selpercatinib hard capsules (Retsevmo®)

Eli Lilly and Company

06 June 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the orphan equivalent medicine process

selpercatinib (Retsevmo®) is accepted for restricted use within NHSScotland.

Indication under review: as monotherapy for the treatment of adults and adolescents 12 years and older with advanced *RET* fusion-positive thyroid cancer who are radioactive iodine-refractory (if radioactive iodine is appropriate).

SMC restriction: patients who require systemic therapy who have not previously received systemic therapy.

In an open-label, single-arm, phase I/II study in adult patients with RET fusion-positive thyroid cancer, 89% of patients who received selpercatinib achieved an objective response.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

SMC has previously issued advice (SMC2370) for selpercatinib for the treatment of adults with advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with lenvatinib and/or sorafenib. This advice remains valid.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Selpercatinib is an inhibitor of the rearranged during transfection (RET) receptor tyrosine kinase. It inhibits wild-type RET and multiple mutated RET isoforms as well as vascular endothelial growth factor receptor (VEGFR)-1 and VEGFR-3.[1] The recommended dose of selpercatinib is 120 mg (<50 kg body weight) or 160 mg (≥50 kg body weight) twice daily, administered orally. Treatment should be continued until disease progression or unacceptable toxicity. For more information please see the Summary of Product Characteristics (SPC).[1]

In September 2021, selpercatinib was accepted for use by SMC on an interim basis for the treatment of adults with advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib (SMC2370). This submission represents an extension to this indication to include adults and adolescents 12 years and older with advanced *RET* fusion-positive thyroid cancer who are radioactive iodine-refractory (if radioactive iodine is appropriate) and who have not previously received systemic therapy.[1]

1.2. Disease background

Thyroid cancer is a rare type of cancer with various subtypes, representing about 1% of all malignancies. The most common are the differentiated cancers, papillary thyroid cancer (80% to 85% of cases) and follicular thyroid cancer (10% to 15% of cases). Rarer, more aggressive forms include poorly differentiated subtypes and anaplastic thyroid cancer (5% to 10% of cases). RET gene fusions are present in approximately 6% to 9% of papillary thyroid cancers and 6% of poorly differentiated subtypes but are not frequently associated with follicular or anaplastic thyroid cancers. The clinical course of RET fusion-positive thyroid cancers can vary considerably; some cases can be cured with surgery whilst others are aggressive, metastatic, and are associated with high mortality. There is also variation between adult patients and children. Although very rare, cases in children tend to be more aggressive and are diagnosed at more advanced stages of disease.[2, 3]

1.3. Company proposed position

Adults and adolescents aged 12 years and older with thyroid cancer who require systemic therapy who have not previously received systemic therapy.

1.4. Treatment pathway and relevant comparators

Standard initial treatment for thyroid cancer includes surgery and radioactive iodine. For the treatment of patients with progressive, locally advanced or metastatic differentiated thyroid cancer, refractory to radioactive iodine, there are two available treatments: lenvatinib (SMC1179/16) and sorafenib (SMC1055/15). Lenvatinib is the preferred option if indicated.[2, 4]

1.5. Category for decision-making process

Eligibility for interim acceptance decision option

Selpercatinib has conditional marketing authorisation from the Medicines and Healthcare Products Regulatory Agency.

Eligibility for a PACE meeting

Selpercatinib meets SMC orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of selpercatinib for the treatment of RET fusion-positive thyroid cancer comes from LIBRETTO-001. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies[2, 5]

Criteria	LIBRETTO-001
Study design	International, single-arm, open-label, phase I/II study.

Eligible patients	• 18 years of age or older (12 years or older in some countries)
	• Patients with a locally advanced or metastatic solid tumour who:
	  ○ Have progressed on or are intolerant to standard therapy
	  ○ No standard therapy exists or would be unlikely to tolerate/benefit from standard therapy (according to investigator)
	  ○ Decline standard therapy.
	• RET alteration (fusion or mutation). RET alterations were not required initially, but only after dose escalation proceeded above 20 mg twice daily of selpercatinib. The subgroup of interest for this submission are patients with RET fusion positive thyroid cancer.
	• Measurable or non-measurable disease (as per RECIST 1.1 or RANO).
	• ECOG performance status 0 to 2 or LPS ≥ 40% (age < 16 years) with no sudden deterioration in preceding 2 weeks.
	• No previous treatment with RET inhibitor.

