NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

MABp1 for previously treated metastatic colorectal cancer

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of MABp1within its marketing authorisation for treating metastatic or unresectable colorectal cancer after oxaliplatin and irinotecan based regimens.

Background

Colorectal cancer is a malignant tumour arising from the lining of the large intestine (colon and rectum). Metastatic colorectal cancer refers to disease that has spread beyond the large intestine and nearby lymph nodes. This type of cancer most often spreads first to the liver, but metastases may also occur in other parts of the body including the lungs, brain and bones.

In 2012, there were 34,322 people diagnosed with colorectal cancer[i] and 13,236 deaths[ii]. Between 10% and 25% of people with colorectal cancer have metastatic disease when first diagnosed[iii,iv], and approximately 50% of people who have surgery for early stage disease will eventually develop metastases[v]. The overall 5 year survival rate for metastatic colorectal cancer is around 7%[vi].

Treatment of metastatic colorectal cancer may involve a combination of surgery, chemotherapy, radiotherapy and supportive care. When possible, surgical removal (resection) or destruction of the primary tumour and metastases may be considered. For people with metastases only in their livers, complete resection appears to offer the best chance of long-term survival, providing 5 year survival rates ranging from 25% to 44%.

Treatment for metastatic colorectal cancer aims to prolong survival, improve quality of life and/or make the primary tumour or metastases suitable for resection. Chemotherapy options include: folinic acid plus fluorouracil plus oxaliplatin (FOLFOX), folinic acid plus fluorouracil plus irinotecan (FOLFIRI), capecitabine plus oxaliplatin (XELOX), single-agent irinotecan, capecitabine or tegafur with uracil (in combination with folinic acid) (NICE clinical guideline 131). Chemotherapy may be combined with biological agents such as EGFR inhibitors (cetuximab or panitumumab) and VEGF inhibitors (bevacizumab). If standard therapies are unsuccessful, not tolerated or contraindicated, people are treated with supportive care to manage the symptoms and complications of the condition.

The technology

MABp1(Xilonix, Xbiotech) is a true human monoclonal antibody targeting anti-interleukin-1-alpha (IL-1α). MABp1 targets an inflammatory cytokine that is essential for tumour growth and spread, and is responsible for symptoms commonly observed in advanced cancer, such as weight loss, fatigue, and appetite loss.

MABp1 does not currently have a marketing authorisation in the UK for treating metastatic or unresectable colorectal cancer. It is being studied in clinical trials in combination with best supportive care compared with placebo in combination with best supportive care in people with colorectal cancer which is metastatic and which is refractory to standard therapy.

Intervention(s)	MABp1 in combination with best supportive care
Population(s)	Adults with metastatic colorectal cancer whose disease has progressed following treatment with oxaliplatin and irinotecan based regimens
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.

Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy' (2014). NICE Technology Appraisal No. 307. Review date August 2016. 'Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy (review of TA150 and part review of TA118)' (2012). NICE Technology Appraisal No. 242. Guidance on static list. 'Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer' (2010). NICE Technology Appraisal No. 212. Guidance on static list. 'Cetuximab for the first-line treatment of metastatic colorectal cancer' (2009). NICE Technology Appraisal No. 176. Currently under review [ID794]. 'Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer' (2007). Technology Appraisal No. 118. Guidance on static list. Partially reviewed as part of TA242. Terminated appraisals 'Regorafenib for metastatic colorectal cancer after treatment for metastatic disease' (terminated appraisal) (2015). NICE Technology Appraisal No. 334. 'Panitumumab in combination with chemotherapy for the treatment of metastatic colorectal cancer' (terminated appraisal) (2011). NICE Technology Appraisal No. 240. Currently under review [ID794]. Appraisals in development 'Colorectal cancer (metastatic) - cetuximab (review TA176) and panitumumab (part review TA240) (1st line)'. NICE technology appraisals guidance [ID794]. Publication expected April 2016. Proposed Appraisals 'Ramucirumab in combination with FOLFIRI for treating metastatic colorectal cancer after progression with bevacizumab, oxaliplatin and fluoropyrimidine'. Proposed NICE technology appraisal [ID867]. Publication date to be confirmed.

	Related Guidelines: 'The diagnosis and management of colorectal cancer' (2011, partially updated December 2014). NICE Clinical Guideline No. 131. Review date to be confirmed. Related Interventional Procedures: 'Selective internal radiation therapy for non-resectable colorectal metastases in the liver' (2011). Interventional Procedures Guidance No. 401 'Radiofrequency ablation for colorectal liver metastases' (2009) Interventional Procedures Guidance No. 327. 'Preoperative high dose rate brachytherapy for rectal cancer' (2006). Interventional Procedures Guidance No. 201. Related Quality Standards: 'Colorectal cancer (2012). Quality Standard No. 20. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: 'Colorectal cancer' (2011). NICE Pathway. http://pathways.nice.org.uk/pathways/colorectal-cancer
Related National Policy	Department of Health, 2013, NHS Outcomes Framework 2014-2015. Domains 1, 2, 4 and 5. Department of Health, 2011, Improving outcomes: a strategy for cancer Department of Health, 2009, Cancer commissioning guidance Department of Health, 2007, Cancer reform strategy NHS England, 2014, Manual for prescribed specialised services 2013/14. Chapter 10. NHS England, 2015, Cancer Drugs Fund list Public Health England, 2011, National Screening Committee policy on bowel cancer screening in adults.

Questions for consultation

Have all relevant comparators for MABp1been included in the scope?
Which treatments are considered to be established clinical practice in the NHS for metastatic or unresectable colorectal cancer following treatment with oxaliplatin and irinotecan based regimens?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom MABp1is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider MABp1will fit into the existing NICE pathway?
http://pathways.nice.org.uk/pathways/colorectal-cancer
http://pathways.nice.org.uk/

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which MABp1 will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider MABp1 to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of MABp1 can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's

Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

1. Office for National Statistics (2012) '10 most common cancers in males and females'. Accessed June 2015.
2. Cancer Research UK (2014) 'Bowel cancer mortality statistics'. Accessed June 2015.
3. Bowel Cancer UK (2014) 'Bowel cancer statistics'. Accessed June 2015.

4. Association of Coloproctology of Great Britain and Ireland (2007) 'Guidelines for the Management of Colorectal Cancer'. Accessed June 2015.

5. Garden OJ, Rees M, Poston GJ et al. (2006) Guidelines for resection of colorectal cancer liver metastases. Gut 55 (Suppl III) iii1–iii8.

6. Cancer Research UK (2014b) 'Bowel cancer survival statistics'. Accessed June 2015.