osimertinib film-coated tablet (Tagrisso®)

AstraZeneca

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

osimertinib (Tagrisso®) is accepted for use within NHSScotland.

Indication under review: in combination with pemetrexed and platinum-based chemotherapy for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

In an open-label, phase III study, addition of pemetrexed and platinum-based chemotherapy to osimertinib significantly improved progression-free survival in adults with NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.

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.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Osimertinib is a tyrosine kinase inhibitor (TKI) that inhibits epidermal growth factor receptor (EGFR) harbouring sensitising-mutations and TKI-resistance mutation T790M. It is taken orally, 80 mg once a day. In this indication it is taken in combination with pemetrexed and platinum-based chemotherapy.[1] Refer to the Summary of Product Characteristics for pemetrexed and cisplatin or carboplatin for dosing information.[2-4] Treatment should continue until disease progression or unacceptable toxicity.[1]

1.2. Disease background

Non-small cell lung cancer (NSCLC) comprises approximately 80% to 90% of lung cancers. At diagnosis, 70% to 80% of patients with NSCLC have locally advanced or metastatic disease. EGFR mutations are found in approximately 50% of Asian patients and 15% of White patients; they are more common in women, never-smokers, and the adenocarcinoma histological subtype. Central nervous system (CNS) metastases are present in about a quarter of patients with EGFR mutations at diagnosis and affect about a half of all patients within 3 years from diagnosis.[5, 6] The most common symptom is cough, but patients also suffer from dyspnoea, haemoptysis and chest pain.[7]

1.3. Treatment pathway and relevant comparators

The standard first-line treatment for advanced NSCLC with EGFR mutations is EGFR-TKIs, of which osimertinib monotherapy is currently preferred. Alternative EGFR-TKIs include gefitinib, erlotinib, afatinib or dacomitinib, all of them administered as monotherapy.[5, 6] Scottish Cancer Network clinical management pathways and clinical experts consulted by SMC indicate that osimertinib monotherapy is the current standard of care.[8] This is confirmed by data from Cancer Medicines Outcome Programme Public Health Scotland (CMOP-PHS).[9]

1.4. Category for decision-making process

Eligibility for a PACE meeting.

Osimertinib meets SMC orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Clinical evidence is from the FLAURA-2 study detailed in Table 2.1.[5, 10]

Table 2.1. Overview of relevant study.[5, 10]

Criteria	FLAURA-2 study (D5169C00001)
Study design	International, open-label, phase III study
Eligible patients	Adults (≥18 years or ≥20 years in Japan) with locally advanced or metastatic (stage IIIB to IVB) non-squamous NSCLC and EGFR mutations (exon 19 deletion or exon 21 L858R substitution) that was not amenable to curative surgery or radiotherapy. They had not previously received an EGFR-TKI or any treatment for advanced disease. They had WHO PS of 0 to 1 and life expectancy > 12 weeks.
Treatments	Osimertinib monotherapy (80 mg orally once daily) or in combination with IV pemetrexed (500 mg/m^2 on day 1 of 21-day cycle) plus four cycles of IV platinum chemotherapy (cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/minute, chosen by

	the investigator pre-randomisation, on day 1 of 21-day cycle). Treatment continued until disease progression* or unacceptable toxicity. There was no crossover.
Randomisation	Randomisation was stratified by ethnicity (Chinese-Asian versus non-Chinese-Asian versus non-Asian patients), WHO PS (0 versus 1), and method of tissue testing (central versus local). Patients were equally assigned to osimertinib-chemotherapy or osimertinib monotherapy.
Primary outcome	Progression-free survival defined as time from randomisation to progression assessed by investigator on RECIST v1.1 or death from any cause.
Secondary outcomes	Overall survival, defined as time from randomisation to death from any cause. Objective response rate, defined as complete or partial response on RECIST v1.1.
Statistical analysis	Efficacy was assessed in full analysis set, which comprised all randomised patients. Overall survival tested if primary outcome achieved in hierarchical testing strategy.

*treatment beyond progression was permitted if the investigator judged that clinical benefit continued; AUC = area under concentration-time curve; EGFR = epidermal growth factor receptor; IV = intravenous; NSCLC = non-small cell lung cancer; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1; TKI = tyrosine kinase inhibitor; WHO PS = World Health Organisation Performance Status.

