastatic colorectal cancer cases in 2009 in the UK		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	n/a		
Costing implications of remit change	No change to costing comments.		
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.		