National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Sugemalimab with chemotherapy for untreated metastatic non-small-cell lung cancer [ID4001]

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments	Action
Appropriateness	EQRx (company)	Yes, we believe that this topic is appropriate to refer to NICE for appraisal.	Comment noted. No action required.
	Novartis Pharmaceuticals UK	The topic is highly appropriate given the rapidly evolving landscape of new therapies in NSCLC, where there still remains an unmet clinical need for effective treatments	Comment noted. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.
Wording	EQRx (company)	Yes, we believe that the wording of the remit reflects the issue(s) about this technology.	Comment noted. No action required.
	Novartis Pharmaceuticals UK	The wording of the remit appropriately reflects the clinical and cost-effectiveness issues that the technology should consider.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments	Action
	AstraZeneca	No comments.	Comment noted. No action required.
Timing Issues	EQRx (company)	Urgency is high based on ILAP designation granted to sugemalimab [redacted]	Comments noted. NICE aims to provide draft guidance to the NHS as close as possible to the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action required.
	Novartis Pharmaceuticals UK	There is urgency for NICE to review this topic to ensure that patients receive access to effective medicines in an area where there is a clear unmet clinical need.	Comments noted. NICE aims to provide draft guidance to the NHS as close as possible to the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.

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Additional comments on the draft remit	EQRx (company)	We do not have any additional comments on the draft remit.	Comment noted. No action required.
	Novartis Pharmaceuticals UK	None	Comment noted. No action required.
	AstraZeneca	No comments received.	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	EQRx (company)	Given the GEMSTONE 302 study excluded patients with EGFR, ALK, ROS, and RET genomic alterations, we recommend omitting the specific treatment options listed under background for patients with those driver mutations. Specifically, we recommend removing the following: • *EGFR-positive mutations: afatinib (NICE technology appraisal guidance 310), dacomitinib (NICE technology appraisal guidance 595), erlotinib (NICE technology appraisal guidance 258), gefitinib (NICE technology appraisal guidance 192), or osimertinib (NICE technology appraisal guidance 654).* • *ALK-positive mutations: alectinib (NICE technology appraisal guidance 536), brigatinib (NICE technology appraisal guidance 670), ceritinib (NICE technology appraisal guidance 500), or crizotinib (NICE technology appraisal guidance 406).*	Comment noted. The background section of the scope has been updated as suggested.

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		• *ROS1-positive mutations: entrectinib (NICE technology appraisal guidance 643) or crizotinib (available for use within the Cancer Drugs Fund only; NICE technology appraisal guidance 529)* We also recommend NICE reference the most recent version of the National Lung Cancer Audit annual report for epidemiology data.	
	Novartis Pharmaceuticals UK	No Comment	Comment noted. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.
The technology/ intervention	EQRx (company)	We note that sugemalimab is incorrectly referenced as Libtayo, Sanofi. We recommend the following description of the technology: "Sugemalimab (EQRx) is a high-affinity, fully-human, full-length immunoglobulin G4 (IgG4) monoclonal antibody. It specifically binds to PD-L1 and inhibits its interaction with (programmed cell death-1) PD-1, which reinvigorates the dysfunctional tumour-infiltrating effector T cells to overcome adaptive immune resistance. Sugemalimab was developed by the OmniAb® Technology (OMT) transgenic animal platform. It has the expected pharmacokinetic (PK) profile. In addition, sugemalimab mirrors the natural human IgG4 antibody which may potentially reduce the risk of immunogenicity and toxicity in patients." Sugemalimab with platinum-based chemotherapy does not currently have a marketing authorisation for use in patients with untreated metastatic NSCLC. It has been studied in a clinical trial compared with platinum-based chemotherapy and placebo in adults with untreated metastatic NSCLC without known EGFR, ALK, ROS, or RET genomic alterations.	Comment noted. The scope has been updated to remove the brand name and correct the company as stated. NICE scope does not aim to provide in-depth description of the new technology. No action required. The scope has been amended to include the clinical trial population as suggested.

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	Novartis Pharmaceuticals UK	No Comment	Comment noted. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.
Population	EQRx (company)	The population should be adult patients with untreated metastatic non-small cell lung cancer without known EGFR, ALK, ROS, or RET sensitizing genomic alterations.	Comment noted. The scope has been updated as suggested.
	Novartis Pharmaceuticals UK	No Comment	Comment noted. No action required.
	AstraZeneca	It should be made clear that the pivotal study of sugemalimab in this indication (GEMSTONE-302), is a single-country trial conducted in China. The generalisability of this data to UK clinical practice is a potentially significant limitation and should be addressed in this appraisal.	Comment noted. The appraisal committee will consider the generalisability of the clinical trials for sugemalimab with platinum-based chemotherapy during the appraisal.
Comparators	EQRx (company)	We believe that pembrolizumab plus chemotherapy, either with pemetrexed and platinum chemotherapy for non-squamous NSCLC or with carboplatin and paclitaxel for squamous NSCLC, is the most relevant comparator. As NICE noted in TA724 “[Pembrolizumab] combinations are widely used in NHS clinical practice” for patients with untreated metastatic NSCLC.[1] [redacted]	Comment noted. The comparator list includes all relevant options which may be offered for treatment of this condition. The committee will consider the appropriate

