NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Pembrolizumab for previously treated biliary, colorectal, endometrial, gastric or small intestine cancer with high microsatellite instability or mismatch repair deficiency (TA914)

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Summary

NICE has recommended pembrolizumab as an option for treating tumours with high MSI or MMR deficiency in adults (please see guidance for specified tumour types).

We estimate that:

- Around 100 people with endometrial carcinoma will be eligible for treatment with pembrolizumab.
- Around 100 people with gastric cancer, 30 people with small intestine cancer and around 90 people with biliary cancer will be eligible for treatment with pembrolizumab.
- People with colorectal cancer are not included in this assessment because they can access pembrolizumab at first line, therefore numbers eligible are very small (less than 30).
- Around 250 people in total will receive pembrolizumab for the above cancer types from year 2024/25 onwards once uptake has reached the percentages given in table 1.
- Around 2,300 fewer attendances at chemotherapy units will be required from year 2024/25. This is because pembrolizumab can be received less frequently (every 6 weeks) compared with other treatment options. This is shown in table 2.

Table 1 Estimated number of people in England receiving pembrolizumab

	2023/24	**2024/25**	**2025/26**	**2026/27**	**2027/28**
Uptake rate for endometrial carcinoma (%)	35	50	50	50	50
Uptake rate for gastric, small intestine and biliary cancer (%)	75	90	90	90	90
People receiving pembrolizumab each year:					
- Endometrial cancer	30	50	50	50	50
- Gastric cancer	80	90	90	90	90
- Small intestine cancer	20	30	30	30	30
- Biliary cancer	70	80	80	80	80
Total	**200**	**250**	**250**	**250**	**250**

Table 2 Estimated reduction in chemotherapy unit attendances in England

	2023/24	2024/25	2025/26	2026/27	2027/28
Endometrial carcinoma*	70	60	50	50	50
Gastric cancer	970	1,170	1,180	1,180	1,200
Small intestine cancer	260	120	90	90	90
Biliary cancer	780	940	950	950	960
Total	**2,080**	**2,290**	**2,270**	**2,270**	**2,300**

*Includes dostarlimab option currently in the CDF.

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

Pembrolizumab is commissioned by NHS England. Providers are NHS hospital trusts.

1 Pembrolizumab

1.2 NICE has recommended pembrolizumab as an option for treating tumours with high microsatellite instability (MSI) or mismatch repair (MMR) deficiency in adults with:

- advanced or recurrent endometrial cancer that has progressed during or after a platinum-based therapy, who cannot have curative surgery or radiotherapy
- unresectable or metastatic gastric, small intestine or biliary cancer that has progressed during or after 1 therapy
- colorectal cancer after fluoropyrimidine combination therapy, only if they cannot have nivolumab with ipilimumab

It is only recommended if:

- pembrolizumab is stopped at 2 years of uninterrupted treatment, or earlier if the cancer progresses, and
- the company provides it according to the commercial arrangement

1.3 This recommendation is not intended to affect treatment with pembrolizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

1.4 A gastrointestinal oncologist explained that from their experience, there is an unmet need for immunotherapies for the gastrointestinal tumour sites. The committee concluded that for many people with cancer in these sites, there is an unmet need for new and effective treatment options such as targeted therapies.

1.5 Pembrolizumab offers a survival benefit with a good quality of life for people eligible to receive treatment. Experts from the committee stated that implementation is unlikely to be a problem because pembrolizumab is commonly used in other tumour types.

1.6 There are potential capacity benefits associated with pembrolizumab compared with current chemotherapy options. This is due to less frequent administrations (every six weeks versus every 2 weeks) resulting in fewer administrations overall, or no requirement for more frequent initial dosing.

2 Resource impact of the guidance

2.1 We estimate that:

- Around 100 people with endometrial carcinoma will be eligible for treatment with pembrolizumab.
- Around 100 people with gastric cancer, 30 people with small intestine cancer and around 90 people with biliary cancer will be eligible for treatment with pembrolizumab.
- People with colorectal cancer are not included in this assessment because they can access pembrolizumab at first line, therefore numbers eligible are very small (less than 30).
- Around 250 people in total will receive pembrolizumab for the above cancer types from year 2024/25 onwards once uptake has reached the percentages given in table 3.
- Around 2,300 fewer attendances at chemotherapy units will be required from year 2024/25. This is because pembrolizumab can be received less frequently (every 6 weeks) compared with other options. This is shown in table 4.

