NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency (TA716)

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Summary

NICE has recommended Nivolumab plus ipilimumab as an option for treating metastatic colorectal cancer with high microsatellite instability (MSI) or mismatch repair (MMR) deficiency after fluoropyrimidine-based combination chemotherapy.

The number of people who are eligible for treatment with nivolumab plus ipilimumab is expected to be affected by the positive recommendation in TA709 Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency because a large proportion of people in the incident population will now receive pembrolizumab as first line treatment rather than a fluoropyrimidine-based combination chemotherapy. There will be an initial prevalent population who did not receive pembrolizumab at first line and will become eligible for treatment with nivolumab plus ipilimumab.

We estimate that:

- An annual incidence of 65 people with previously treated metastatic colorectal cancer with high MSI or MMR deficiency will be eligible for treatment with nivolumab plus ipilimumab each year. Of these, 48 people will start treatment with nivolumab plus ipilimumab from year 2022/23 onwards once uptake has reached 73% (source: company submission)
- A further 325 people in the prevalent population will progress to second line treatment with 163 people assumed to start second line treatment in 2021/22 and a further 163 people assumed to start second line treatment in 2022/23. It is estimated that there will be an uptake of 37% in 2021/22 and 119 people will start treatment with nivolumab plus ipilimumab in year 2022/23 once uptake has reached 73%.

Table 1 Estimated number of people in England starting nivolumab plus ipilimumab

	2021/22	2022/23	2023/24	2024/25	2025/26
Incident population starting nivolumab plus ipilimumab each year	24	48	48	48	48
Prevalent population starting nivolumab plus ipilimumab each year	59	119	0	0	0
Total population starting nivolumab plus ipilimumab each year	**83**	**167**	**48**	**48**	**48**

This report is supported by a local resource impact template because the list prices of nivolumab and ipilimumab have a commercial arrangement (commercial access agreement) discount that is commercial in confidence. The discounted price of nivolumab and ipilimumab 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 Nivolumab plus ipilimumab

1.1 NICE has recommended nivolumab plus ipilimumab as an option for treating metastatic colorectal cancer with high microsatellite instability (MSI) or mismatch repair (MMR) deficiency after fluoropyrimidine-based combination chemotherapy, only if:

- The company provides nivolumab and ipilimumab according to the commercial arrangements.

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 People with previously treated metastatic colorectal cancer that has high MSI or MMR deficiency are usually offered combination chemotherapy including FOLFOX, FOLFIRI or trifluridine-tipiracil, and best supportive care. This guidance means that nivolumab and ipilimumab is now an option for these people.

1.4 However, NICE has recently published positive guidance in TA709 Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency. When people receive pembrolizumab at first line, they are not expected to receive nivolumab plus ipilimumab at second line. It is only people with untreated metastatic colorectal cancer that has high MSI or MMR deficiency who have fluoropyrimidine-based combination chemotherapy initially that are expected to receive nivolumab plus ipilimumab.

1.5 The uptake for pembrolizumab as a first line treatment is expected to be high and therefore only a small incident population is expected to be eligible for nivolumab plus ipilimumab each year.

There will be an initial prevalent population who did not receive pembrolizumab at first line and will therefore become eligible for treatment with nivolumab plus ipilimumab.

1.6 Clinical experts explained that treatment options for previously treated metastatic colorectal cancer depend on previous treatments, fitness level and patient and clinician preference.

2 Resource impact of the guidance

2.1 We estimate that:

An annual incidence of 65 people with previously treated metastatic colorectal cancer with high MSI or MMR deficiency will be eligible for treatment with nivolumab plus ipilimumab each year. Of these, 48 people will start treatment with nivolumab plus ipilimumab from year 2022/23 onwards once uptake has reached 73%

A further 325 people in the prevalent population will progress to second line treatment with 163 people assumed to start second line treatment in 2021/22 and a further 163 people assumed to start second line treatment in 2022/23. It is estimated that there will be an uptake of 37% in 2021/22 and 119 people will start treatment with nivolumab plus ipilimumab in year 2022/23 once uptake has reached 73%.

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

Table 2 Estimated number of people in England starting nivolumab plus ipilimumab

	2021/22	2022/23	2023/24	2024/25	2025/26
Incident population starting nivolumab plus ipilimumab each year	24	48	48	48	48
Prevalent population starting nivolumab plus ipilimumab each year	59	119	0	0	0
Total population starting nivolumab plus ipilimumab each year	**83**	**167**	**48**	**48**	**48**

2.3 This report is supported by a local resource impact template. The company has a commercial arrangement (commercial access agreement). This makes nivolumab and ipilimumab available to the NHS with a discount. The discounted prices of nivolumab and ipilimumab can be put into the template and other variables may be amended. For enquiries about the patient access scheme contact UKCommercialEnquiries@bms.com.

Savings and benefits

2.4 The faster and less frequent administration of nivolumab plus ipilimumab might help to reduce visits to hospital and make better use of clinical capacity compared with chemotherapy combination treatments.

2.5 Nivolumab plus ipilimumab could also reduce administration costs relative to the complex prolonged infusions needed for the combination chemotherapy option. This is modelled in the template.

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 Nivolumab plus ipilimumab falls within the programme budgeting category PB02C: Cancer, LGI.

4 How we estimated the resource impact

The population

4.1 In 2018, around 36,000 new cases of adults with colorectal cancer were recorded in England (Public Health England, 2020).

4.2 The eligible population is based on the proportion of people with metastatic colorectal cancer and who test positive for high MSI or MMR deficiency as shown in tables 3 and 4.

Table 3 Number of people eligible for treatment in England (incident population)

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 nivolumab plus ipilimumab [4]	5	465
People who have had first line treatment with a fluoropyrimidine-based combination chemotherapy[4]	20	93
People expected to start second line treatment[4]	70	65
Uptake of people starting treatment with nivolumab plus ipilimumab[5]	73	48

[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

[5] Company submission

Table 4 Number of people eligible for treatment in England (prevalent population)

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 nivolumab plus ipilimumab [4]	5	465
People who have had first line treatment with a fluoropyrimidine-based combination chemotherapy and progress to second line treatment[4]	70	325
Proportion assumed progress to second line treatment in each of the first 2 years[4]	50	163
Uptake of people starting treatment with nivolumab plus ipilimumab in year 1	37	59
Uptake of people starting treatment with nivolumab plus ipilimumab in year 2[5]	73	119

[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
[5] Company submission

Assumptions

4.3 The resource impact template assumes that:

- 5-fluorouracil, folinic acid, and oxaliplatin (FOLFOX), 5-fluorouracil, folinic acid and irinotecan (FOLFIRI), trifluridine–tipiracil and best supportive care are the relevant comparators for nivolumab plus ipilimumab for previously treated metastatic

colorectal cancer with high microsatellite instability or mismatch repair deficiency.

- In future 73% (source: company submission) of the eligible population will start nivolumab plus ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency. There will be a 37% uptake in year 2021/22 to reflect routine commissioning for the part-year.
- The average treatment duration with nivolumab is 19 months. This is based on data from clinical trials as per the company submission.
- The average treatment duration with ipilimumab is 3 months. This is based on data from clinical trials as per the company submission.
- The recommended dose is 1 mg/kg nivolumab in combination with 3 mg/kg ipilimumab administered intravenously every 3 weeks for the first 4 doses. This is then followed by a second phase in which nivolumab monotherapy is administered intravenously at either 240 mg every 2 weeks or at 480 mg every 4 weeks.

Other factors

4.4 Treatment with nivolumab plus ipilimumab 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

4.5 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 Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency and should be read with it.