At the 3 April 2023 cut-off, median follow-up for progression-free survival (PFS) was 19.5 and 16.5 months in the osimertinib-chemotherapy and osimertinib monotherapy groups, respectively. The primary outcome, investigator-assessed PFS, was significantly improved with osimertinib-chemotherapy compared with osimertinib monotherapy. At the latest interim analysis of overall survival (OS), cut-off 8 January 2024, statistical significance was not achieved at the pre-specified boundary. Objective response rate (ORR) was not formally tested. Results are detailed in Table 2.2.[5, 10]

Table 2.2: Primary and secondary outcomes of FLAURA-2 study.[5, 10]

	Osimertinib-chemotherapy	**Osimertinib monotherapy**
	N=279	**N=278**
Progression-free survival assessed by investigator on RECIST v1.1; cut-off 3 April 2023		
PFS events, n	120	166
Hazard ratio (95% CI)	0.62 (0.49 to 0.79), p<0.001	
Median PFS, months	25.5	16.7
KM estimated PFS at 24 months	57%	41%
Overall survival; cut-off 8 January 2024		
Deaths	100	126
Hazard ratio (95% CI)	0.75 (0.57 to 0.97), p=0.028	
Median OS, months	NC	36.7
KM estimated OS at 36 months	64%	50%
Objective response rate assessed by investigator on RECIST v1.1; cut-off 3 April 2023		
Objective response, n (%)	232 (83%)	210 (76%)
Complete response, n (%)	1 (0.4%)	2 (0.7%)
Partial response, n (%)	231 (83%)	208 (75%)
Odds ratio (95% CI)	1.61 (1.06 to 2.44)	
Median duration of response, months	24.0	15.3

CI = confidence interval; KM = Kaplan-Meier; NC = not calculable; OS = overall survival; PFS = progression-free survival; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

Survival without central nervous system progression (CNS PFS), assessed by blinded independent central review (BICR) in 40% of the study population with measurable and non-measurable CNS metastases at baseline, was an exploratory outcome. There appeared to be improvement with

osimertinib-chemotherapy versus osimertinib monotherapy, with a hazard ratio (HR) of 0.58 (95% confidence interval [CI]: 0.33 to 1.01). Median CNS PFS was 30.2 and 27.6 months in the respective groups.[5, 10]

2.2. Health-related quality of life outcomes

Health-related quality of life (HRQoL) was assessed using European Organisation for Research and Treatment of Cancer (EORTC) core questionnaire, QLQ-C30, and lung cancer questionnaire, QLQ-LC13. The questionnaires were completed by > 91% in both treatment arms at baseline and by ≥ 80% of patients until Week 82 (Month 19).[5]

In the osimertinib-chemotherapy group, compared with the osimertinib monotherapy group, improvement was smaller for global health status and physical function and for the symptoms, fatigue, dyspnoea and chest pain, but greater for cough, with differences in change from baseline between the groups typically less than five points (except fatigue, 6.28). In the osimertinib-chemotherapy group appetite loss increased, but decreased with osimertinib monotherapy, with a difference between groups of 7.45. The clinical relevance of these differences, which were assessed on 100-point scales, is uncertain.[5]

3. Summary of Safety Evidence

In the FLAURA-2 study, at 3 April 2023 cut-off, median exposure to osimertinib was 21.8 and 19.0 months in the osimertinib-chemotherapy and osimertinib monotherapy groups, respectively. Median exposure to cisplatin/carboplatin was 2.76 months and to pemetrexed was 8.28 months.[5]

The regulator concluded that the safety profile of osimertinib-chemotherapy appears consistent with the established adverse effects of the individual medicines and there were no new safety signals. However, the addition of chemotherapy increased the overall toxicity profile, including the rates of adverse events with at least grade 3 severity (64% versus 27%), that were serious (38% versus 19%) and that had a fatal outcome (6.5% versus 2.9%).[5]

Adverse events with at least grade 3 severity, which occurred at higher rates with osimertinib-chemotherapy than osimertinib monotherapy were mainly haematological: anaemia (20% versus 0.4%), neutropenia (13% versus 0.7%), neutrophil count decreased (11% versus 0.7%), platelet count decreased (7.6% versus 0), thrombocytopenia (6.9% versus 1.1%), febrile neutropenia (4.0% versus 0) and white blood cell count decreased (3.3% versus 0.4%). Other events occurred at rates less than 3%.[5]

