Healthcare Improvement Scotland

National Cancer Medicines Advisory Group (NCMAG) Programme

NCMAG128 Pazopanib | Advice Document v1.0 | July 2026

For the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma who have received prior chemotherapy for metastatic disease or who have progressed within 12 months of (neo) adjuvant therapy [A]

NCMAG Decision | this on-label use of an off-patient medicine is **supported**

This advice applies only in the context of the confidential pricing agreements in NHSScotland, upon which the decision was based, or confidential pricing agreements or list prices that are equivalent or lower.

[A] NCMAG considers proposals submitted by clinicians for use of cancer medicines outwith SMC 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 and cost-effectiveness for pazopanib in the proposed population.

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	Scottish Sarcoma Managed Clinical Network
Medicine Name	Pazopanib
Cancer type	Soft tissue sarcoma
Proposed off-patent on-label indication	For the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy.

	Efficacy and safety have only been established in certain STS histological tumour subtypes.
Medicine Details	Form: oral film-coated tablets (200 mg or 400 mg) Dose: 800 mg daily
Advice eligibility criteria	**Inclusion criteria:** • aged 18 years or older • advanced, metastatic STS: Fibroblastic (adult fibrosarcoma, myxofibrosarcoma, sclerosing epithelioid fibrosarcoma, malignant solitary fibrous tumours), so-called fibrohistiocytic (pleomorphic malignant fibrous histiocytoma [MFH], giant cell MFH, inflammatory MFH), leiomyosarcoma, malignant glomus tumours, skeletal muscles (pleomorphic and alveolar rhabdomyosarcoma), vascular (epithelioid hemangioendothelioma, angiosarcoma), uncertain differentiation (synovial, epithelioid, alveolar soft part, clear cell, desmoplastic small round cell, extra-renal rhabdoid, malignant mesenchymoma, PEComa, intimal sarcoma), malignant peripheral nerve sheath tumours, undifferentiated soft tissue sarcomas not otherwise specified (NOS) and other types of sarcoma (not listed as ineligible). • have received prior chemotherapy for advanced or metastatic disease. **Exclusion criteria:** adipocytic sarcoma (all subtypes), all rhabdomyosarcoma that were not alveolar or pleomorphic, chondrosarcoma, osteosarcoma, Ewing tumours/primitive neuroectodermal tumours (PNET), GIST, dermofibromatosis sarcoma protuberans, inflammatory myofibroblastic sarcoma, malignant mesothelioma and mixed mesodermal tumours of the uterus. Liposarcoma and de-differentiated liposarcoma (considered to be underrepresented in the PALLETE study).

1. Current Management Context

Soft tissue sarcoma symptoms, incidence and prognosis.

Soft tissue sarcoma (STS) is a rare form of cancer of mesenchymal origin affecting the connective tissue and can occur anywhere throughout the body. There are approximately 80 types of STS defined by the World Health Organisation[1]. The most common early presentation of STS is a painless, enlarging mass (5cm or greater) which becomes painful as it grows. Soft tissue sarcomas are most commonly found in the upper and lower limbs and trunk but can affect the stomach and intestines (GIST) as well as behind the abdomen (retroperitoneal). Due to the range of subtypes and tumour sites including muscles, nerves, tendons, blood vessels and fatty or fibrous tissues, symptoms can vary making STS difficult to recognise and they can be mistaken as benign abnormalities such as lipomas or cysts. Advanced STS can be associated with fatigue, pain or respiratory symptoms.

Soft tissue sarcomas can occur at any age but are most commonly seen in Scotland for those aged 60 to 65 years. In Scotland there were 147 people diagnosed with connective tissue cancers in 2023 [2]. This corresponds to an incidence of fewer than 5 per 10,000 people per year in NHSScotland and meets orphan-equivalent criteria. Metastatic STS has a median survival of approximately 12 to 18 months from diagnosis[3] and 5-year overall survival rates of 17% in this setting[3].