2.2 The current treatment and future uptake figure assumptions are based on from gastrointestinal oncologists and are shown in the resource impact template. Table 3 shows the number of people in

England who are estimated to receive pembrolizumab by financial year.

Table 3 Estimated number of people in England receiving pembrolizumab

	2023/24	2024/25	2025/26	2026/27	2027/28
Uptake rate for endometrial carcinoma (%)	35	50	50	50	50
Uptake rate for gastric, small intestine and biliary cancer (%)	75	90	90	90	90
People receiving pembrolizumab each year:					
- Endometrial cancer	30	50	50	50	50
- Gastric cancer	80	90	90	90	90
- Small intestine cancer	20	30	30	30	30
- Biliary cancer	70	80	80	80	80
Total	**200**	**250**	**250**	**250**	**250**

Table 4 Estimated reduction in chemotherapy unit attendances in England

	2023/24	2024/25	2025/26	2026/27	2027/28
Endometrial carcinoma*	70	60	50	50	50
Gastric cancer	970	1,170	1,180	1,180	1,200
Small intestine cancer	260	120	90	90	90
Biliary cancer	780	940	950	950	960
Total	**2,080**	**2,290**	**2,270**	**2,270**	**2,300**

*Includes dostarlimab option currently in the CDF.

2.3 This report is supported by a local resource impact template. Pembrolizumab has a commercial arrangement (commercial access agreement). This makes pembrolizumab available to the NHS with a discount. The size of the discount is commercial in confidence. The discounted price of pembrolizumab can be put into the template and other variables may be amended. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Implications for commissioners

3.1 This technology is commissioned by NHS England. Providers are NHS hospital trusts.

3.2 A comparator treatment for endometrial carcinoma (dostarlimab) is currently funded in the CDF. The costs are not included in the resource impact, however the change in capacity impact for chemotherapy attendances can be assessed.

3.3 Pembrolizumab falls within the programme budgeting categories '2B Cancers and tumours upper GI'; '2C Cancers and tumours lower GI'; and '2G Cancers and tumours Gynaecological'.

4 How we estimated the resource impact

The population

4.1 The eligible populations for each solid cancer type are based on cancer statistics, published studies and clinical expert opinion. These are given in Appendix 1 of this report.

4.2 Around 90% of people who have colorectal cancer receive first line treatment with pembrolizumab, therefore a very low number of people (less than 30) would receive it at second line and only where nivolumab with ipilimumab are unsuitable. Colorectal cancer is therefore not included in the resource impact template.

Assumptions

4.3 The resource impact template assumes that:

- The impact on subsequent treatments is not expected to be significant because most people receive best supportive care.
- The average number of 6 weekly cycles for pembrolizumab for endometrial cancer is 10 (received over more than 1 year), for

gastric cancer this is 4, small intestine cancer 17 cycles (received over more than 1 year) and biliary cancer 8 cycles.

- The average number of 2 weekly cycles for folinic acid, fluorouracil and oxaliplatin (FOLFOX) and folinic acid, fluorouracil and irinotecan (FOLFIRI) regimens for treating gastric, small intestine and biliary cancer is 10.

- The average number of 28-day cycles (3 doses per cycle) of paclitaxel for treating gastric cancer is 5.

- The average number of dostarlimab cycles /doses, currently in the CDF, is 11.