Treatments	In phase 2 of the study, nearly all patients received the recommended dose of 160 mg orally twice daily. Patients continued treatment until disease progression, death, unacceptable toxicity, or withdrawal of consent. Patients with documented disease progression could continue selpercatinib if they were deriving clinical benefit.
Randomisation	Not applicable.
Primary outcome	Objective response (complete response or partial response) as determined by independent review committee according to RECIST version 1.1 criteria
Secondary outcomes	DOR, PFS, OS.
Statistical analysis	Efficacy analyses were performed in two analysis sets: patients with RET fusion-positive thyroid cancer that have had no prior systemic therapy and/or other systemic therapy other than radioactive iodine; patients with RET fusion-positive thyroid cancer previously treated with systemic therapy (lenvatinib, sorafenib) or other systemic therapy. Patients in both sets had received at least one dose of selpercatinib and had at least 6 months of follow-up time from first dose of selpercatinib.

Abbreviations: DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; OS = overall survival; PFS = progression-free survival; RANO = Response Assessment in Neuro-Oncology; RECIST 1.1 = response evaluation criteria in solid tumours version 1.1; RET = rearranged during transfection.

At the 13 January 2023 cut-off for LIBRETTO-001, in 65 patients with RET fusion-positive thyroid cancer who received selpercatinib, the percentage who had an objective response was 89% and in those who had not received previous systemic therapy (n=24) it was 96%. See Table 2.2 for details.

Table 2.2. Key efficacy results from LIBRETTO-001 in the RET fusion-positive thyroid cancer systemic therapy naïve population and any-line population (data-cut 13 January 2023).[2, 6, 7]

	RET fusion-positive TC Systemic therapy naïve (n=24)	RET fusion-positive TC Any-line population (n=65)
Objective response rate (assessed by IRC as per RECIST 1.1)		
%	96%	89%
Best overall response (assessed by IRC as per RECIST 1.1)		
Complete response	21%	15%
Partial response	75%	74%
Stable disease	4.2%	11%
Progressive disease	0	0
Not evaluable	0	0
Duration of response (assessed by IRC)		
Median follow-up	17.8 months	*
Responders	*	*
Median DOR	NE	*
DOR rate at 24 months	91%	*
Progression-free survival (assessed by IRC)		
Median follow-up	24.9 months	*
Events	*	*
Median PFS	NE	*
PFS rate at 24 months	95%	*
Overall survival		
Median follow-up	38.7 months	*
Events	*	*
Median OS	NE	*
OS rate at 24 months	94%	*

Abbreviations: DOR = duration of response; IRC = independent review committee; NE = not estimable; OS = overall survival; PFS = progression-free survival; RECIST 1.1 = Response evaluation criteria in solid tumours version 1.1; RET = rearranged during transfection; TC = thyroid cancer. * results considered confidential by the company

2.2. Health-related quality of life outcomes

Exploratory, post-hoc health-related quality of life (HRQoL) data were provided by the submitting company. However, given that LIBRETTO-001 is a single-arm, open-label study and these data were exploratory and post-hoc, results should be interpreted with caution.[8]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing selpercatinib with lenvatinib, sorafenib, and best supportive care, the submitting company presented a naïve indirect treatment comparison. This has been used to inform the economic base case.

Table 2.2: Summary of indirect treatment comparison

Criteria	Overview
Design	Naïve indirect treatment comparisons.
Population	Adults with locally advanced or metastatic thyroid cancer, refractory to radioactive iodine.
Comparators	Lenvatinib, sorafenib, best supportive care.
Studies included	LIBRETTO-001[2, 9], SELECT[10], and DECISION[11]
Outcomes	PFS and OS
Results	Selpercatinib was associated with improved PFS and OS compared with lenvatinib and best supportive care, and selpercatinib was associated with improved PFS compared with sorafenib but there was no evidence of a difference for OS.