Soft tissue sarcoma treatment pathway in NHSScotland

Within NHSScotland there is no current nationally agreed treatment pathway, however clinicians follow European Society of Medical Oncology (ESMO)[4-6] and British Sarcoma Group guidelines[3]. Current first-line treatment for advanced or metastatic and clinically unresectable STS, excluding gastrointestinal stromal tumours (GIST), would include an anthracycline medicine such as doxorubicin. Depending on histology, clinician choice and other factors this can be used alone or in combination with ifosfamide. Second line and subsequent treatment options vary depending on histology subtype, prior treatment and patient fitness and include ifosfamide if not previously used, gemcitabine with docetaxel for younger fitter patients and trabectidin. Both eribulin and pazopanib (the proposed treatment) are accessed through individual patient treatment requests. Pazopanib is licensed for treatment of adult patients with selective subtypes of advanced soft tissue sarcoma who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy. However, when it was on patent it was not recommended following health technology assessment review, so is not routinely accessible in NHSScotland for this use[7].

International context for proposed use

The national comprehensive cancer network (NCCN) recognises the use of pazopanib for specified STS subgroups[8]. European Society of Medical Oncology and the British Sarcoma guidelines include pazopanib as an alternative treatment option after first-line chemotherapy[3, 6]. However, the

evidence in rarer subtypes is limited due to lower patient numbers and choice or treatment option will depend on individual patient circumstances.

Pharmacology of pazopanib

Pazopanib is an oral multi-targeted kinase inhibitor that works through inhibiting multiple pathways including the growth of blood vessels around tumours, known as VEGF inhibition, thus potentially shrinking and halting tumour growth[9].

2. Evidence Review Approach

A literature search to identify clinical and economic evidence was conducted on key electronic databases including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, 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 pazopanib, soft tissue sarcoma, metastatic, and advanced. Titles and abstracts were screened by one reviewer with a second opinion sought by another reviewer when required. The included key studies were critically appraised using the Cochrane risk of bias version 2.0 tool and Risk of bias in non-randomised studies – of interventions tool version 1 (ROBINS-1).

3. Clinical Evidence Review Summary

Clinical Efficacy Evidence

The PALETTE study was identified as providing evidence with the highest relevance[10]. It was a phase III, randomised, double blind, placebo-controlled study with the primary aim of determining the safety and tolerability of pazopanib in patients with locally advanced or metastatic soft tissue sarcoma. The study included patients who were 18 years of age with measurable disease according to the modified Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1, had a World Health Organization (WHO performance status of 0 or 1, with either progressive disease following first-line chemotherapy or within 12 months following (neo)adjuvant therapy. Patients with at least one prior line of chemotherapy and a maximum of four previous lines of systemic therapy for metastatic disease were permitted. The study included all of the most common subtypes of soft tissue sarcoma but excluded the following: all types of adipocytic sarcoma, embryonal rhabdomyosarcoma, chondrosarcoma, osteosarcoma, Ewing tumours, primary neuroectodermal tumour, gastrointestinal stromal tumour, dermatofibrosarcoma protuberans, inflammatory myofibroblastic sarcoma, malignant mesothelioma and mixed mesodermal tumours of the uterus. Patients were randomised 2:1 to receive oral pazopanib 800 mg once daily (n=246) or placebo (n=123), stratified by number of previous lines (none or one versus two or more) and WHO performance status (0 versus 1)[10].

The primary outcome was progression-free survival (PFS), defined as time from randomisation to either first disease progression (independent radiographical review) or death from any cause. Secondary outcomes include overall survival (OS), response, defined as either a partial response or stable disease, safety, and quality of life[10].

Results from the PALETTE study

The median duration of treatment was 16.4 weeks (interquartile range [IQR] 6.3 to 30.0) in the pazopanib group versus 8.1 (IQR 4.0 to 13.6) in the placebo group. At the primary data cut of 22 November 2010, the median duration of follow up was 14.9 months (IQR 11.0 to 18.2) in the pazopanib group and 14.6 months (IQR 11.3 to 19.7) in the placebo group. Patients in the pazopanib group tended to be older compared to placebo (57 versus 52 years). The remaining baseline characteristics were well balance between groups. Overall, 55 to 58% of patients had two to four prior lines of treatment and approximately half of patients had a WHO PS of 0[10].

