

Putting NICE guidance into practice

Resource impact report: Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency (TA709)

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Summary

NICE has recommended [pembrolizumab](#) as an option for untreated metastatic colorectal cancer with high microsatellite instability (MSI) or mismatch repair deficiency (MMR) in adults only if pembrolizumab is stopped after 2 years and no documented disease progression, and the company provides pembrolizumab according to the commercial arrangement.

We estimate that:

- 465 people with untreated metastatic colorectal cancer with high MSI or MMR deficiency are eligible for treatment with pembrolizumab each year
- 310 people will start treatment with pembrolizumab from year 2022/23 onwards once uptake has reached 67%.
- Some people will go on to receive second year treatment with pembrolizumab each year from 2022/23 onwards. Because there is no data on treatment discontinuations, the number of people should be estimated at a local level and input into the [resource impact template](#).

Table 1 Estimated number of people in England having pembrolizumab

	2021/22	2022/23	2023/24	2024/25	2025/26
Uptake rate for pembrolizumab (%)	35	67	67	67	67
Population starting pembrolizumab each year	160	310	310	310	310

This report is supported by a local resource impact template because the list price of pembrolizumab has a commercial arrangement (commercial access agreement) discount that is commercial in confidence. The discounted price of pembrolizumab can be put into the template and other variables may be amended.

This technology is commissioned by NHS England. Providers are NHS trust hospitals.

1 Pembrolizumab

1.1 NICE has recommended [pembrolizumab](#) as an option for treating untreated metastatic colorectal cancer with high microsatellite instability (MSI) or mismatch repair deficiency (MMR) in adults, only if:

- pembrolizumab is stopped after 2 years and no documented disease progression, and
- the company provides pembrolizumab according to the commercial arrangement.

1.2 Metastatic colorectal cancer with high MSI or MMR deficiency occurs in around 5% of metastatic colorectal cancer. It is associated with a poorer prognosis and a greater risk of death than metastatic colorectal cancer without high MSI or MMR deficiency.

1.3 There are currently no specific treatments for untreated colorectal cancer with high MSI or MMR deficiency tumours. People are usually offered the same treatments as the wider metastatic colorectal cancer population, that is, combination chemotherapy including FOLFOX and FOLFIRI or CAPOX. For RAS wild-type cancer, cetuximab or panitumumab is added to FOLFOX or FOLFIRI.

1.4 Pembrolizumab is the first colorectal cancer treatment specific for people with untreated metastatic high MSI or MMR deficiency colorectal cancer at first line.

1.5 As part of the NHS response to Covid-19, NHS England is already commissioning pembrolizumab for people with high MSI or MMR deficiency colorectal cancer.

2 Resource impact of the guidance

2.1 We estimate that:

- 465 people with untreated metastatic colorectal cancer with high MSI or MMR deficiency are eligible for treatment with pembrolizumab each year
- 310 people will start treatment with pembrolizumab from year 2022/23 onwards once uptake has reached 67%.
- Some people will go on to receive second year treatment with pembrolizumab each year from 2022/23 onwards. Because there is no data on treatment discontinuations, the number of people should be estimated at a local level and input into the [resource impact template](#). See section 4.4.

2.2 The current treatment and future uptake figure assumptions are based on NHS England clinical expert opinion and company submission and are shown in the resource impact template. Table 2 shows the number of people in England who are estimated to start pembrolizumab by financial year.

Table 2 Estimated number of people having pembrolizumab using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
Uptake rate for pembrolizumab (%)	35	67	67	67	67
Population starting pembrolizumab each year	160	310	310	310	310

2.3 This report is supported by a local resource impact template. The company has a commercial arrangement (commercial access agreement). This makes pembrolizumab available to the NHS with a discount. The discounted price of pembrolizumab can be put into

the template and other variables may be amended. For enquiries about the patient access scheme contact patient.access@nhs.uk.

Savings and benefits

- 2.4 Pembrolizumab has preferable adverse effects compared with current standard of care. Experts highlight that the current treatments are highly toxic, which could lead to hospital admissions during treatment and permanent adverse effects like nerve damage.
- 2.5 Pembrolizumab is administered once every three weeks or once every six weeks. Less frequent administrations may reduce visits to hospital and make better use of clinical capacity compared with chemotherapy combination treatments.
- 2.6 Pembrolizumab could also reduce administration costs relative to the complex prolonged infusions needed for the combination chemotherapy option. Pembrolizumab is administered over 30 minutes.

