

National Cancer Medicines Advisory Group (NCMAG) Programme

NCMAG129 Aspirin | Advice Document v1.0 | October 2026

For the adjuvant treatment of adults with resected stage I to III rectal cancer or stage II to III colon cancer with PI3K pathway alterations ^A

NCMAG Decision | this off-label use is **supported**

^A NCMAG considers proposals submitted by clinicians for use of cancer medicines outwith Scottish Medicines Consortium remit. For more detail on NCMAG remit please see our website.

Decision Rationale

After consideration of the available evidence regarding the clinical benefits and harms, the Council were **satisfied** with the clinical effectiveness case for aspirin in the proposed population. After consideration of all relevant information under the Decision-making Framework for Value Judgements the Council made a decision to **support** this use.

Governance Arrangements

Each NHS board must ensure all internal governance arrangements are completed before medicines are prescribed. The benefits and risks of the use of a medicine should be clearly stated and discussed with the patient to allow informed consent.

Proposal Details	
Proposers	NHSScotland oncologists treating colorectal cancer
Medicine Name	Aspirin
Cancer type	Colon and rectal cancers
Proposed off-label use ^B	Adjuvant treatment of resected colorectal cancers with somatic PI3K pathway alterations. • Stage I to III rectal cancers • Stage II to III colon cancers
Medicine Details	<u>Form</u>: Aspirin oral tablet <u>Dose</u>: 150mg once daily for three years
Advice eligibility criteria	Inclusion criteria

	• Stage II or III colon cancer or stage I, II or III rectal cancer • prior radical resection of their primary tumour with or without pre-operative therapies and • confirmed PIK3CA, PIK3R1 or PTEN somatic alterations
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^B Aspirin has a marketing authorisation for multiple non-cancer indications including but not limited to:

- Secondary prevention of thrombotic cerebrovascular
- Primary and secondary prevention of cardiovascular disease and myocardial infarction
- For the relief of mild to moderate pain
- Reduction of inflammation

See Summary of Product Characteristics for further licensed indications¹

1. Current Management Context

Colorectal cancer symptoms, incidence and prognosis

Colorectal cancer is a collective term including cancers that originate in the colon or rectum and are often grouped together as they have many similar features. Symptoms are often associated with larger tumours and/or advanced disease stages and commonly include alterations in bowel habit, abdominal pain, weight loss without other specific causes, weakness, iron deficiency and anaemia². Genetic mutations can occur within colorectal tissue leading to cancer cell development. The phosphatidylinositol 3-kinase (PI3K) cell signalling pathway, associated with cell division and replication, most commonly involve mutations in PIK3CA, PIK3R1 and PTEN³.

Disease stage is an important determinant of prognosis and treatment approach. Cancer staging is determined by size of the cancer, its progression beyond the inner or outer linings of the bowel or extension into adjacent organs, its spread into blood vessels or lymph nodes, or spread into distant organs. Reported 5-year colon cancer survival rates after surgical resection alone are 68% to 86% for stage II and 45% to 65% for stage III disease². Reported 5-year rectal cancer survival is 70 to 80% for stage II and 60 to 70% for stage III disease when treated with surgery, often alongside pre-operative chemotherapy and radiation. Survival rates are improved by 5 to 20% with the addition of post-operative chemotherapy for stage III and high-risk stage II colorectal cancers. In Scotland in 2023, there were 4,329 colorectal cancer diagnoses, of which 3,074 were colon and 1,255 were rectal cancers. The highest incidence was found in patients aged 70 to 74 years at diagnosis, with 670 cases³. In Scotland in 2022, 855 (22%) patients were diagnosed with stage II and 974 (25%) stage III colorectal cancer. Approximately 37% of colorectal cancers involve mutations in PIK3CA (17%), or in PIK3R1 or PTEN (19% combined)⁴⁻⁶. The incidence of patients with stage I to III rectal cancer or stage II to III colon cancer with PI3K pathway alterations is fewer than 5 per 10,000 per year in Scotland and meets orphan-equivalent criteria.

Colorectal cancer treatment pathway in NHSScotland

Within NHSScotland genetic testing for specific markers is undertaken at diagnosis for all colorectal cancer patients. Currently, PIK3CA, PIK3R1 or PTEN somatic alterations are not standardly tested for, or reported, across NHSScotland. Cancer staging is determined by pathological evaluation of the surgical specimen and radiological imaging.