Abbreviations: OS = overall survival; PFS = progression-free survival.

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

Evidence to support the safety of selpercatinib comes from the thyroid cancer safety population of LIBRETTO-001, defined as all patients with RET fusion-positive thyroid cancer who received at least one dose of selpercatinib (n=54, data-cut 15 June 2021). Most patients in this population (94%) had a selpercatinib starting dose of 160 mg. Any treatment-emergent adverse event (TEAE) related to selpercatinib was reported by 98% (53/54) of patients; 68% had a grade ≥3 TEAE and 32% were related to selpercatinib; 37% had a serious TEAE and 5.6% were related to selpercatinib; 3.7% had a TEAE that led to discontinuation and 0 were related to selpercatinib.[2]

The most frequently reported TEAEs of any grade with an incidence ≥20% in the thyroid cancer safety population were: dry mouth (46%), fatigue (46%), hypertension (39%) constipation (37%), abdominal pain (32%), oedema (26%), nausea (26%), vomiting (26%), rash (26%), arthralgia (24%), back pain (24%), hypocalcaemia (24%), headache (22%), pyrexia (22%), ALT increased (20%), decreased appetite (20%), lymphopenia (20%). The most common TEAEs grade ≥3 were hypertension (17%), hyponatraemia (7.4%), and lymphopenia (7.4%).[2]

The safety profile of selpercatinib in patients with thyroid cancer not previously treated with systemic therapy other than radioactive iodine is consistent with the overall safety population and with what has previously been reported. Longer-term follow-up from LIBRETTO-001 is required.[2]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Selpercatinib is the first medicine to be approved specifically for RET-altered thyroid cancer.
- ORR, as assessed by independent review committee and using RECIST 1.1 criteria, was 96% in adult patients with treatment naïve RET fusion-positive thyroid cancer (proposed positioning population); 21% achieved complete response and 75% achieved partial response. Results were consistent with investigator-assessed analysis, which is reassuring, and even the lower boundary confidence interval represents a reasonable treatment effect. Overall, these results can be considered promising. [2]

4.2. Key uncertainties

- LIBRETTO-001 is a single-arm, open-label phase I/II study, and such studies are prone to various biases. The lack of a control group is an important limitation; the treatment effect of selpercatinib relative to active comparators is therefore highly uncertain.[2]
- Data from LIBRETTO-001 are immature; median duration of response, PFS, and OS could not be estimated. Whilst ORR is an appropriate primary outcome for a phase I/II study and can demonstrate anti-tumour activity, it may be unclear to what extent ORR corresponds to more robust measures of clinical benefit such as survival.[2, 12]
- The relevant sample sizes for treatment naïve patients (n=24) and patients at "any-line" (n=65) were very limited.[2]
- The results of the naïve indirect treatment comparisons are highly uncertain. Naïve indirect treatment comparisons are inherently at high risk of bias. There were limitations with heterogeneity, immature data, wide confidence intervals, the populations differed from the company's proposed positioning and there were no quality of life or safety outcomes measured. These limitations are largely due to the available data; no alternative approaches could provide more robust results.
- No data have been provided to support the use of selpercatinib in adolescent patients as per the proposed positioning.
- Quality of life data from LIBRETTO-001 were exploratory, post-hoc and potentially biased by the single-arm, open-label study design and are therefore highly uncertain.

4.3. MHRA conditional marketing authorisation specific obligations

The marketing authorisation holder will submit final data from LIBRETTO-001 (December 2025, systemic treatment naïve patients) and LIBRETTO-121 (June 2025) to further confirm the efficacy and safety of selpercatinib in the treatment of patients with RET fusion-positive thyroid cancer.

4.4. Clinical expert input

Clinical experts consulted by SMC considered that selpercatinib fills an unmet need in this therapeutic area. They consider it to be a therapeutic advancement for the small group of patients with RET fusion-positive disease since selpercatinib is a highly targeted and effective treatment. They also suggest that selpercatinib could have a favourable safety profile over currently available treatments and would likely displace lenvatinib in eligible patients.

4.5. Service implications

Selpercatinib is an oral treatment which is a convenient route of administration for both patients and the service. No service implications are anticipated with the introduction of this treatment.

