**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Fruquintinib for previously treated metastatic colorectal cancer

**Draft scope**

## Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of fruquintinib within its marketing authorisation for treating metastatic colorectal cancer.

## 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 often first spreads to the liver, but metastases may also occur in other parts of the body, including the lungs, brain and bones. Most colorectal cancers are adenocarcinomas, these start in glands that line the insides of the colon and rectum.

There are around 42,900 new cases of colorectal cancer each year in the UK, accounting for 11% of all cancers.[1] Around 4 in 10 (43%) new cases of colorectal cancer in the UK were in people aged over 75 years, but it can affect young people too[1].

Metastatic colorectal cancer treatment aims to prolong survival and improve quality of life. Treatment can involve a combination of surgery (to resect the primary tumour or the metastases), chemotherapy (to make the tumour or metastases resectable, or to manage the cancer), biological therapy, and radiotherapy. For people with untreated metastatic colorectal cancer:

- NICE technology appraisal 61 recommends intravenous fluorouracil/folinic acid (5-FU/FA) or capecitabine.
- NICE guideline 151 recommends either folinic acid plus fluorouracil plus oxaliplatin (FOLFOX) or capecitabine plus oxaliplatin (CAPOX).
- NICE technology appraisal 439 recommends cetuximab for people with EGFR-expressing, RAS wild-type metastatic disease, and panitumumab for people with RAS wild-type metastatic disease.
- NICE technology appraisal 709 recommends pembrolizumab for people with high microsatellite instability or mismatch repair deficiency.

For people with previously treated metastatic colorectal cancer:

- NICE guideline 151 recommends folinic acid plus fluorouracil plus irinotecan (FOLFIRI), after either FOLFOX or CAPOX, or single-agent irinotecan (after FOLFOX) or raltitrexed (for patients with advanced colorectal cancer who are intolerant to 5-FU/FA, or for whom these drugs are not suitable).
- NICE technology appraisal 405 recommends trifluridine–tipiracil, and NICE technology appraisal 866 recommends regorafenib, if fluoropyrimidine-, oxaliplatin- or irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-EGFR agents have failed or when these therapies are not suitable.

- NICE technology appraisal TA716 recommends nivolumab with ipilimumab as a treatment for those with high microsatellite instability or mismatch repair deficiency after fluoropyrimidine-based combination chemotherapy.
- NICE technology appraisal TA668 recommends encorafenib plus cetuximab as a treatment option for those with BRAF V600E mutation-positive metastatic colorectal cancer who have had previous systemic treatment.

If standard therapies are unsuccessful, not tolerated or contraindicated, people are treated with best supportive care to manage the symptoms and complications of the condition.

**The technology**

Fruquintinib (Fruzagla, Takeda) does not currently have a marketing authorisation in the UK for the treatment of adults with metastatic colorectal cancer. It is being studied in clinical trials compared with best supportive care in adults with advanced, metastatic colorectal cancer who had progressed after second line or above standard chemotherapy and people with refractory metastatic colorectal cancer who have progressed on, or were intolerant to chemotherapy, anti-VEGF and anti-EGFR biologics, and TAS-102 (trifluridine-tipiracil) or regorafenib.

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| **Intervention(s)** | Fruquintinib |
| **Population(s)** | People with metastatic colorectal cancer (mCRC) who have had two or more previous treatments |
| **Comparators** | • Trifluridine-tipiracil monotherapy<br>• Regorafenib<br>• Nivolumab with ipilimumab (where high microsatellite instability or mismatch repair deficiency is present)<br>• Encorafenib plus cetuximab for people with BRAF V600E mutation-positive metastatic colorectal cancer<br>• Best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<br>• adverse effects of treatment<br>• health-related quality of life |

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| **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.<br><br>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. |
| **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. |

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| **Related NICE recommendations** | **Related Technology Appraisals:**<br>'Regorafenib for previously treated metastatic colorectal cancer' (2023). NICE technology appraisal 866.<br>'Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency' (2021). NICE Technology Appraisal 716.<br>'Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency' (2021). NICE Technology Appraisal 709.<br>'Encorafenib plus cetuximab for previously treated BRAF V600E mutation-positive metastatic colorectal cancer' (2021). NICE Technology Appraisal 668.<br>'Cetuximab and panitumumab for previously untreated metastatic colorectal cancer' (2017). NICE Technology Appraisal 439.<br>'Trifluridine–tipiracil for previously treated metastatic colorectal cancer' (2016). NICE Technology Appraisal 405.<br>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 307.<br>'Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy: Cetuximab (monotherapy or combination chemotherapy), bevacizumab (in combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy' (2012). NICE Technology Appraisal 242.<br>'Laparoscopic surgery for colorectal cancer' (2006). NICE Technology Appraisal 105.<br>'Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer' (2003). NICE Technology Appraisal 61.<br>**Related appraisals in development (including suspended appraisals):**<br>'Trifluridine–tipiracil with bevacizumab for treating metastatic colorectal cancer after 2 systemic treatments'. NICE technology appraisals guidance (ID6298). In development.<br>'Tucatinib with trastuzumab for previously treated HER2-positive colorectal cancer'. NICE technology appraisals guidance (ID6227). In development.<br>'Pembrolizumab with lenvatinib for previously treated metastatic colorectal cancer'. NICE technology appraisals guidance (ID5112). Appraisal suspended. |

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| | 'Nivolumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency'. NICE technology appraisals guidance (ID1136). Appraisal suspended.<br>**Related Guidelines:**<br>'Colorectal cancer' (2021). NICE guideline 151.<br>'ColonFlag for identifying people at risk of colorectal cancer' (2018). Medtech innovation briefing 142.<br>'Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care' (2017). Diagnostics guidance 30.<br>'Virtual chromoendoscopy to assess colorectal polyps during colonoscopy' (2017). Diagnostics guidance 28.<br>'Colorectal cancer prevention: colonoscopic surveillance in adults with ulcerative colitis, Crohn's disease or adenomas' (2011). Clinical guideline 118.<br>**Related Interventional Procedures:**<br>'Selective internal radiation therapy for unresectable colorectal metastases in the liver' (2020). NICE interventional procedures guidance 672.<br>'Radiofrequency ablation for colorectal liver metastases' (2009). NICE interventional procedures guidance 327<br>**Related Quality Standards:**<br>'Colorectal cancer' (2022). NICE quality standard 20.<br>'Suspected Cancer' (2017) NICE Quality Standard 124 |
| **Related National Policy** | The NHS Long Term Plan (2019) NHS Long Term Plan<br>NHS England (2018) NHS manual for prescribed specialist services (2018/2019) |

**Questions for consultation**

Where do you consider fruquintinib will fit into the existing care pathway for metastatic colorectal cancer?

Which treatments do you consider to be the comparators of fruquintinib?

Would fruquintinib be used as an alternative treatment option to nivolumab with ipilimumab for people with high microsatellite instability or where high mismatch repair is present?

Would fruquintinib be used as an alternative treatment option to encorafenib plus cetuximab for people with BRAF V600E mutation-positive metastatic colorectal cancer?

When would best supportive care be used in the treatment of metastatic colorectal cancer?

Would fruquintinib be a candidate for managed access?

Do you consider that the use of fruquintinib can result in any potential 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 committee to take account of these benefits.

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 fruquintinib 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

However, please state if you consider that there is potential for using the cost comparison process for this technology. Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?

- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

**References**

1. Cancer Research UK, Bowel cancer statistics. Accessed September 2023.