Depending on disease presentation, surgical intervention alone may be appropriate, however for others systemic anticancer therapies (SACT), radiotherapy or combined chemo-radiotherapy may be administered before or following surgical removal of the cancer (surgical resection). SACT treatments may include 3 to 6 months of fluoropyrimidine-containing regimens such as capecitabine plus oxaliplatin (CAPOX) or folinic acid plus fluorouracil and oxaliplatin (FOLFOX). Treatment for colorectal cancer is determined by disease site, stage, tumour characteristics, surgical resectability, patient fitness and clinician and patient preference.

International context for proposed use

The National comprehensive cancer network (NCCN) supports the use of aspirin daily for three years as an adjuvant treatment in patients with stage II and III colorectal cancers with alterations that activate PI3K^{7,8}.

Pharmacology of Aspirin

Aspirin is an anti-inflammatory medicine and suppresses the PI3K pathway in two places: upstream through COX-2 and PGE-2 pathway inhibition, and downstream through reduction of mTOR signalling⁹. It is understood that this inhibition reduces the risk of polyp formation, thereby decreasing the likelihood that polyps will undergo malignant transformation into colorectal cancer.

2. Evidence Review Approach

A literature search was conducted by a health services researcher (HSR) on key electronic databases including MEDLINE, Embase, major international health technology agencies, as well as a focused internet search. The search strategy comprised both Medical Subject Headings and keywords. The main search concepts were aspirin, colorectal cancer, adjuvant, secondary prevention and PI3K. No filters were applied to limit the retrieval by study type. One HSR independently screened titles and abstracts, eligible full text articles were retrieved and assessed for inclusion. The included publications were critically appraised by one HSR using the Cochrane risk of bias tool 2.

3. Clinical Evidence Review Summary

Clinical Efficacy Evidence

Two studies were identified as being potentially relevant in support of the proposed use, the SAKK 41/13 and ALASCCA studies. The SAKK 41/13 study was a phase III double blind randomised controlled trial in patients with stage II and III colon cancer harbouring the PIK3CA mutation; the study did not include rectal patients or any of the other somatic variants and used a lower 100 mg dose. Finally, the study was stopped early and therefore underpowered to detect differences and was therefore excluded from the review and will not be discussed any further¹⁰.

The ALASCCA study was identified as providing evidence with the highest relevance for the proposed use⁶. It was a phase III, randomised, double blind, placebo-controlled study with the primary aim of evaluating the efficacy of adjuvant aspirin in patients with colorectal cancer and was conducted in Sweden, Norway, Denmark, and Finland. The study included patients who were aged between 18 and 80 years with stage I to III rectal cancer or stage II or III colon cancer with alterations in PI3K pathway. Staging was assessed according to the criteria in the American Joint Committee on Cancer staging manual, 7th edition. Somatic alterations were classified as group A (prespecified hotspot mutations in exons 9 and 20 of PIK3CA) or group B (other moderate or high impact somatic variants in PIK3CA, PIK3R1 or PTEN). Patients were randomised 1:1, within 12 weeks post-surgery to receive oral aspirin 160 mg (group A, n=157 and group B, n=156) or

matched placebo (group A, n=157 and group B, n=156) once daily for 3 years. Aspirin or placebo were started after randomisation and given either alone or alongside adjuvant chemotherapy, if this was recommended, based on local practice. Randomisation was stratified by tumour location (colon or rectal), pathological staging (I, II or III), and genetic alterations⁶.

The primary outcome was colorectal cancer recurrence, assessed as 3-year cumulative incidence with recurrence defined as a locoregional recurrence, distant metastasis or death from colorectal cancer in patients with group A alterations. Time to recurrence was defined as the time from randomisation to the first recurrence of colorectal cancer. Secondary outcomes included disease-free survival, defined as time from randomisation to the first recurrence, distant metastasis, any new primary cancer or death from any cause; overall survival, defined as time from randomisation to death of any cause; and safety. These outcomes were also assessed in patients with group B alterations.⁶

Results

Randomisation within 12 weeks following surgery was achieved in 92% of patients, with a median time from surgery to randomisation of 7.7 weeks (range 1.6 to 23 weeks). Baseline characteristics were well balanced between groups: 52% of patients were women, 33% had rectal cancer, median age was 66 years (range 31 to 80) across groups A and B. No differences were noted between groups A and B or between groups treated with aspirin or placebo⁶.

Results for the primary and secondary outcomes were presented for patients with group A or B alterations and the subgroups with rectal and colon cancer and are summarised in Table 1. The analysis was conducted after all patients remaining in the study had been on study treatment for three years. In total, three patients were lost to follow-up.