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		For non-squamous patients, pembrolizumab combination therapy has been shown to be superior and cost-effective compared to pemetrexed and platinum therapy alone.[2] For non-squamous “high PD-L1” patients, the most plausible ICERs for pembrolizumab combination therapy has been shown to be within the range NICE considers to be cost-effective relative to pembrolizumab monotherapy.[2] For squamous patients, pembrolizumab combination therapy has been shown in clinical trials to be superior compared to carboplatin and paclitaxel alone.[3] Contingent on it being deemed cost-effective in forthcoming NICE guidance [4], we believe pembrolizumab combination therapy is the most relevant comparator for the squamous population as it is already “widely used in NHS clinical practice”.[1]
		
		We request removing the following comparators given patients with EGFR, ALK, and/or ROS genomic alterations are excluded from our pivotal study supporting our anticipated indication:
		
		For adults with non-squamous histology and
		• EGFR- sensitizing mutations
		  ○ Afatinib
		  ○ Dacomitinib
		  ○ Erlotinib
		  ○ Gefitinib
		  ○ Osimertinib
		• ALK-sensitizing genomic rearrangements
		  ○ Alectinib
		  ○ Brigatinib
		  ○ Ceritinib
		  ○ Crizotinib
		• ROS1-fusions
			comparator(s). See section 6.2 of the NICE Guide to the methods of technology appraisal. Treatments for EGFR, ALK, ROS1, or RET genomic alterations have been removed from the scope.

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		○ Entrectinib	
	Novartis Pharmaceuticals UK	The draft scope comprehensively describes the comparators according to histology and mutation status	Comment noted. No action required.
	AstraZeneca	Patients were excluded from enrolling in GEMSTONE-302 if they had known sensitising EGFR, ALK, ROS1, or RET genomic alterations. Therefore any therapies licensed for EGFR, ALK and ROS1-positive mutations should be excluded as comparators.	Comment noted. Treatments for EGFR-, ALK-, ROS1- or RET-positive mutations have been excluded from the scope.
Outcomes	EQRx (company)	The following outcome measures will be provided: • progression-free survival • overall survival • response rates • adverse effects of treatment	Comment noted. No action required.
	Novartis Pharmaceuticals UK	The outcome measures should reflect those assessed in the key trial for the intervention being appraised	Comment noted. The NICE scope aims to capture all outcomes relevant to the appraisal. No amendment necessary.
	AstraZeneca	No comments.	Comment noted. No action required.

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Economic analysis	EQRx (company)	We propose conducting a cost comparison analysis rather than a cost effectiveness analysis. We are recommending a cost comparison because we anticipate that sugemalimab is likely to provide similar or greater health benefits at similar or lower cost than pembrolizumab plus chemotherapy, either with pemetrexed and platinum chemotherapy for non-squamous NSCLC or with carboplatin and paclitaxel for squamous NSCLC. Wherever possible and appropriate, cost data and sources will be consistent with the data and sources that were used in the previously published NICE guidance for the comparators in the same indication and will be updated to reflect the most up-to-date cost information available for these sources. We are confident that costs, with the exception of acquisition cost of the medicine, will be similar and this will be demonstrated in the submission. We recommend using two years as the time horizon, based on the two-year stopping rules that are currently in place. Costs will not be discounted. We propose using univariate sensitivity analyses to understand the sensitivity of costs to inputs with uncertainty (e.g., adverse event rates, duration of treatment). For pembrolizumab, the publicly available list price will be used for acquisition costs.	Comment noted. No action required.
	Novartis Pharmaceuticals UK	The economic analysis is appropriate and consistent with the NICE reference case.	Comment noted. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.

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Equality and Diversity	EQRx (company)	The proposed remit does not need to be changed in order to meet NICE's stated equality objectives.	Comment noted. No action required.
	Novartis Pharmaceuticals UK	No comment.	Comment noted. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.
Other considerations	EQRx (company)	We have no further suggestions to add.	Comment noted. No action required.
	Novartis Pharmaceuticals UK	No comment.	Comment noted. No action required.
	AstraZeneca	No comments.	Comment noted. No action required.
Innovation	EQRx (company)	An innovation passport was granted to sugemalimab on September 10, 2021. This was granted primarily on the basis of EQRx pricing to enable affordable access to life-saving drugs, which have demonstrated clinical comparability to relevant comparators through cross-trial comparison. EQRx plans to conduct an indirect comparison and cost comparison versus pembrolizumab combination treatment to demonstrate the impact of sugemalimab on public health and patient access.	Comment noted. The appraisal committee will consider the innovative nature of sugemalimab with platinum-based chemotherapy during the appraisal.
	Novartis Pharmaceuticals UK	No comment.	Comment noted. No action required.