The results were presented in the intention to treat analysis, which included all patients who were randomised and analysed according to their assigned treatment irrespective of whether they completed or adhered to the treatment and are summarised below (Table 1)[10].

Table 1 | Key efficacy results of the PALETTE study[10]

	Pazopanib (n=246)	Placebo (n=123)
Primary Outcome: Independently assessed PFS (Data cut off November 22, 2010)		
Events n (%)	168 (68%)	106 (86%)
Median PFS, months (95% CI)	4.6 (3.7 to 4.8)	1.6 (0.9 to 1.8)
Hazard Ratio (95% CI)	0.31 (0.24 to 0.40), p<0.001[a]	
Overall survival (Data cut off October 24, 2011)		
Events n (%)	185 (75%)	95 (77%)
Median OS, months (95% CI)	12.5 (10.6 to 14.8)	10.7 (8.7 to 12.8)
Hazard Ratio (95% CI)	0.86 (0.67 to 1.11)	
Response		
Partial response n (%)	14 (6%)	0
Stable disease n (%)	164 (67%)	47 (38%)
Subsequent treatments		
Chemotherapy	103 (45%)	75 (61%)
Targeted	22 (9.6%)	17 (14%)

PFS = progression-free survival, OS = overall survival; CI: confidence interval
[a] statistically significant

Supportive Evidence

One study was identified as supportive to this proposal, a national prospective observational cohort study, which included adults with STS who were treated in Italy with pazopanib (as per PALETTE protocol)[11]. The primary outcome was time to treatment discontinuation (TTD), defined as the time from the first administration of pazopanib to the last administration before treatment discontinuation for any cause, including death or loss to follow up. Secondary outcomes included number of treatment cycles, and dose reductions.

Between 2013 and 2019, 1,964 patients were treated with pazopanib for STS, more than half of the patients were female (62%), median age at treatment onset was 59.7 years (IQR 50 to 70) and

94% of patients had an Eastern Cooperative Oncology Group (ECOG) PS 0 or 1. Metastatic disease was reported in 94% of patients and 98% had received at least one prior line of therapy. The median number of cycles per patient was 3 (IQR 2-6). The median TTD was 106 days (95% CI 98 to 112) and 495 patients were reported to have had a dose reduction after the first cycle, at a median time of 56 days (IQR 28 to 112 days)[11].

Patient reported outcomes

The PALETTE study collected patient reported outcomes using the European Organisation for the Research and Treatment of Cancer (EORTC QLQ-C30) (version 3) questionnaire, global health status/quality of life score and EQ5D at baseline, and weeks 4, 8, and 12[10, 12]. There was good compliance with the completion of the QoL outcomes throughout the duration of the study, with 81% completion at week 12. For the global health status there was no difference found between pazopanib and placebo across the 12 weeks, where a decline was noted across both groups. Subscales for diarrhoea, fatigue, nausea and vomiting were all worse on pazopanib[10, 12].

Safety evidence

This is an on-label use which has been considered by the UK medicines regulator to have an acceptable safety profile. In the PALETTE study when compared with placebo (n=123), pazopanib (n=239) patients experienced higher rates of grade 3 or greater fatigue (13% versus 5%), diarrhoea (5% versus 1%), hypertension (7% versus 3%), and anorexia (6% versus 0%). There was one death reported in the pazopanib group that may have been related to the pazopanib or antibiotics[10].

Comparator evidence

The main comparators relevant within NHSScotland are trabectedin and ifosfamide, but there is no published evidence comparing pazopanib with these treatments. Other potential comparators include gemcitabine as single agent or in combination with docetaxel, eribulin and oral cyclophosphamide but these are not included in the review due to limited data availability.

Evidence in support of trabectedin comes from a phase III randomised, open label, active controlled, parallel multicentre study (ET743-SAR-3007)[13, 14]. The primary aim was to compare the safety and efficacy of trabectedin versus dacarbazine. Patients were included if they were 15 years or older, had a confirmed liposarcoma or leiomyosarcoma that was unresectable and/or metastatic with relapse or progressive disease after prior treatment with an anthracycline and ifosfamide-containing regimen, with an ECOG performance status of 0. Patients were randomised 2:1 to receive trabectedin, starting dose 1.5 mg/m^2 body surface area (BSA) as a 24-hour intravenous (IV) infusion (n=345) versus dacarbazine, starting dose 1 g/m^2 BSA as a 20- to 120-minute IV infusion (n=173). The primary outcome was OS, and secondary outcomes include PFS[13, 14].