Table 1 | Key efficacy results from the ALASCCA study⁶

	Group A		Group B	
	Aspirin (n=157)	Placebo (n=157)	Aspirin (n=156)	Placebo (n=156)
Colorectal Cancer Recurrence				
Events n (%)	12 (7.6%)	23 (15%)	12 (7.7%)	27 (17.3%)
3-yr cumulative incidence (95% CI)	7.7 (4.2 to 12)	14 (9.2 to 20)	7.7 (4.2 to 13)	17 (11 to 23)
Hazard ratio (95% CI)	0.49 (0.24 to 0.98), p=0.04		0.42 (0.21 to 0.83)	
Rectal cancer recurrence				
Events n (total)	3/47	11/47	6/57	13/56
Hazard ratio (95% CI)	0.23 (0.06 to 0.83)		0.44 (0.17 to 1.15)	
Colon cancer recurrence				
Events n (total)	9/110	12/110	6/99	14/100
Hazard ratio (95% CI)	0.75 (0.32 to 1.78)		0.41 (0.16 to 1.06)	
Disease free survival				
Events n (%)	19	30	19	35
3-yr disease free survival (95% CI)	88% (82 to 93)	81% (74 to 87)	89% (83 to 93)	79% (71 to 84)
Hazard ratio (95% CI)	0.61 (0.34 to 1.08)		0.51 (0.29 to 0.88)	

Key: CI: confidence interval;

In the ALASCCA study, aspirin reduced the 3-year risk of colorectal cancer recurrence from 14% to 7.7% and from 16% to 7.7% in patients with group A and B alterations respectively (Table 2). The 5-year overall survival rate was estimated to be 92% with aspirin versus 90% in placebo (HR 0.79, 95% CI 0.37 to 1.68) in group A, and 93% with aspirin versus 90% in placebo (HR 0.68, 95% CI 0.30 to 1.51) in group B.

Table 2 | 3-year number needed to treat results⁶

	Group A		Group B	
	ARR	NNT	ARR	NNT
Colorectal Cancer	6.4%	16	9.1%	11
Rectal Cancer	17%	6	13%	8
Colon Cancer	2.7%	27	7.9%	13

Key: ARR: absolute risk reduction. NNT: number needed to treat

Patient reported outcomes

The ALASCCA study did not collect any patient reported outcomes.

Safety Evidence

This off-label use and dose of aspirin in the ALASCCA study was associated with non-severe adverse events in 43% of the patients receiving aspirin compared to 35% receiving placebo. Severe adverse events (SAEs), categorised as grade 3 or above, occurred in 17% and 12% of the groups, respectively. The most commonly reported SAEs reported for aspirin versus placebo were gastrointestinal disorders (6.5% versus 3.9%); cardiovascular disorders (5.8% versus 4.2%) and events resulting in hospitalisation for >24 hours or extended medical care (11% versus 7.4%)⁶.

Four severe adverse events (1.3%) were considered by the principal investigator to be potentially related to aspirin: allergic reaction, gastrointestinal bleeding, subarachnoid haemorrhage and spontaneous haematoma associated with anaemia; one death was considered potentially related to aspirin⁶.

Risk of Bias Assessment

The ALASCCA trial was assessed for bias using the Cochrane risk of bias version 2 tool. Across all domains it was judged to have a low risk of bias¹¹.

Clinical Effectiveness Considerations

Aspirin, when added to standard of care treatment, has been shown to reduce the risk of cancer recurrence following surgical removal of colorectal cancers with alterations in PIK3CA pathway

The ALASCCA study met its primary outcome, demonstrating that when added to standard of care, aspirin is associated with a statistically significant reduction in cancer recurrence compared with placebo in patients with hotspot mutations in exons 9 and 20 of PIK3CA. A similar treatment effect was reported for a cohort of patients with other moderate or high impact somatic variants in PIK3CA, PIK3R1 or PTEN. The study sample size calculation was updated while the study was

ongoing to account for the distribution across cancer stages among patients already randomised. This led to a reduction in the study sample size while maintaining the same level of power to detect a difference between study treatments. The data from ALASCCA was robust with a low risk of bias, providing reassurance around the estimated relative effects of the treatment.

There is some uncertainty on the longer-term efficacy of aspirin

The key secondary outcomes of disease-free survival (DFS) and overall survival (OS) were not formally tested. Although central estimates favoured aspirin, event rates were low and confidence intervals were wide, crossing 1.0 (possibility of no difference between treatment arms) for both DFS and OS in group A and OS in group B; the lack of mature survival data is an uncertainty. Aspirin treatment stopped after 3 years and there may be uncertainty on the optimal duration. Three-year disease-free survival is a widely recognised surrogate for overall survival in colorectal cancer adjuvant trials, but this endpoint was not described¹².