In addition to haematological events (71% versus 24%), adverse events of special interest included cardiac events, which occurred at higher rates with osimertinib-chemotherapy than osimertinib monotherapy (9.4% versus 3.6%), with the difference primarily due to cardiac failure and decreased ejection fraction. Other events of special interest were interstitial lung disease and pneumonitis, which were at similar rates across the respective groups (3.3% and 3.6%).[5]

Gastrointestinal effects, of any severity, were also common, with similar rates of diarrhoea across the respective groups (44% and 41%) but there were higher rates with osimertinib-chemotherapy of nausea (43% and 10%), decreased appetite (31% and 9.5%), constipation (30% and 10%), vomiting (26% and 6.2%) and stomatitis (25% and 18%).[5]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In the FLAURA-2 study, addition of pemetrexed and platinum-based chemotherapy to osimertinib significantly improved median investigator-assessed PFS by about 8.8 months. Similar results were observed for PFS assessed by BICR. An exploratory analysis of CNS PFS in the subgroup of patients with CNS metastases at baseline suggested a possible benefit of about 2.6 months. [5, 10]
- This new indication is the first regimen to combine a EGFR-TKI with pemetrexed and platinum-based chemotherapy for first-line treatment of advanced NSCLC with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.[1]

4.2. Key uncertainties

- The study is ongoing, at the latest interim analysis (cut-off January 2024), OS data were immature and did not reach statistical significance at the pre-specified p-value.[5]
- The open-label design of FLAURA-2 may impact subjective assessments such as quality of life and safety outcomes. Also, the magnitude of differences between the groups for quality of life outcomes is of uncertain clinical relevance.[5, 10]
- The analysis of CNS PFS was limited as it was an exploratory outcome in a subgroup of patients. It may be supported by subgroup analysis of PFS that suggests a possibly greater magnitude of benefit with osimertinib-chemotherapy versus osimertinib monotherapy in those with CNS metastases compared to those without, with HR 0.47 (95% CI: 0.33 to 0.66) and 0.75 (95% CI: 0.55 to 1.03) in the respective subgroups. However, the analyses were not adjusted for multiplicity and cannot support a definitive conclusion. FLAURA-2 excluded patients with unstable CNS metastases and therefore does not provided evidence in this group.[5, 10]
- FLAURA-2 excluded patients who had ever received an EGFR-TKI, for example, osimertinib in the adjuvant setting, which is accepted by SMC (advice SMC2383). In NHSScotland, it is possible that some patients with advanced disease may differ from the FLAURA-2 study population, as they may have received adjuvant osimertinib. However, this is likely to be a small number as 70% to 80% of patients with NSCLC have locally advanced or metastatic disease at diagnosis and some patients who receive adjuvant osimertinib may never relapse.[5]
- In FLAURA-2, 64% of patients were Asian and 28% were White, which differs from the population in Scotland. However, subgroup analysis by ethnicity (Asian-Chinese versus Asian-non-Chinese versus non-Asian patients) were generally consistent with the PFS primary analysis, with HR of 0.49 (95% CI: 0.30 to 0.81), 0.76 (95% CI: 0.53 to 1.09) and 0.55 (95% CI: 0.37 to 0.83), respectively.[5, 10]
- The median age of FLAURA-2 patients was 61 years, with 61% < 65 years.[5] Subgroup analyses suggests less certainty in the benefit for older patients, however, these were exploratory subgroup analyses that cannot support definitive conclusions. CMOP-PHS data

indicated that the median age of patients undergoing first-line single-agent EGFR-TKI treatment for NSCLC was 70 years and the majority were older than the median age of FLAURA-2 patients.[9]

4.3. Clinical expert input

Clinical experts consulted by SMC considered that osimertinib in combination with pemetrexed and platinum-based chemotherapy is a therapeutic advance in the first-line treatment of adult patients with advanced NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations due to its efficacy. They note that it would be used in place of current treatments, such as osimertinib monotherapy, but may not be suitable for patients unable to tolerate chemotherapy.