Evidence to support ifosfamide comes from a phase II randomised study to evaluate the safety and efficacy of two doses of ifosfamide in patients with metastatic soft tissue sarcoma given as first or second line chemotherapy. Patients were included if they have confirmed STS, excluding Ewings sarcoma, embryonal rhabdomyosarcoma, mesothelioma, paraganglioma, chondrosarcoma,

neuroblastoma and osteosarcoma. Patients with either locally recurrent or metastatic disease and ECOG PS of 0 or 1 were included. Patients were randomised 1:1 to receive either ifosfamide 5 g/m^2 BSA given as a 24-hour infusion (n=36) or ifosfamide 3 g/m^2 BSA given over 4-hours on three consecutive days (n=40) with both repeating every 3-weeks. Randomisation was stratified by centre and by treatment (first- or second-line). The outcomes included ORR, time to progression and OS.

Results

The results for the trabectedin and ifosfamide 3g/m^2 arms of their respective trials are summarised in Table 2 below.

Table 2| summary results for trabectedin[13, 14] and ifosfamide

	ET743-SAR-3007 Trabectedin n=345	EORTC STSBG Second line[a] (3 g/m^2)[b] ifosfamide n=40
Overall Survival		
Events n (%)	258 (67%)[c]	NR
Median OS	13.7 months	8.3 months
Progression-free survival		
Events n (%)	217 (63%)[d]	NR
Median PFS, months	4.2	NR
Time to progression	NR	14 weeks
Response		
ORR n (%)	23 (7%)	8%

Key: NR: not reported, OS: overall survival, PFS: progression free survival, ORR: objective response rate, DoR: Duration of response
[a]Subgroup including second line patients only
[b]Reflective of the most common dose used within NHSScotland
[c]Data cut off 5 December 2015
[d]Data cut off 16 September 2013

Risk of Bias Appraisal

The PALETTE study was assessed for bias using Cochranes risk of bias version 2 tool. Across all domains it was judged to have a low risk of bias.

Clinical effectiveness considerations

Compared with placebo, pazopanib increased median PFS, however relative effects for OS are uncertain due to the use of subsequent anti-cancer treatments.

The PALETTE study met its primary outcome, showing a statistically significant increase in PFS for pazopanib compared with placebo, 4.6 months versus 1.6 months, when used as a second or subsequent line of treatment in metastatic disease. As the treatment groups had similar baseline characteristics and the study was at low risk of bias, this seems to be a robust finding[10].

The comparison for OS did not show a statistically significant difference between the study groups, however 65% of the study population went on to receive subsequent anti-cancer treatments, which is likely to confound the OS results. Subsequent treatment in the pazopanib and placebo groups included chemotherapy (45% versus 61%), targeted therapy (9.6% versus 14%) and radiotherapy (16% versus 23%). From the placebo group 3.3% received pazopanib at a subsequent treatment line[10].

There is a lack of direct evidence comparing pazopanib with the medicines used to treat the proposed population in NHSScotland, however indirect evidence suggests similar effects for progression-free survival and overall survival

Due to the lack of head-to-head comparison with the treatments used in NHSScotland (ifosfamide, trabectedin) there is uncertainty of the comparative efficacy of pazopanib to other treatments. In previous HTA assessments, naïve (pazopanib versus ifosfamide) and unanchored matching adjusted indirect comparisons (MAIC) (trabectedin versus pazopanib) were presented[7, 15]. These analyses suggest broadly similar outcomes between pazopanib and ifosfamide or trabectedin for key efficacy outcomes. In the comparison between ifosfamide and pazopanib, time-to-progression and PFS were similar. In the comparison between trabectedin and pazopanib, similar PFS and OS were reported. Both indirect comparisons were based on naïve and unanchored comparisons, which have significant limitations including not accounting for all differences in study populations and differences in methodologies. The pazopanib comparison with ifosfamide is further limited as different outcomes (PFS and time-to-progression) were compared. This makes the relative efficacy of pazopanib compared to alternative treatments such as trabectedin and ifosfamide very uncertain. Gemcitabine plus docetaxel was not considered as a comparator in the proposed population as it is likely to have limited use in the older or frailer population that would receive pazopanib.