The adverse event profile for adjuvant aspirin is broadly consistent with its profile in other clinical areas

Aspirin is associated with increased bleeding tendencies and gastrointestinal disorders such as nausea, vomiting, dyspepsia and diarrhoea¹. The most common SAEs within the ALASCCA study were post operative complications such as deep-vein thrombosis, embolism and infection however these were not considered treatment related by the principal investigator. Severe treatment related adverse events were reported for 1.3% of the study group receiving 3 years of aspirin including 1 treatment related death. The adverse event profile for aspirin in the ALASCCA study is similar to the profile for on-label uses for primary and secondary prevention in vascular disease; however, due to different disease states and comorbidities the incidence is not comparable.

Due to the absence of aspirin products to support use of the ALASCCA study 160mg oral dose in NHSScotland, the proposal is for a 150mg oral dose. These doses are considered to be broadly equivalent.

The ALASCCA study utilised an aspirin oral dose of 160mg daily, however no licensed products in the UK can be used to make this dose. Based on the available oral aspirin products in the UK a 150mg dose is possible. No direct evidence demonstrates superiority of 160mg over 150mg aspirin and both doses are thought to be pharmacologically equivalent. It has become routinely accepted that 150mg is equivalent to 160mg for clinical studies^{13, 14}. The NCCN guidelines recommend a dosing range of 100 to 162mg daily for stage II and III colon and rectal cancers with PI3K pathway alternations^{7, 8}.

The ALASCCA study findings are likely generalisable to NHSScotland although there are some uncertainties.

The ALASCCA study was conducted within four northern European countries excluding the UK; however, health systems and treatment guidelines are similar^{2, 6}. Within the ALASCCA study adjuvant treatments included fluoropyrimidine regimes containing fluorouracil and capecitabine with or without oxaliplatin, aligning with NHSScotland treatment options.

In the ALASCCA study 53% of the colon cancer patients had stage II disease and 47% had stage III disease respectively; 51% of all the stage II and III colon cancer patients were treated with adjuvant chemotherapy, demonstrating similar treatment thresholds to the NHSScotland population. On average 50% of rectal cancer patients in the ALASCCA study had neoadjuvant treatment including radiotherapy, chemoradiotherapy or total neoadjuvant therapy. After surgery, 37% had stage III pathology, and 25% of all patients were given adjuvant chemotherapy. Whilst direct comparisons are not possible, these treatments and proportions are in line with treatments seen in NHSScotland and provide some reassurance.

The median age of the study population was 66 years whereas in NHSScotland the most common age range at diagnosis is 70 to 74 years; older patients may have comorbidities, so patients in NHSScotland could represent a frailer population than the study population, potentially with reduced tolerance to treatment.

4. Patient Group Summary

We received a statement from Bowel Cancer UK who are a registered charity. Bowel Cancer UK reported 3.5 to 4% of their annual funding came from the pharmaceutical industry in 2025. A representative from Bowel Cancer UK attended the NCMAG council meeting. The key points from the Bowel Cancer UK statement include:

Patient feedback highlighted the significant physical and psychological burden associated with colorectal cancer, including fatigue, pain, changes in bowel function and anxiety regarding disease recurrence. Participants reported that fear of recurrence can have a substantial impact on quality of life and future planning.

Respondents were generally supportive of aspirin as a potential strategy to reduce recurrence risk, reflecting the importance patients place on preventing their cancer returning. No specific concerns were raised regarding impacts on family members or carers; however, clear communication regarding the benefits and risks of aspirin would be important to support patient understanding and acceptance of treatment.

5. Benefit-risk Balance

The proposal is for the off-label use and dosing of aspirin for adjuvant treatment of colorectal cancer in patients with resected colorectal cancers with somatic PI3K pathway alterations. In the ALASCCA study combined cohort aspirin showed a 7.7% absolute reduction in 3-year disease recurrence rates (7.7% versus 15.4% in the placebo group) and this was consistent across both genetic alteration cohorts. Mature overall survival data, with greater than 5 years of follow-up, has not been published. There were no unexpected safety signals compared to on-label uses of aspirin with gastrointestinal events reported as the most common severe adverse events¹.