Table 5 Assumptions made on current and future practice

People eligible for pembrolizumab		
Current Practice	**Future practice (year 5)**	**Rationale**
Endometrial cancer		
0% of people receive pembrolizumab 100% of people receive dostarlimab (CDF)	**50%** of people receive pembrolizumab 50% receive dostarlimab (CDF)	Estimate based on expert opinion from gastrointestinal oncologists.
Gastric cancer		
0% of people receive pembrolizumab 70% receive paclitaxel 30% receive FOLFIRI	90% of people receive pembrolizumab 7% receive paclitaxel 3% receive FOLFIRI	Estimate based on clinical expert opinion from gastrointestinal oncologists.
Small intestine cancer		

0% of people receive pembrolizumab 10% receive FOLFIRI 90% receive FOLFOX	90% of people receive pembrolizumab 1% receive FOLFIRI 9% receive FOLFOX	Estimate based on clinical expert opinion from gastrointestinal oncologists.
Biliary cancer		
0% receive pembrolizumab 10% receive FOLFIRI 90% receive FOLFOX	90% of people receive pembrolizumab 1% receive FOLFIRI 9% receive FOLFOX	Estimate based on clinical expert opinion from gastrointestinal oncologists.
Totals = 100%	**Totals = 100%**	

Other factors

4.4 Extra routine testing is needed to determine high MSI (MSI-H) and MMR deficiency (dMMR). The cost of dMMR testing is £150 (based on clinical experts from the committee). MSI-H testing can become part of biomarker panel tests in cancer treatment. Both tests are currently funded in the NHS for colorectal and endometrial cancer. For gastric, small intestine and biliary cancer, funding will be secured by NHSE.

Appendix 1 Eligible population for each solid tumour type in England

Tumour site	Endometrial		Gastric		Small intestine		Biliary	
	%	Number of people	%	Number of people	%	Number of people	%	Number of people
Adults aged 18 and over (adjusted for population growth) [1]		46,263,200		46,263,200		46,263,200		46,263,200
Incidence % of adults aged 18 and over [2]	0.2	8,200	0.01	5,800	0.004	1,700	0.01	2,700
People with advanced / stage 4 metastatic cancer (8,200 x 18%) [3]	18	1,470	48	2,800			70	1,900
People with early-stage endometrial cancer who experience disease recurrence each year (8,200x13%)[4]	13	1,060						
People with advanced or recurrent endometrial cancer [5]		**2,530**						
People receiving platinum-based chemotherapy/first line treatment [6]	64	1,620	85	2,400			85	1,600
People whose cancer progresses on or after platinum chemo / first line treatment and eligible for further treatment [7]	36	580	50	1,200	23	400	50	800
Eligible population - People with MSI-H or dMMR tumours [8]	17	**100**	9	**100**	8	**30**	11	**90**
Total number of people estimated to receive pembrolizumab each year from year 2024/25 [9]	50	**50**	90	**90**	90	**30**	90	**80**

References:

1) Office for National Statistics, see population data below. Population uplifted from baseline 2020 population.
2) Endometrial cancer: C54.1 Cancer registration statistics 2019 - adjusted for population growth
   Gastric cancer: C16 Cancer registration statistics 2019
   Small intestine cancer: C17 Cancer registration statistics 2019
   Biliary cancer: C22.1, C24.0, C24.8 and C24.9 Cancer registration statistics 2019
3) Cancer Research UK. 2020. Uterine cancer incidence by stage at diagnosis. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/uterine-cancer/incidence#heading-Three [accessed 27 April 2021].
   Valle JW, Lamarca A, Goyal L, et al. New Horizons for Precision Medicine in Biliary Tract Cancers. *Cancer Discov*. 2017; 7(9):943-62.
4) Odagiri T, Watari H, Hosaka M, et al. Multivariate survival analysis of the patients with recurrent endometrial cancer. Journal of gynecologic oncology 2011;22:3-8.
5) TA779 company submission. 2021. Clinical Expert Feedback.
6) Endometrial cancer - TA779 company submission 2021. Gastric cancer, Biliary cancer - Company assumption
7) Endometrial cancer - TA779 company submission 2021. Gastric cancer, Biliary cancer - Company assumption
8) Endometrial, Gastric, Small intestine source: Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science*. 2017; 357(6349):409-13.
   Biliary cancer – NHSE submission
9) Company estimate.

About this resource impact report

This resource impact report accompanies the NICE guidance on Pembrolizumab for previously treated biliary, colorectal, endometrial, gastric or small intestine cancer with high microsatellite instability or mismatch repair deficiency and should be read with it.