The safety profile for pazopanib is well-characterised for this on-label use and is different to standard chemotherapy treatments.

The pazopanib adverse event profile appears to include substantially less haematological toxicity compared to ifosfamide treatment in the second-line setting; however, there is no head-to-head comparison. Serious adverse effects have been noted with pazopanib, including grade 3 or greater fatigue, diarrhoea, hypertension, loss of appetite, nausea and vomiting[10].

The impact of pazopanib on HRQoL relative to the key comparators is uncertain. Data from the PALETTE study, versus placebo, is also uncertain due to a drop in compliance with assessments. The results broadly suggested a similar decline in HRQoL for both patient groups. HRQoL data is only available for 12 weeks therefore it is uncertain how long-term treatment effects impact the overall HRQoL[10, 12].

There are some differences between the PALETTE study and real-world data, however results are likely generalisable.

The NHSScotland Cancer Medicines Outcomes Program - Public Health Scotland (CMOP-PHS) provided a real word data report of the treatment of adults with soft tissue sarcoma following

prior chemotherapy[16]. This report showed 39 patients were treated in the second or subsequent line setting for STS over the 2-year review period and there were no patients treated who had progressed within 12 months of (neo) adjuvant therapy. Findings of the report should be interpreted with caution due to data limitations relating to subtypes of STS and the sample size. The median age (56 years), pazopanib treatment duration (4.8 months, IQR 3.7 to 11 months) and subsequent treatments reported, in the NHSScotland real-world data are similar to those reported for the PALETTE study. The report showed that 13 (33%) patients, in the eligible population, were being treated with the proposed medicine[16]. Access to treatment with pazopanib was likely through individual patient requests in some health boards. The patient group aligned with the published evidence and similarities across the baseline characteristics and outcomes may provide reassurance that the evidence reported in the PALETTE and other studies are generalisable to the Scottish population.

A study using real-world data from the Italian national registry found the median time with pazopanib treatment for patients with advanced STS was similar to that on the PALETTE study, 106 days compared to 114 days respectively[10]. This study included patients with a median age of 59 years and 651 patients received pazopanib as second line treatment and 703 in third line treatment. This prospective study showed that patients who had a PS of 0 rather than a PS of 1 to 2 remained on treatment longer.

There are some differences between the PALETTE study and the NHSScotland populations, however the results are likely generalisable. The study included a 60% European population, where healthcare systems follow similar treatment pathways, including use of first-line doxorubicin, which aligns with practice in NHSScotland.

Patients included in the PALETTE trial were PS 0 to 1 which aligns with the proposal criteria. The real world data report showed those treated with pazopanib, compared to all other treatments, had an older median age, 66 versus 53.5 years[16]. Pazopanib is an oral treatment with a reduced appointment burden and may be preferable in an older and frailer population.

4. Patient group summary

We received a statement from Sarcoma UK who are a registered charity. Sarcoma UK reported 0.12% of their annual funding came from the pharmaceutical industry in 2026. A representative from Sarcoma UK attended the NCMAG council meeting. The key points from the Sarcoma UK statement include:

Soft tissue sarcoma is a rare and serious cancer associated with poor outcomes and a substantial burden on patients and their families. Patients experience significant physical symptoms such as pain, fatigue and reduced mobility, alongside considerable mental health impacts driven by uncertainty and isolation. Financial strain is also common, as the disease and its treatment can limit individuals' ability to work and maintain income.

Current chemotherapy treatments are often described as highly burdensome, due to their side effect profiles, frequent hospital visits and long recovery periods. Pazopanib, an oral treatment,

may offer a more manageable alternative for some patients, reducing the need for hospital-based care and associated travel while supporting maintenance of daily activities. Although there are side effects with pazopanib, patients report a willingness to tolerate these in exchange for improved convenience and reduced disruption, with potential benefits also extending to carers through a lower overall care burden.