6. Council Review | Clinical Benefit-risk Balance Evaluation

After consideration of the available evidence regarding the clinical benefits and risks, the Council were **satisfied** that the case had been made for the clinical effectiveness of aspirin.

7. Economic Evidence Review Summary

Economic Overview

The literature search for economic evidence returned no cost-effectiveness publication which evaluated aspirin for the adjuvant treatment of adults with resected stage I to III rectal cancer or stage II to III colon cancer with PI3K pathway alterations.

Type of economic evaluation

In the absence of a cost-effectiveness analysis, a de-novo cost-comparison analysis was performed to support this assessment.

Population, intervention, comparator and outcomes

The proposed eligible patients for treatment included those with resected stage I to III rectal cancer or stage II to III colon cancer with PI3K pathway alterations.

The selection of eligible patients for treatment requires all new colorectal cancer patients to undergo genetic testing for PI3K pathway alterations in addition to the current panel of genetic tests routinely performed at diagnosis. Therefore, the intervention was testing for mutations in PIK3CA, PIK3R1 and PTEN (referred as extended mutation panel) and subsequent oral aspirin 150mg once daily for three years following surgery in the eligible patients.

There is currently no national approach for the routine testing of PI3K pathway alterations in this patient population. Therefore, the comparator was standard of care without additional genetic testing and without subsequent aspirin (hereafter referred to as NHSScotland SOC).

As a cost-comparison analysis in the specific treatment setting only has been performed, quality-adjusted life-years (QALYs) were not included in the analysis.

Costs

Costs included were medicine acquisition, adverse event and monitoring costs, in the specific treatment setting only – excluding costs related to the management of cancer recurrence, for three years following surgery and one-off genetic testing cost. The lowest price of oral aspirin was derived from Scottish Drug Tariff (accessed July 2026) as it is likely to be prescribed and dispensed from primary care¹⁵.

Adverse event costs were estimated for events resulting in hospitalisation for more than 24 hours or extended medical care reported in ALASCCA study⁶. Based on clinical expert opinion, patients experiencing these events were assumed to receive an average of three days of inpatient care under General Medicine speciality area. The corresponding inpatient unit cost was sourced from

Public Health Scotland (2023/24). This was assumed to cover the cost of administration, monitoring and treatment for Grade 3 or above adverse events.

The monitoring cost included one general practitioner (GP) consultation lasting 10 minutes based on clinical expert opinion. This cost was sourced from PSSRU Unit Costs of Health and Social Care Manual 2025¹⁶.

The cost of genetic testing was estimated in consultation with Scottish Strategic Network for Genomic Medicine (SSNGM). The total costs and expected testing population across genetic laboratories in NHSScotland were used to estimate the weighted average per-test cost of introducing extended mutation testing panel to the existing colorectal panel. In the absence of relevant information, an assumption was made that extended testing for mutations in PIK3CA, PIK3R1 and PTEN would incur three times the unit cost per test. In addition, the testing cost per eligible patient was adjusted to include the cost of testing both positive and negative patients, as all patients must be tested to identify eligible patients for treatment with aspirin. At diagnosis approximately 53% of colorectal cancers are stage I to III rectal or stage II to III colon cancer and 37% of colorectal cancers involve mutations in PIK3CA, PIK3R1 or PTEN, corresponding to 5.1 patients needed to be tested to identify one patient eligible for treatment. This results in total testing cost per eligible patient of £46.

Results

All figures in the cost-comparison analysis exclude value added tax (VAT).

Table 3 | Summary of cost-comparison results in the specific treatment setting only

Cost category	Aspirin	NHSScotland SOC ^a	Cost difference
Medicine acquisition	£127	£0	£127
Adverse event	£177	£123	£55
Monitoring	£45	£0	£45
Genetic testing	£46 ^b	£0	£46
Total costs per-patient	£396	£123	£273
Total costs per-patient (excluding genetic testing costs)	£350	£123	£227

^a Refers to standard of care without genetic testing and without subsequent aspirin

^b Genetic testing cost per eligible patient accounts for cost of testing both positive and negative patients

Compared with the NHSScotland SOC in this setting, aspirin increased total costs per patient by £273 over a three-year period (Scottish Drug Tariff, accessed July 2026)¹⁵. On excluding genetic testing costs, the additional per-patient cost of treatment over the same period was £227 compared with the NHSScotland SOC.

Generalisability

The Scottish Drug Tariff price for 28 tablet pack of 75 mg aspirin was used as it is likely to be dispensed from primary care¹⁵. The lowest price generic versions were used for calculation. The clinical and genetic testing experts from NHSScotland and SSNGM were consulted to validate resource implications of additional genetic testing and patient monitoring requirements.