Diagnostic test required to identify patients eligible for treatment: contact local laboratory for information.

5. Patient and Clinician Engagement (PACE)

A patient and clinician engagement (PACE) meeting was held to consider the added value of selpercatinib, as an orphan equivalent medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- RET fusion-positive advanced thyroid cancer is a very rare, incurable cancer that typically metastasises in the neck, bones, lungs, liver, or brain, which can cause debilitating symptoms such as bone pain, swallowing, difficulties, breathing difficulties, and potential voice changes. Patients with advanced thyroid cancer usually have already undergone one or more surgeries and possibly received radioactive iodine as well. Advanced thyroid cancer can also lead to a reduction in activities of daily living and a poorer quality of life. The psychological impact can also be substantial with low mood, anxiety, and fatigue commonly reported. In very rare cases, RET fusion-positive advanced thyroid cancer can affect adolescent patients.

- Many patients with advanced thyroid cancer have had positive results with the currently available treatments lenvatinib and sorafenib. However, these medicines can cause significant and challenging side effects for patients so there is still an unmet need in this area

- The benefits of selpercatinib reported in clinical studies are expected to translate into improved quality of life for patients, including long-lasting responses to treatment, better symptom control, and management of pain. This would in turn allow patients to maintain independence and to spend more time with family and friends and could allow some patients to return to work and other family or social commitments. As a highly targeted medicine, PACE participants expect selpercatinib to be better tolerated than currently available treatments. Fewer overall side effects and more manageable minor side effects would improve quality of life and again enable patients to return to normal daily activities such as work or education.

- Family members and carers understandably suffer from hardship and distress when a loved one has advanced thyroid cancer. As a terminal diagnosis, it is likely to extend to every aspect of a family member/carer's life: physical, psychological, and financial. Patients may require less care if they have better symptom control and less side effects. Patients returning to work may have financial benefits for families. Patients may be able to spend more quality time with family. Altogether, PACE participants agreed that the potential benefits of selpercatinib could translate to marked improvements in quality of life for family members and carers.

- Selpercatinib is an oral treatment which is a convenient route of administration for both patients and the service. PACE participants stated that the number of patients that would be eligible for selpercatinib each year for this indication would be very small. RET mutation testing is now routinely carried out in NHSScotland.

Additional Patient and Carer Involvement

We received a joint patient group submission from the British Thyroid Foundation and the Butterfly Thyroid Cancer Trust, both organisations are registered charities. The British Thyroid Foundation has received 2.35% pharmaceutical company funding in the past two years, with none

from the submitting company. The Butterfly Thyroid Cancer Trust has not received any pharmaceutical company funding in the past two years. Both patient groups participated in the PACE process and the key points of the joint submission have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The submitting company presented an economic case, summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	A lifetime time horizon of 35 years was used in the analysis with a weekly cycle length.
Population	The population of the economic model was stated as patients aged 12 years and over with advanced RET fusion-positive thyroid cancer who require systemic therapy (and who have not previously received systemic therapy).
Comparators	The comparators were lenvatinib, sorafenib, and best supportive care (BSC). BSC was assumed to consist of routine care and monitoring. The main comparator was lenvatinib.
Model description	A three-state partitioned survival model was used, with health states of progression-free, progressed disease and death. Patients enter the model in the progression-free health state. Patients may either remain progression-free, transition to post-progression, or transition directly to death. Patients in the post-progression state may subsequently transition to death.
Clinical data	PFS and OS data for selpercatinib were from the LIBRETTO-001 RET fusion-positive thyroid cancer any-line population (n=65, data-cut 13 January 2023). Adverse event rate data for selpercatinib were from the LIBRETTO-001 thyroid cancer safety analysis set (n=66, data-cut 13 January 2023).[2, 6, 7] The efficacy data for sorafenib, lenvatinib and BSC were obtained from the studies in the naïve indirect treatment comparison. Pseudo patient-level data were derived from the published Kaplan–Meier curves and number of event information from these studies.[13] PFS, OS and adverse event rate data for sorafenib were from the intention to treat (ITT) population receiving sorafenib in the DECISION study (n=207).[11] PFS, OS and adverse event rate data for lenvatinib and BSC were from the ITT populations receiving lenvatinib and placebo, respectively, in the SELECT study (n=261, n=131).[10] The OS data used from this study were the rank preserving structural failure time (RPSFT)-adjusted data from NICE TA535 to account for patient cross-over in SELECT.
Extrapolation	OS for all treatments was extrapolated using a piecewise exponential model. As the extrapolated OS estimates for selpercatinib and sorafenib exceeded the submitting company's clinical expert opinion, adjustment factors were applied to the OS extrapolations to align with the expert expectations. For selpercatinib an adjustment factor of 1.2 was applied from 60 months. For sorafenib an adjustment factor of 2.7 was applied from 26 months onwards. PFS for all treatments was extrapolated using a stratified Weibull model. The submitting company noted that in these models all parameters can vary by treatment and proportional hazards assumptions can be relaxed. Selpercatinib time to treatment discontinuation (TTD) was set equivalent to PFS, with the addition of the mean time from progression to treatment discontinuation as observed in the RET fusion positive systemic therapy naïve thyroid cancer population of the LIBRETTO-001