5. Benefit-risk balance

Pazopanib, for the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma who have received prior chemotherapy for metastatic disease or who have progressed within 12 months of (neo) adjuvant therapy, is on-label and the UK medicines regulator has judged the regimen to have a favourable benefit-harm balance[9]. Pazopanib has been shown to improve median PFS compared with placebo. There is a lack of direct evidence comparing pazopanib to other available treatment options. Pazopanib has a different mechanism of action, administration (oral versus intravenous) and safety profile compared to the alternative treatment options.

6. Council Review |Clinical benefit-risk balance evaluation

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

7. Economic Evidence Review Summary

Economic Overview

A literature search was conducted and a cost-effectiveness publication which evaluated pazopanib for the treatment of advanced STS was found[13]. The researchers conducted a cost-utility analysis. A variation of the model used in this publication was provided by the manufacturing pharmaceutical company of the originator product. Inputs have been updated where appropriate to generate the results to support this assessment.

Type of economic evaluation

A cost-utility analysis was used for the economic evaluation over a time horizon of 10 years. A partitioned survival analysis approach was used in the model, where patients transitioned between the following health states: progression-free, progressed disease and death.

Population, intervention, comparator and outcomes

- The population used in the study were patients with advanced STS who had received prior treatment with chemotherapy and were eligible for second- or subsequent line treatment with pazopanib or chemotherapy. This was aligned with the population of the PALETTE study.
- The intervention was pazopanib, administered orally at a daily dosage of 800mg.
- The comparators included:

  - Best supportive care (BSC): This was included in the economic analysis to consider patients not suitable or eligible for pazopanib.
  - Ifosfamide administered intravenously: 5g/m^2 BSA once every three weeks. Concomitant mesna administered intravenously alongside ifosfamide.
  - Trabectedin administered intravenously: 1.5mg/m^2 BSA once every three weeks.

- As a cost-utility analysis was performed, health outcomes were measured in terms of quality-adjusted life-years (QALYs). These were informed by the clinical evidence in the PALETTE study and the literature.
- EQ-5D data were collected in the PALETTE study only at baseline and 4 weeks, and cancer-specific questionnaire EORTC-QLQ30 data were collected at 8 and 12 weeks. The EORTC-QLQ30 data were mapped to EQ-5D. The full EQ-5D results were used to generate the utility values. Given that the PALETTE study collected health outcomes data for placebo and pazopanib only, the utility values were adjusted to be made suitable in the comparison versus ifosfamide and trabectedin.
- For the progression-free state, utility values were 0.681 for pazopanib and 0.679 for BSC. For the progressed disease health state, decrements of 0.235 and 0.250 were applied for pazopanib and BSC respectively, giving mean health state utility values of 0.446 for pazopanib and 0.429 for BSC. As the PALETTE study assessed pazopanib versus placebo only, the utility values for ifosfamide and trabectedin were assumed to be the same as pazopanib.
- Disutility decrements due to adverse events were also included in the analysis, and the evidence for this was sourced from the PALETTE study and the literature.

Costs

Costs included were medicine acquisition (up to time to progression), administration, adverse event costs and 'other' one-time costs associated with treatment initiation and disease progression, and direct costs for patients in the progression-free and progressed disease health states. Monitoring costs were not included because they were assumed to be equivalent between treatments. Confidential NHSScotland National Framework prices for off-patent medicines were used (accessed May 2026). The cheapest available prices were used for each medicine.

The administration cost for intravenous medicines was based on delivery of complex chemotherapy. A weighted average was calculated across costs for inpatient stay, outpatient and day case treatments to generate a unit cost for administration (NHS National Reference costs 2024-25).

The costs associated with adverse events were based on initial calculations of NHS National Reference costs 2010-11, NHS Trusts and Primary Care Trusts combined. These were inflated to 2023-24 prices. Adverse event incidence for pazopanib and BSC were sourced from the PALETTE study, and from the literature for ifosfamide and trabectedin. 'Other costs', which included health

state-related costs were calculated or sourced from the literature or PALETTE study and were also inflated to 2023-24 prices.