Limitations of the cost comparison

Uncertainty in estimating the cost of genetic testing for alterations in PI3K pathway

There was uncertainty regarding the cost of adding genetic tests to existing colorectal testing panels across laboratories in NHSScotland. Expert opinion suggests that the incremental cost may range from minimal to substantial, depending on existing infrastructure and laboratory capacity. Moreover, in the absence of relevant information, an assumption was made that extended testing for mutations in PIK3CA, PIK3R1 and PTEN would incur three times the unit cost per test which may not be the case in the real-world. The base case results with and without genetic testing costs are presented in Table 3.

Clinical evidence suggests lower recurrence rates in patients on aspirin compared with placebo. However, subsequent treatment costs relating to recurrence are not considered in the cost-comparison.

Due to an absence of a cost-effectiveness analysis, the analysis only compared costs in the specific setting described and excluded costs relating to the management of cancer recurrence. As detailed in Section 3, the ALASCCA study demonstrated that when added to standard of care, aspirin was associated with an eight percent absolute reduction in cancer recurrence compared with placebo in patients with PI3K alterations. A reduction in cancer recurrence with aspirin would be expected to decrease associated long-term treatment costs and has the potential to be cost-effective. Published evidence covers a broad spectrum of cancer management contexts with some estimates for the cost of treatment (after adjustment for inflation) ranging from approximately £15,000 to £38,000^{17, 18}. However, an estimate of cost-effectiveness can only be made by modelling the costs and benefits over a lifetime time horizon. Due to its absence, an incremental cost-effectiveness ratio (ICER) was not available, and the cost-effectiveness remained unknown.

Summary

The cost-comparison in the proposed setting only, excluding costs related to the management of cancer recurrence, indicated that aspirin was a cost-increasing intervention compared with NHSScotland SOC. However, in the absence of a cost-effectiveness analysis, it was not possible to quantify treatment benefits in relation to costs, and the actual cost-effectiveness remained unknown.

8. Council Review | Cost-effectiveness Evaluation

After considering the available evidence, the Council accepted that in the absence of a cost-effectiveness analysis, the cost effectiveness is unknown. In this situation Council was able to

consider additional relevant information including service impact and estimated net medicines budget impact under the Decision-making Framework for Value Judgements.

9. Service Impact

Consultation with experts from the SSNGM suggests regional variation in PI3K alteration testing and no reporting, due to a lack of clinical need. Greater challenges have been identified for introducing the extended mutation panel (explored in group B of the ALASCCA trial). Testing for PTEN and PIK3R1 is not currently done, and review by the SSNGM is required before these additional tests can be delivered.

Aspirin is routinely prescribed in primary care for a range of on-label uses. Management of the proposed population is expected to be similar to other patient groups. Recommendations for use of aspirin would be on advice of the oncology service.

It is not possible to capture the impact a reduced recurrence rate would have on the service, however a reduction in service use would be expected in the longer term.

10. Budget Impact

In the absence of a cost-effectiveness analysis, a detailed budget impact analysis was conducted.

Patient uptake

The base case budget impact analysis included patient uptake associated with testing and treatment. Consultation with experts from the SSNGM suggests that testing for PI3K alterations is likely to be conducted at diagnosis, before cancer staging is determined. Approximately 4,329 patients in Scotland are diagnosed with colorectal cancer each year and were assumed to constitute the eligible testing population.

After testing, a proportion of patients with either stage I to III rectal cancer or stage II to III colon cancer and mutations in PIK3CA, PIK3R1 or PTEN were proposed eligible for adjuvant treatment with aspirin. The base case assumed that 100% of eligible patients would receive aspirin. A lower treatment uptake excluding patients who may not be suitable for treatment was explored in Scenario 1 (Table 5).

Per patient medicine cost and treatment duration

The intervention was genetic testing for mutations in PIK3CA, PIK3R1 and PTEN and subsequent oral aspirin 150mg once daily for three years following surgery. The base case budget impact analysis included costs associated with testing and treatment.

Medicine acquisition costs were based on two doses of 75mg oral aspirin taken once daily for three years. As aspirin will be prescribed and supplied from primary care, medicine price was sourced from the Scottish Drug Tariff (accessed July 2026)¹⁵. As treatment duration is three years, the number of patients receiving aspirin is expected to accumulate until a steady state is reached from Year 3 onwards.