	study. Due to a lack of TTD data for active comparators, sorafenib and lenvatinib TTD was assumed equal to their respective PFS. No discontinuation was applied to BSC.
Quality of life	The utility values in the model were derived from EORTC-QLQ-C30 data collected in the RET fusion-positive thyroid cancer any-line thyroid population in the LIBRETTO-001 study mapped to the EQ-5D-3L.[14] The utility values were health state dependent and were the same for all treatments. Adverse event disutilities were applied and the utilities were adjusted for age.
Costs and resource use	Costs included in the model were medicine acquisition, administration, monitoring, adverse events, end of life and diagnostic testing. Resource use was costed using annual health state costs. Selpercatinib was subject to a dose distribution based on the recorded doses received in the LIBRETTO-001 study. Within the first treatment cycle patients received doses between 160 to 80mg twice daily. In subsequent treatment cycles, to account for dose reductions, patients were assumed to receive doses between 160mg to 10mg twice daily, such that the mean dose intensity matched that observed in the LIBRETTO-001 study.
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. A PAS discount is in place for lenvatinib and sorafenib and these were included in the results used for decision-making by using estimates of the comparator PAS price. SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present results comparing selpercatinib to lenvatinib or sorafenib due to competition law issues.

6.2. Results

The economic analysis considered both the incremental costs of implementing selpercatinib as a treatment option as well as the incremental health gains. The use of selpercatinib was estimated as generating better health outcomes for patients than any of the other included comparators.

Confidential discounts are in place for lenvatinib and sorafenib, meaning that SMC is unable to present the economic results comparing selpercatinib against these medicines, due to competition law issues.

Considering BSC as the comparator, inclusive of the PAS discount on selpercatinib, the incremental cost-effectiveness ratio was estimated as £26,702.

*Other data were also assessed but remain confidential.**

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered, and descriptions of these key scenarios are provided in Table 6.3 below. Results for the comparisons between selpercatinib and lenvatinib and sorafenib cannot be displayed due to the presence of confidential discounts. The results presented for the comparison between selpercatinib and BSC are inclusive of the PAS discount on selpercatinib.

Table 6.3: Scenario analysis results (inclusive of selpercatinib PAS)

				ICER (£/QALY)		
	Parameter	**Base case**	**Scenario**	**versus lenvatinib**	**versus sorafenib**	**versus BSC**
	Base case	-	-	CIC	CIC	26,702
1a	PFS extrapolation	Stratified Weibull	Exponential	CIC	CIC	28,197
1b			Spline two knot	CIC	CIC	29,450