3 Implications for commissioners

- 3.1 This technology is commissioned by NHS England. Providers are NHS Hospital trusts.
- 3.2 There is no additional infrastructure needed to be put in place, and there are no anticipated implementation issues.
- 3.3 Pembrolizumab falls within the programme budgeting category PB02C: Cancer, LGI.

4 How we estimated the resource impact

The population

- 4.1 In 2018, around 35,900 new cases of adults with colorectal cancer were recorded in England ([Public Health England, 2020](#)).

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4.2 The eligible population is based on the proportion of people who test positive for high MSI, or MMR deficiency as shown in table 3.

Table 3 Number of people eligible for treatment in England

Population	Proportion of previous row (%)	Number of people
Total population ¹		55,286,961
Adult population ¹		44,263,393
Incidence of colorectal cancer ²	0.81	36,000
People with metastatic colorectal cancer (mCC) ³	25.8	9,300
People with mCC with high microsatellite instability or mismatch repair deficiency and eligible for treatment with pembrolizumab ⁴	5	465
Total number of people estimated to start treatment with pembrolizumab each year from year 2022/2023 ⁴	67	310
¹ Office for National Statistics ² Public Health England, 2020 ³ National Cancer Registration and Analysis Service: Cancer breakdown by stage ⁴ NHS England clinical expert opinion		

Assumptions

4.3 The resource impact template assumes that:

- 5-fluorouracil, folinic acid, and oxaliplatin (FOLFOX), 5-fluorouracil, folinic acid and irinotecan (FOLFIRI) and oxaliplatin and capecitabine (CAPOX) are the relevant comparators for pembrolizumab in untreated high MSI and MMR deficiency metastatic colorectal cancer.
- Cetuximab or panitumumab with FOLFOX or FOLFIRI are also comparators for pembrolizumab in the treatment for RAS wild-type colorectal cancer.

- Pembrolizumab is administered once every 3 or 6 weeks for 30 minutes intravenously.
- FOLFOX, FOLFIRI and panitumumab or cetuximab with FOLFOX or FOLFIRI need to be administered as a three-day treatment, once every 2 weeks.
- The median treatment duration with pembrolizumab is 13.3 months. This is based on data from clinical trials as per the company submission.
- Treatment costs with FOLFOX, FOLFIRI, CAPOX and cetuximab or panitumumab with FOLFOX or FOLFIRI include administration cost of £319 for each treatment cycle (Healthcare resource group SB13Z: Deliver more complex parenteral chemotherapy at first and SB15Z Deliver Subsequent Elements of a Chemotherapy Cycle). Taken from [NHS national tariff 2020/21](#).
- The administration cost used for pembrolizumab is £159 per cycle (Healthcare resource group SB12Z: Deliver Simple Parenteral Chemotherapy at First Attendance). Taken from [NHS national tariff 2020/21](#).
- The recommended dosage regimen of pembrolizumab monotherapy is either 200 mg every 3 weeks or 400 mg every 6 weeks. The frequency of dosage impacts on the administration costs of pembrolizumab. The template assumes people receive 200 mg every 3 weeks for 3 months, and thereafter, 400 mg every 6 weeks. Users can amend the template in line with local practice.
- Pembrolizumab will not require additional monitoring compared with established clinical practice in England.

Other factors

4.4 The guidance recommends pembrolizumab is stopped at 2 years and no documented disease progression. Therefore, costs could be higher if more people respond to treatment and still receive

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treatment at 2 years. Users can amend the treatment duration for year 2 in the unit costs worksheet of the [resource impact template](#) to reflect local practice.

4.5 Treatment with pembrolizumab requires colorectal cancer tumours to be tested for MSI-H and dMMR. The test is already recommended by the NICE diagnostic guidance 27 [on molecular testing strategies for Lynch syndrome in people with colorectal cancer](#)

4.6 Tests are already routinely commissioned by NHS England. However, experts explained that uptake is currently low in some places. Therefore, testing will increase as it will be offered to all newly diagnosed people before starting treatment.

About this resource impact report

This resource impact report accompanies the NICE guidance on [pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency](#) and should be read with it.

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