The cost of genetic testing was estimated in consultation with SSNGM. The total costs and expected testing population across genetic laboratories in NHSScotland were used to estimate the weighted average per-test cost of adding extended testing panel to the existing colorectal panel. In the absence of relevant information, an assumption was made that extended testing for mutations in PIK3CA, PIK3R1 and PTEN would incur three times the unit cost per test.

Comparator displacement

Oral aspirin is proposed for use alongside NHSScotland SOC. Therefore, no comparator was displaced.

Results

All figures in the budget impact include VAT.

The Year 1 budget impact was estimated to be £82K. The steady state budget impact was estimated to be £169K per year. The Scenario 2 (Table 5) explored net medicine budget impact excluding genetic testing costs.

Table 4 | Budget impact analysis base case results (Including VAT)

	Year 1	Steady state (Year 3 onwards)
Medicine acquisition cost		
Aspirin 150mg once daily	£51	£51
Patient uptake		
Eligible for genetic testing		
Eligible for extended panel mutation testing	4,329	4,329
Cost per sample of testing and reporting	£9	£9
Eligible for treatment		
Patients with stage I to III rectal cancer and stage II to III colon cancer	2,288	2,288
Patients testing positive for mutations in PIK3CA, PIK3R1 and PTEN	847	2,540 ^a
Budget Impact		
Net budget impact	£82,342	£168,696

^a As treatment duration is three years, the number of patients receiving aspirin accumulates until a steady state is reached, resulting in higher patient uptake Year 3 onwards.

Scenario considerations

The following table presents three budget impact scenarios to explore alternate assumptions.

Table 5 | Budget impact base case and scenario analysis results (including VAT)

#	Scenario	Base case	Net annual budget impact	
			Year 1	Steady state (Year 3 onwards)
	-	Base case	£82,342	£168,696
1	45% of eligible patients get treatment (excluding patients not clinically suitable for aspirin)	100% of eligible patients get treatment	£58,595	£97,454
2	Medicine acquisition costs alone	Medicine acquisition and genetic testing cost	£43,177	£129,531
3	Genetic testing limited to PIK3CA mutation	Extended testing for mutations in PIK3CA, PIK3R1 and PTEN	£56,232	£142,586
4	Testing cost sourced from SMC advice SMC2399 ¹⁹	Testing cost estimate based on SSNGM expert opinion	£484,735	£571,089

Limitations

The calculations are based on stable incidence and patient uptake which may vary in the real world. No adjustment was made to the treatment duration based on discontinuation rates, mortality and disease progression. Some eligible patients may not be suitable for aspirin due to contraindications or other patient-specific factors, while others may already be receiving aspirin for comorbidities. Due to these factors, the net budget impact may be overestimated. Alternate assumptions regarding testing and treatment uptake were tested in scenario analysis (Table 5).

There was uncertainty regarding the cost of adding genetic tests to existing colorectal testing panels across laboratories in NHSScotland. Expert opinion suggests that the incremental cost may vary depending on existing infrastructure and laboratory capacity. An alternative unit cost of £34 per test (for adding new genetic test to existing next-generation sequencing panel), based on a previously published SMC advice document, was explored in Scenario 4¹⁹. In the absence of relevant information, an assumption was made that extended testing for mutations in PIK3CA, PIK3R1 and PTEN would incur three times the unit cost.

Summary

The use of aspirin in the specific treatment setting will increase the net medicines budget impact when compared with NHSScotland SOC. Based on genetic testing of all colorectal cancer patients and treatment of 847 patients in Year 1 and 2,540 patients in steady state, the estimated net budget impact was estimated to be £82K in Year 1, rising to £169K Year 3 onwards. These figures are based on Scottish Drug Tariff price and include VAT.

Separate information will be supplied to the boards to facilitate local budget impact assessment.

11. Council Review | Overall Proposal Evaluation

After consideration of all relevant information under the Decision-making Framework for Value Judgements the Council made a decision to support this use.

12. Acknowledgements

NCMAG would like to acknowledge our patient group partner, Bowel Cancer UK for their valuable input.