All costs and health outcomes were discounted at an annual rate of 3.5%.

Results

All figures in the cost-utility analysis exclude VAT.

Based on medicine acquisition costs alone, pazopanib was more costly per patient than BSC but cost-saving versus ifosfamide and trabectedin. When total costs are accounted for, including medicine acquisition, administration, adverse event and other costs, pazopanib was cost-saving versus all comparators. These savings were largely driven by differences in post-progression health state costs. Pazopanib also generated more QALYs per patient than all comparators, ranging between 0.031 versus trabectedin and 0.097 versus BSC. Therefore, pazopanib dominated all comparators with lower costs and better health outcomes.

Table 3 | Summary of cost-effectiveness results (confidential price, excluding VAT)

Cost category	Medicine acquisition (£)	Medicine administration (£)	Adverse event[A] (£)	Other costs[B] (£)	Total costs per patient (£)	Total LYs per patient[C]	Total QALYs per patient[D]	ICER (£/QALY)
Pazopanib	CIC	0	336	15,032	CIC	1.375	0.692	
BSC	0	0	72	18,970	19,042	1.261	0.596	
Ifosfamide	CIC	9,519	240	15,647	CIC	1.336	0.652	
Trabectedin	CIC	4,008	3,297	15,644	CIC	1.334	0.662	
Difference versus BSC	CIC (cost-increasing)	0	264 (cost-increasing)	-3,938 (cost-saving)	**CIC (cost-saving)**	**0.114**	**0.096**	**Dominant[E]**
Difference versus Ifosfamide	CIC (cost-saving)	-9,408 (cost-saving)	96 (cost-increasing)	-726 (cost-saving)	**CIC (cost-saving)**	**0.039**	**0.040**	**Dominant**
Difference versus Trabectedin	CIC (cost-saving)	-3,897 (cost-saving)	-2,961 (cost-saving)	-722 (cost-saving)	**CIC (cost-saving)**	**0.041**	**0.030**	**Dominant**

Abbreviations: BSC = best supportive care, CIC = commercial in confidence, ICER = incremental cost effectiveness ratio, LY = life year, QALY = quality adjusted life year

[A] Rates of grade 3 and above adverse events were included in the costing, where a minimum 5% patient prevalence was recorded for at least one treatment, and the adverse event was expected to incur notable hospital cost.

[B] 'Other' costs included one-time costs associated with therapy initiation and disease progression, and monthly direct costs according to patient health state (i.e. progression-free or progressed disease)

[C] Total life year gains have been presented to show differences in survival outcomes between treatments

[D] QALYs were calculated using the clinical evidence in the original 2012 evaluation conducted by the manufacturing company.

[E] When an intervention is dominant, it is cost-saving and produces better health outcomes than the comparator

Sensitivity Analysis

Sensitivity analyses were conducted to explore uncertainty surrounding parameters used in the model. These included probabilistic and scenario analyses.

Scenario Analysis

In scenario analysis, a range of inputs that may affect cost-effectiveness outcomes were explored. These included the following:

- Changing the distribution curve to extrapolate progression-free survival
- Adjusting the hazard ratios for progression-free survival in the comparator arms to their lower and upper bounds of 95% confidence interval
- Varying the cost of AEs by ±50% of their base case values
- Varying 'other' costs by ±50% of their base case values
- Varying disutility values by ±50% of their the base case values
- Applying 5-year time horizon

In results versus BSC, pazopanib dominated in all scenarios. There were cost savings in every scenario and health outcome gains ranged between 0.070 and 0.180 QALYs.

In results versus ifosfamide, pazopanib dominated in most scenarios. There were cost savings in every scenario and incremental health outcomes ranged between 0.026 reduction and 0.065 increase in QALYs. The only scenario in which pazopanib demonstrated worse health outcomes was the one in which the hazard ratio for progression-free survival in ifosfamide was below 1, that is ifosfamide had better survival outcomes than in the base case.

In results versus trabectedin, pazopanib dominated in most scenarios. There were cost savings in every scenario and incremental health outcomes ranged between 0.018 reduction and 0.056 increase in QALYs. The only scenario in which pazopanib demonstrated worse health outcomes was the one in which the hazard ratio for progression-free survival in trabectedin was below 1, that is trabectedin had better survival outcomes than in the base case.