2a	OS extrapolation	Piecewise exponential	Weibull	CIC	CIC	25,301
2b			Stratified Weibull	CIC	CIC	30,531
3a	Adjustment factor selpercatinib OS	Applied at 5 years using a 1.2x adjustment factor	1.4 adjustment factor to align with lower bound of 10-year clinical OS estimates	CIC	CIC	28,420
3b			1.9 adjustment factor align with lower bound of 20-year clinical OS estimates	CIC	CIC	32,283
3c			Adjustment factor removed	CIC	CIC	24,893
4	Adjustment factor sorafenib OS	Applied at 26 months using a 2.7x adjustment factor	Adjustment factor removed	CIC	CIC	26,702
5	TTD approach	Selpercatinib TTD is assumed equal to PFS, with a delay	Selpercatinib TTD is assumed equal to PFS	CIC	CIC	25,724
6	Utility values	EORTC-QLQ- to EQ-5D data	Fordham et al. 2015	CIC	CIC	27,243
7	Dose reductions	Treatment cycle 1 160 to 80mg. Treatment cycle 2+, 160 to 10mg	All patients on 160mg twice daily	CIC	CIC	34,063

Abbreviations: BSC = best supportive care; CIC = commercial in confidence; ICER = incremental cost-effectiveness ratio; KM = Kaplan–Meier; OS = overall survival; PFS = progression-free survival; QALYs = quality-adjusted life year.

6.4. Key strengths

- The included comparators in the analysis were appropriate.
- The company conducted an SLR to identify any relevant supplementary utility data.

6.5. Key uncertainties

- The OS extrapolations for selpercatinib and sorafenib were subject to overestimation compared to company clinical expert predictions, and as a result the company applied adjustment factors to reduce OS for these treatments. This approach was viewed as uncertain and scenarios testing alternative assumptions led to changes in the estimated cost-effectiveness (see Scenarios 3a, 3b, 3c and 4 in Table 6.3).
- There were limitations in the clinical data used within the economic evaluation. Selpercatinib PFS and OS data from LIBRETTO-001 were immature and had a small sample size. Additionally, efficacy data across the comparators were not fully consistent with the proposed treatment population. Data on selpercatinib were drawn from the RET fusion-positive thyroid cancer any-line population in LIBRETTO-001. Data on Lenvatinib were from the differentiated thyroid cancer any-line population in the SELECT, and data for sorafenib were from the differentiated thyroid cancer systemic therapy naïve population in DECISION. The company noted this was due to small sample sizes in the LIBRETTO-001 study and data paucity in the comparator populations from the indirect treatment comparison studies, however this remained a source of uncertainty. Thirdly, the efficacy data for comparators were obtained from the ITC, which was a naïve comparison with

multiple limitations. Finally, no data have been provided to support the use of selpercatinib in adolescent patients as per the proposed positioning. These clinical data concerns are challenging to resolve.

- The dose distribution for selpercatinib was uncertain. Within the first treatment cycle a dose distribution from 160mg to 80mg (twice daily) was applied. However, it was not clear how this was derived and whether this was due to data from the dose finding phase of LIBRETTO-001 being included in the analysis. From the second treatment cycle onwards dose reductions were applied, with these based on a relative dose intensity from LIBRETTO-001, leading to patients receiving doses between 160 to 10 mg (twice daily). The proportion receiving 160mg (twice daily) from treatment cycle 2 onwards noticeably decreased compared to treatment cycle 1. Since these data were derived from the percentage of all doses after week 4 at each dose level in LIBRETTO-001 (all thyroid cancer population), they may have been generated over a longer period, with the timepoint of application in the model potentially underestimating selpercatinib acquisition costs. Therefore, a conservative scenario was presented to understand the bound of this consideration, where all patients were costed as receiving 160mg (twice daily) (Scenario 7).

7. Conclusion

The Committee considered the benefits of selpercatinib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as selpercatinib is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted selpercatinib for restricted use in NHSScotland.

8. Guidelines and Protocols

NICE thyroid assessment and management guidelines (NG230) were published in 2022.[15]

ESMO Clinical Practice Guideline update on the use of systemic therapy in advanced thyroid cancer were published in 2019 and updated in 2022.[4]

9. Additional Information

9.1. Product availability date

31 January 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
selpercatinib	**120 or 160 mg orally twice daily**	**85,176 to 113,568**

Costs from BNF online on 5 March 2025. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 4 patients eligible for treatment with selpercatinib in year 1 and 7 patients in year 5.

SMC is unable to publish the with PAS budget impact 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 the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 10 April 2025.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium 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.