13. References

1. Novartis Pharmaceuticals UK Ltd. Aspirin. Summary of product characteristics. Electronic medicines Compendium. <https://www.medicines.org.uk/emc/product/102206/smpc>. Last updated [27 Aug 2026].
2. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T, *et al.* Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2020;31(10):1291–305.
3. Public Health Scotland, Cancer incidence and prevalence in Scotland To December 2023, <https://publichealthscotland.scot/media/35152/20250930-cancer-incidence-2023-report-finalv.pdf>, accessed June 2026.
4. Kim J, Jang H-L, Hong JY, Kim ST, Park SH, Park JO, *et al.* Prevalence and clinical implications of PIK3CA aberrations across cancer types: A real-world next-generation sequencing approach. *Cancer Genetics*. 2025;296-297:133–43.
5. Hamada T, Nowak JA, Ogino S. PIK3CA mutation and colorectal cancer precision medicine. *Oncotarget*. 2017;8(14):22305–6.
6. Martling A, Lindberg J, Myrberg IH, Nilbert M, Mayrhofer M, Gronberg H, *et al.* Low-dose aspirin to reduce recurrence rate in colorectal cancer patients with PI3K pathway alterations: 3-year results from a randomized placebo-controlled trial. *Journal of Clinical Oncology*. 2025;43(Supplement 4).
7. National Comprehensive Cancer Network: Clinical practice guidelines in oncology: Rectal cancer Version 2.2006. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed May 2026.
8. National Comprehensive Cancer Network: Clinical practice guidelines in oncology: Colon cancer Version 2.2006. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf Accessed August 2026.
9. Bonilla-Velez J, Whitlock KB, Ganti S, Zenner K, Cheng CV, Jensen DM, *et al.* Acetylsalicylic acid suppression of the PI3K pathway as a novel medical therapy for head and neck lymphatic malformations. *Int J Pediatr Otorhinolaryngol*. 2021;151:110869. Epub 20210805.
10. Guller U, Hayoz S, Horber D, Jochum W, De Dosso S, Koeberle D, *et al.* Adjuvant Aspirin Treatment in PIK3CA-Mutated Colon Cancer Patients: The SAKK 41/13 Prospective Randomized Placebo-Controlled Double-Blind Trial. *Clinical Cancer Research*. 2025;31(15):3142–9.

11. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
12. Sargent D, Shi Q, Yothers G, Van Cutsem E, Cassidy J, Saltz L, *et al.* Two or three year disease-free survival (DFS) as a primary end-point in stage III adjuvant colon cancer trials with fluoropyrimidines with or without oxaliplatin or irinotecan: data from 12,676 patients from MOSAIC, X-ACT, PETACC-3, C-06, C-07 and C89803. *Eur J Cancer*. 2011;47(7):990–6. Epub 20110121.
13. Burn J, Borthwick GM, Elliott F, Macrae F, Ong KR, Kraus AC, *et al.* Aspirin for cancer prevention in individuals with Lynch syndrome: first results from the CaPP3 multicentre, randomised, double-blind, non-inferiority trial. *The Lancet Gastroenterology & Hepatology*.
14. Rothwell PM, Cook NR, Gaziano JM, Price JF, Belch JFF, Roncaglioni MC, *et al.* Effects of aspirin on risks of vascular events and cancer according to bodyweight and dose: analysis of individual patient data from randomised trials. *The Lancet*. 2018;392(10145):387–99.
15. Public Health Scotland; Scottish Drug Tariff - Medical practice and pharmaceuticals - Resources and tools - Public Health Scotland <https://publichealthscotland.scot/resources-and-tools/medical-practice-and-pharmaceuticals/scottish-drug-tariff/drugs-and-preparations/search-part-7/> accessed September 2026.
16. University of Kent: New Unit Costs of Health and Social Care Programme; Care and Outcomes Research Centre: unit costs 2022-2027: <https://research.kent.ac.uk/corec/unit-costs-2022-2027/> Accessed September 2026.
17. Snowsill T, Coelho H, Huxley N, *et al.* Molecular testing for Lynch syndrome in people with colorectal cancer: systematic reviews and economic evaluation. Southampton (UK): NIHR Journals Library; 2017 Sep. (Health Technology Assessment, No. 21.51.) Chapter 5, Independent economic assessment. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK453193/>.
18. Pearson C, Jones DA, Baily G, Cherry R, Gray E, Hiom S, *et al.* Influence of stage at cancer diagnosis on NHS hospital care costs in England: a national, retrospective, population-based cohort study using individual patient-level data. *The Lancet Oncology*. 2026;27(3):361–71.
19. Scottish Medicines Consortium. SMC2399. pemigatinib (Pemazyre®) 14 January 2022 . Available: <https://scottishmedicines.org.uk/media/6668/pemigatinib-pemazyre-final-jan-2022-for-website.pdf>.

This advice represents the view of the NCMAG Council and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Minor document amendments

Date	Previous version	Amendment	Updated version	Approved by