An additional scenario was tested where survival outcomes were set equal across all treatments. In this scenario, pazopanib had higher QALYs versus ifosfamide and trabectedin due to lower AE disutility decrements and therefore dominated those comparators. However, compared to BSC, pazopanib had lower QALYs of 0.025 due to a worse AE profile.

Probabilistic Sensitivity Analysis

Probabilistic sensitivity analysis involves varying all model inputs simultaneously and randomly according to their maximum and minimum expected ranges. This generates 1,000 iterations which represent the full range of possible ICER outcomes.

In results, pazopanib demonstrated 100% probability of being cost-saving versus all comparators. However, it demonstrated a 90% probability of generating higher incremental QALYs than BSC, 70% probability versus ifosfamide and 75% probability versus trabectedin. In the remaining iterations, pazopanib generated marginally lower QALYs than the comparators, with a maximum reduction in QALYs of 0.209 versus BSC, 0.138 QALYs versus ifosfamide and 0.124 QALYs versus trabectedin.

Cost-effectiveness considerations

Generalisability of the cost-comparison

The dosing schedule of pazopanib reflects the proposed dosing in NHSScotland. NHSScotland National Framework prices for medicines were considered in confidence to increase the generalisability of the net costs. Where appropriate NHS reference prices were not available, inflation adjustments were made using health price inflation factors. This helped improve the external validity to NHSScotland.

Limitations of the cost-comparison

Direct clinical evidence versus ifosfamide and trabectedin were not available

The PALETTE study was the primary source of health outcomes data used in the economic analysis. However, as there was no direct clinical evidence comparing pazopanib to ifosfamide or trabectedin, an accurate utility value could not be applied for ifosfamide or trabectedin. Therefore, there is uncertainty surrounding true health outcomes and ICER results, particularly where QALY gains are marginal.

Uncertainty surrounding 'other' costs

The unit costs provided by the manufacturer for 'other' costs were retained and inflated to current prices. Health state-specific 'other' costs were based on monitoring resources, supportive care, concomitant medications, treatment of STS-related AEs, home and hospice care. However, as data were limited on costs of treatment for STS patients, the company generated estimates based on an unpublished retrospective cohort study. Conducting rigorous methodology to generate updated estimates was not feasible within the scope of this analysis.

Summary

There is a high degree of uncertainty in the direction and magnitude of the overall QALY gain. As no alternative utility sources were available, it was not possible to explore the effect on QALY gains, particularly in results versus ifosfamide and trabectedin. Although pazopanib shows a high probability of being cost-saving versus all comparators, this is largely dependent upon savings in 'other' costs, where there is some uncertainty.

Council review | Cost-effectiveness evaluation

After considering the available evidence, the Council were satisfied with the cost effectiveness of the proposed use.

8. Service Impact

Pazopanib is an oral therapy which, when compared to current treatments of intravenous trabectedin or ifosfamide would reduce the burden for hospital setting administration of IV chemotherapy, including nursing and pharmacy capacity and chair time. This treatment could displace or delay current second-line options or subsequent treatment lines and may allow for an additional treatment option in this patient group.

9. Budget Impact

The total estimated number of new patients nationally expected to routinely access pazopanib for the proposed use on an annual basis is 5, based on NHSScotland real-world data from the CMOP-PHS report which indicates that, on average, approximately 5 patients each year receive 'other' medicines for second or subsequent-line treatment of STS. This category includes ifosfamide and trabectedin, amongst other treatments[16].

A budget impact was calculated using only medicine acquisition costs with value added tax applied (VAT). This used the same dosing for pazopanib, trabectedin and ifosfamide as in the cost-comparison analysis.

The estimated results for the budget impact suggest a budget decrease. The uptake is assumed to remain constant in subsequent years.

Budget impact costs were calculated over the full time on treatment for the regimens. Discontinuation and mortality rates were not included.

NCMAG is unable to publish the budget impact using confidential pricing due to commercial-in-confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with PAS contract pricing.

10. Acknowledgements

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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