4.4. Service implications

Clinical experts consulted by SMC noted that the introduction of osimertinib in combination with pemetrexed and platinum-based chemotherapy may have service implications related to resource use in day units and hospital pharmacies associated with the administration of chemotherapy, which may extend for a prolonged period for pemetrexed. There may also be an impact on General Practitioners and services that manage adverse events, however patient numbers are expected to be small.

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

5. Patient and clinician engagement (PACE)

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

The key points expressed by the group were:

- EGFR-mutated NSCLC is an incurable and progressively debilitating disease that often affects younger patients who may have jobs and caring responsibilities. Symptoms of breathlessness, chronic cough and fatigue limit the patient's ability to care for themselves and undertake activities of daily living, including work, which can lead to financial difficulties. Patients may have brain metastases, which prevent them from driving and limits their independence. Overall, it has a significant psychological impact, and many patients suffer anxiety and depression. Many patients require help from their family and carers to manage their condition and to attend hospital appointments.

- The current first-line treatment for EGFR-mutated NSCLC is TKI monotherapy with osimertinib, but it does not control the disease indefinitely, and there is an unmet need for medicines that extend progression-free survival.

- Addition of chemotherapy to osimertinib can prolong progression-free survival, including limiting the progression of brain metastases. It can give the patient a longer period when the symptoms of their disease are controlled and they can lead a more normal life where they are better able to care for themselves, undertake activities of daily living and spend time with family. If brain metastases are controlled for at least a year it may allow patients to regain their driving licence. Accessing this regimen may reassure patients that they have

received the optimal treatment for their condition. Overall, these benefits may provide some psychological relief and reduce anxiety.

- The patient's family and carers may benefit from more time when the patient is able to care for themselves, take part in activities of daily life, and spend time with them. This could provide an extended period when their caring responsibilities are reduced although, there would be an initial increase in these through the initial intensive 12 weeks of chemotherapy.

- Clinicians advised that osimertinib is likely to be used in combination with chemotherapy in line with its licensed indication. They note that this regimen may not be suitable for all, for example, some older patients and those without brain metastases may prefer to receive osimertinib as monotherapy. They noted that the chemotherapy course and additional visits to manage side effects would be associated with increased medical, nursing and pharmacy resources, although, patient numbers are expected to be small.

- Patients would attend hospital to receive additional intravenous chemotherapy and may need additional visits to manage side effects. However, many patients are happy to undertake this to obtain prolonged progression-free survival.

Additional Patient and Carer Involvement

We received patient group submissions from Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum. Roy Castle Lung Cancer Foundation is a registered charity. The Scottish Lung Cancer Nurses Forum is an unincorporated organisation. Roy Castle Lung Cancer Foundation has received 7.6% pharmaceutical company funding in the past two years, including from the submitting company. The Scottish Lung Cancer Nurses Forum has not received any pharmaceutical company funding in the past two years. Representatives from the Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum participated in the PACE meeting. The key points of the submissions from both organisations have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	20 years
Population	Adult patients with previously untreated locally advanced or metastatic NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.
Comparators	Osimertinib monotherapy
Model description	A de novo, cohort-based, partitioned survival model was used with three health states: progression-free (PF), progressed disease (PD) and death.
Clinical data	PFS, OS, safety data and patient characteristics were taken from the FLAURA-2 study.[10] Estimates of subsequent treatments from the FLAURA-2 study were adjusted by the submitting company in consultation with clinical experts.
Extrapolation	Long-term OS and PFS for osimertinib plus chemotherapy and osimertinib monotherapy were extrapolated using parametric survival modelling. Curve selection was based on goodness of fit statistics, visual fit and clinical plausibility. This resulted in the selection of the following

	parametric models to estimate curves for OS, PFS and time-to-treatment discontinuation (TTD): **Osimertinib monotherapy** / **Osimertinib plus chemotherapy** **OS**: 2-knot hazard spline / 2-knot normal spline **PFS**: Weibull / Weibull **TTD**: Gamma / osimertinib: Gompertz pemetrexed (chemotherapy): Exponential
Quality of life	The model base case implements EQ-5D data which were collected in the FLAURA-2 trial to inform the PFS state utility values. For the PD state, the utility value (0.64) was sourced from a real-world study of health state utilities in Canadian patients with lung cancer (Labbé et al. 2017).[11] Health state utilities were age-adjusted. Disutilities due to adverse events were applied to the first model cycle. Disutility values and adverse event durations were obtained from the TA654 NICE submission.[12]
Costs and resource use	Costs included medicine acquisition and administration costs, management of adverse events, health state unit costs and resource use costs for progression-free and progressed disease health states, subsequent treatment, treatment monitoring, CNS metastases related costs (awaiting confirmation) and terminal care costs.
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 this PAS, a discount was offered on the list price of osimertinib.

