NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Atezolizumab with chemotherapy for adjuvant treatment of stage 3 colorectal cancer with high microsatellite instability or mismatch repair deficiency ID6646

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for stage 3 colorectal cancer with high microsatellite instability or mismatch repair deficiency.

Background

Colorectal cancer is a malignant tumour arising from the lining of the large intestine (colon and rectum). Stage 3 colorectal cancer refers to disease that has spread beyond the large intestine to nearby lymph nodes but has not spread to distant parts of the body. Most colorectal cancers are adenocarcinomas. These start in glands that line the insides of the colon and rectum.

Around 46,600 new cases of colorectal cancer were reported in the UK per year between 2018-2019, accounting for 12% 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].

Mismatch repair (MMR) is a process where cells of the body recognise and repair nucleotide mismatches or insertion of excess DNA during replication of the DNA as cells divide. Deficiencies in MMR (dMMR) are associated with the accumulation of mutations in simple repetitive DNA sequences known as microsatellites; this is known as microsatellite instability (MSI)[2].A high frequency of these alterations is classified as an MSI high (MSI-H) phenotype. If the instability occurs in regions of the genome associated with apoptosis (programmed cell death) and cell growth, it can result in the development of tumours. Approximately 9-12% of stage 3 colorectal cancers are categorised as dMMR or MSI-H [3,4].

NICE diagnostics guidance (DG27) recommends testing all people diagnosed with colorectal cancer for mismatch repair proteins or microsatellite instability.

Stage 3 colorectal cancer treatment aims to prolong survival and improve quality of life. The type of treatment depends on whether the cancer started in the colon or the rectum [5]. Treatment can involve a combination of surgery (to resect the primary tumour) and chemotherapy (to make the tumour resectable, or to manage the

cancer), biological therapy, and radiotherapy. Adjuvant therapy is additional treatment given after the primary treatment to lower the risk of the cancer recurring.

NICE clinical guideline 151 recommends capecitabine in combination with Oxaliplatin (CAPOX) for people with stage 3 rectal cancer after radiotherapy or no previous treatment before surgery. If this is not suitable, either oxaliplatin in combination with 5-fluorouracil and folinic acid (FOLFOX) or a single agent fluoropyramidine such as capecitabine is recommended. NICE TA100 recommends capecitabine with oxaloplatin in the adjuvant treatment of stage 3 (Duke's C) colon cancer.

There are currently no NICE recommended biologic therapies for adjuvant treatment of stage 3 colorectal cancer.

The technology

Atezolizumab (Tecentriq, Roche) does not currently have a marketing authorisation for the treatment of stage 3 colorectal cancer with high microsatellite instability or mismatch repair deficiency. It has been studied in phase 2 and 3 clinical trials as monotherapy or in combination with chemotherapy in people with MSI-high or dMMR stage 3 colorectal cancer.

Intervention(s)	Atezolizumab with chemotherapy followed by atezolizumab monotherapy
Population(s)	People with stage 3 colorectal cancer with high microsatellite instability or mismatch repair deficiency
Comparators	Established clinical management without atezolizumab, including: • Capecitabine plus oxaliplatin (CAPOX) • Folinic acid plus fluorouracil plus oxaliplatin (FOLFOX) • Capecitabine
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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. 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.
Related NICE recommendations	**Related NICE guidelines:** Colorectal cancer (2020) NICE Guideline NG151 **Related quality standards:** Related quality standards: Colorectal cancer (2012) NICE Quality Standard QS20

Questions for consultation

Where do you consider will fit into the existing care pathway for stage 3 colorectal cancer with high MSI/dMMR?

Would real-world evidence (RWE) add value to the evaluation of this technology? If so, which aspects of the evaluation would RWE be particularly helpful? (For example: comparator use in practice, long-term outcomes)

Please select from the following, will atezolizumab be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would atezolizumab be a candidate for managed access?

Do you consider that the use of atezolizumab 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.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

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 atezolizumab 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).

References

1. Cancer Research UK, Bowel cancer statistics. Accessed March 2026

2. Lorenzi, M et al. Epidemiology of Microsatellite Instability High (MSI-H) and Deficient Mismatch Repair (dMMR) in Solid Tumours: A Structured Literature Review. Journal of Oncology (2020) Accessed March 2026

3.Cohen R et al.Microsatellite Instability in Patients With Stage III Colon Cancer Receiving Fluoropyrimidine With or Without Oxaliplatin: An ACCENT Pooled Analysis of 12 Adjuvant Trials. Journal of oncology (2020) 20;39(6):642-651.doi: 10.1200/JCO.20.01600. Accessed April 2026

4. Mulet-Margalef N et al. Challenges and Therapeutic Opportunities in the dMMR/MSI-H Colorectal Cancer Landscape. Cancers (Basel). 2023 Feb 6;15(4):1022. doi: 10.3390/cancers15041022. Accessed April 2026

5. Cancer Research UK, Treatment options for colon cancer. Accessed March 2026