6.2. Results

The base case results are presented in Table 6.2. Using PAS prices for osimertinib, the estimated incremental cost-effectiveness ratio (ICER) is £10,914 per quality-adjusted life-year (QALY) gained for osimertinib plus chemotherapy compared to osimertinib monotherapy.

Table 6.2 Base case results (with osimertinib PAS)

	ICER (£/QALY)
osimertinib plus chemotherapy	-
osimertinib monotherapy	£10,914

Abbreviations: ICER= incremental cost-effectiveness ratio; PAS = patient access scheme; QALY= quality adjusted life year

6.3. Sensitivity analyses

To explore areas of uncertainty the company conducted deterministic sensitivity analysis, probabilistic sensitivity analysis and scenario analysis. These analyses suggested that economic results were most sensitive to alternative survival projection assumptions and the progressed state utility value. A range of sensitivity and scenario analyses were considered, and descriptions of these key scenarios are provided in Table 6.3 below.

Table 6.3 Sensitivity and scenario analysis results (PAS price)

	Parameter	Base case	Scenario	ICER (£/QALY)
	Base case			£10,914
1	Time horizon	20 years	10 years	£11,602
2	Cost of wastage	Excluded	Included	£13,724
3	Discount rate	3.5%	1.5%	£10,235
4	Utility source		FLAURA-2	£11,438

	Parameter	Base case	Scenario	ICER (£/QALY)
5		FLAURA2 (PF); Labbé et al. (PD 0.640)	FLAURA PF and FLAURA-2 PD	£12,126
6	PFS extrapolation	Weibull	Gamma (osimertinib)	£11,091
7			Gompertz (osimertinib plus chemotherapy)	£14,730
8	OS extrapolation	osimertinib monotherapy: 2-knot hazard spline; osimertinib plus chemotherapy: 2-knot normal spline	2 spline odds (both arms)	£13,928
9			Weibull (both arms)	£8,718
10			Gamma (both arms)	£8,635
11			2-spline normal (both arms)	£12,549
12			3 spline odds (osimertinib monotherapy)	£19,172
13	TTD survival	osimertinib monotherapy: Gamma; osimertinib plus chemotherapy: Gompertz pemetrexed (chemotherapy): Exponential	Osimertinib plus chemotherapy and osimertinib extrapolation – Gen gamma	£4,362
14			Osimertinib extrapolation – Weibull	£13,461
15			Osimertinib plus chemotherapy: Gamma	£30,831
16	PFS source	BICR	Investigator	£12,731
17	Administration cost of chemotherapy	Included	Excluded	£1,192
18	Treatment waning	No treatment waning	HR= 1 after 2 years	£14,814
19			HR= 1 after 3 years	£13,592
20	Combined scenario		Utility values using FLAURA-2 PF and PD and TTD in both arms using gamma	CIC
21	Combined scenario		Utility values using FLAURA PF and FLAURA-2 PD and TTD in both arms using gamma.	CIC
22	Combined scenario		Utility values using FLAURA-2 PF and PD, TTD in both arms using gamma and OS using 2 spline normal	CIC

Abbreviations: BICR, blinded independent central review, BSC = best supportive care; CIC = commercial in confidence; HR = hazard ratio; Incr. = Incremental; ICER =incremental cost-effectiveness ratio; OS = overall survival; PF = progression-free; PD = progressed disease; PFS = progression-free survival; QALY = quality adjusted life year; RDI =Relative dose intensity

6.4. Key strengths

- The model structure was appropriate and consistent with the approach used in the assessment of other oncology treatments and the choice of comparator was appropriate.
- Availability of randomised evidence from the FLAURA-2 study to estimate the relative efficacy of osimertinib plus chemotherapy compared with osimertinib monotherapy, which was a relevant comparator.

6.5. Key uncertainties

- The model assumes a treatment effect with osimertinib plus chemotherapy for a 20-year time horizon. However, log cumulative hazard curves cross each other after the 2-year point, which could suggest that the relative risk between the treatment groups changes over time. Additionally, OS data from the FLAURA-2 study are short-term and at the second interim OS analysis data remained immature (41%). Therefore, the life year gains predicted by the model based on these data remain uncertain. Treatment waning assuming a hazard of death equal across treatment groups after 2 and 3 years was explored in scenarios 18 and 19.
- The economic model predicted a life year gain with osimertinib plus chemotherapy. However, this is based on extrapolation techniques used to predict long-term survival beyond the observed data from FLAURA-2 and sensitivity analysis showed the ICER is sensitive to the choice of survival curve. The statistical feedback received by SMC highlighted the limitations of the approach used by the company for OS curve selection, particularly for the osimertinib monotherapy arm, as there is wide variability among clinical experts consulted by the submitting company with 5-year survival estimates ranging from 10% to 40%. Alternate spline models appear closer to clinical expert survival estimate of 10% at 10-years for this arm. Therefore, the size of any OS benefit compared to osimertinib monotherapy is uncertain. Other spline models were explored on request with the company noting that some gave results that they considered implausible (10-year OS being higher in the monotherapy arm). The most conservative of these scenarios used the survival curve with 3-spline odds for osimertinib monotherapy (scenario 12).
- There were concerns about the face validity of the base case utility values. The utility value for progression-free health state was higher than values used in previous submissions and compared to general population values in patients of this age. The base case analysis used progressed disease health utility sourced from a real-world study of health state utilities in Canadian patients as they considered the value from FLAURA-2 higher than expected. Alternate progression- free and progressed disease utility values were explored in scenarios 4 and 5.
- The choice of TTD curve has a high impact on the ICER. The company preferred Gompertz for osimertinib + chemotherapy, and Gamma for osimertinib monotherapy. However, the argument provided by the company explaining why the Gamma model is an inappropriate choice of model for TTD for osimertinib + chemotherapy was not found satisfactory. The Gamma model would be the preferred choice for this treatment group due to two reasons. First, consistency across both TTD curves for osimertinib (either given as monotherapy, or in combination with chemotherapy). Second, a more plausible long-term estimate of TTD (it

would make sense that osimertinib TTD is longer when given in combination with chemotherapy versus when given as monotherapy). This is backed up further by the total median exposure being higher in the osimertinib plus chemotherapy arm (22.31 months) compared with the osimertinib monotherapy arm (19.32 months). Scenario 15 explored using the Gamma model for TTD curve in the osimertinib plus chemotherapy arm.

7. Conclusion

The Committee considered the benefits of osimertinib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as osimertinib 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 osimertinib for use in NHSScotland.

8. Guidelines and Protocols

In March 2024, the National Institute for Health and Care Excellence (NICE) updated NICE guideline number 122, 'Lung cancer: diagnosis and management.'[13]

In January 2023, the European Society for Medical Oncology (ESMO) published 'Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up.'[6]

In February 2014, the Scottish Intercollegiate Guidelines Network (SIGN) published guideline number 137, 'Management of lung cancer.'[14]

9. Additional Information

9.1. Product availability date

9 September 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 21-day cycle (£)
Osimertinib Pemetrexed Cisplatin	80 mg orally once daily 500 mg/m^2 IV on Day 1 of 21-day cycle 75 mg/m^2 IV on Day 1 of 21-day cycle for 4 cycles	5,011
Osimertinib Pemetrexed Carboplatin	80 mg orally once daily 500 mg/m^2 IV on Day 1 of 21-day cycle 5 mg/mL/minute AUC IV on Day 1 of 21-day cycle for 4 cycles	5,222

Costs from BNF online on 21 January 25. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration. Costs based on a body surface area of 1.8 m^2. AUC = area under the concentration-time curve; IV = intravenously.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be around 72 patients eligible for treatment with osimertinib plus chemotherapy in each year, with 10 patients estimated to receive treatment in year 1 rising to 22 patients in year 5. However, based on clinical expert opinion consulted by SMC, these figures may be a slight underestimate.

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.

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

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14. Scottish Intercollegiate Guidelines Network (SIGN). Publication number 137: Management of lung cancer, February 2014.

This assessment is based on data submitted by the applicant company up to and including 17 March 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.