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	AstraZeneca	The existing therapies for patients with untreated metastatic non-small-cell lung cancer (without EGFR, ALK and ROS1-positive mutations) are anti-PD-1/PD-L1 therapies. Sugemalimab is anti-PD-L1 monoclonal antibody and has an identical mechanism of action to existing therapy. The technology under appraisal therefore does not represent a step-change in the management of the condition and cannot be considered innovative.	Comment noted. The appraisal committee will consider the innovative nature of sugemalimab with platinum-based chemotherapy during the appraisal.
Questions for consultation	EQRx (company)	**How are treatment decisions made where multiple options exist for tumours with the same biological marker and histology?** *EQRx Response:* When multiple options exist for tumours with the same biologic marker and NSCLC pathologic subtype, treatment options are based on multiple factors such as the stage of the disease, patient's performance status, presence of comorbidities and ability to tolerate the treatment. **Have all relevant comparators for sugemalimab with chemotherapy been included in the scope?** *EQRx Response*: We believe that pembrolizumab plus chemotherapy, either with pemetrexed and platinum chemotherapy for non-squamous NSCLC or with carboplatin and paclitaxel for squamous NSCLC, is the most relevant comparator. As NICE noted in TA724 "[Pembrolizumab] combinations are widely used in NHS clinical practice" for patients with untreated metastatic NSCLC.[1] [redacted] For non-squamous patients, pembrolizumab combination therapy has been shown to be superior and cost-effective compared to pemetrexed and platinum therapy alone.[2] For non-squamous "high PD-L1" patients, the most plausible ICERs for pembrolizumab combination therapy has been shown to be within the range NICE considers to be cost-effective relative to pembrolizumab monotherapy.[2] For squamous patients, pembrolizumab	Comments noted. Please see previous responses for further information. No action required.

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		combination therapy has been shown in clinical trials to be superior compared to carboplatin and paclitaxel alone.[3] Contingent on it being deemed cost-effective in forthcoming NICE guidance [4], we believe pembrolizumab combination therapy is the most relevant comparator for the squamous population as it is already "widely used in NHS clinical practice".[1] We request removing the following comparators given patients with EGFR, ALK, and/or ROS genomic alterations are excluded from our pivotal study supporting our anticipated indication: For adults with non-squamous histology and • EGFR- sensitizing mutations o Afatinib o Dacomitinib o Erlotinib o Gefitinib o Osimertinib • ALK-sensitizing genomic rearrangements o Alectinib o Brigatinib o Ceritinib o Crizotinib • ROS1-fusions o Entrectinib **Are the outcomes listed appropriate?** *EQRx Response:* Yes, all outcomes listed are appropriate. **Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom sugemalimab with**	

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		chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately? *EQRx Response:* The subgroups suggested in 'other considerations' are appropriate. **Where do you consider sugemalimab with chemotherapy will fit into the existing NICE pathway, non-small-cell lung cancer?** *EQRx Response:* For initial systemic treatment of patients with squamous or non-squamous NSCLC and no known EGFR, ALK, ROS, or RET sensitizing genomic alterations. [redacted] **NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims.** *EQRx Response:* The proposed remit does not need to be changed in order to meet NICE's stated equality objectives. **Do you consider sugemalimab with chemotherapy to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** *EQRx Response:* An innovation passport was granted to sugemalimab on September 10, 2021. This was granted primarily on the basis of EQRx pricing to enable affordable access to life-saving drugs.	

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		Do you consider that the use of sugemalimab with chemotherapy can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? *EQRx Response:* We do not anticipate any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation. **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.** *EQRx Response:* As noted in the previous question, we do not believe there are any benefits that would not be captured in the QALY calculation. **To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.** *EQRx Response:* We do not expect any barriers to adoption. **NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process.** *EQRx Response:* EQRx intends to be appraised via the Fast-Track Appraisal (FTA) path for all indications included in this scope, given a relevant comparator, pembrolizumab combination therapy, is either currently commissioned or is anticipated to be commissioned by the NHS by the time of the submission to NICE.	

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		NICE has published an addendum to its guide to the methods of technology appraisal which states the methods to be used where a cost comparison case is made. **Would it be appropriate to use the cost comparison methodology for this topic?** *EQRx Response*: Per NICE's Guide to the Methods of Technology Appraisal, "a cost comparison case can be made if a health technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication". We believe sugemalimab meets these criteria. **Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?** *EQRx Response*: Clinical efficacy is anticipated to be similar to pembrolizumab combination therapy. Resource use is also anticipated to be comparable, outside of drug acquisition cost, which will be lower than pembrolizumab combination therapy. **Is the primary outcome that was measured in the trial or used to drive the model for the comparators still clinically relevant?** *EQRx Response*: Yes, progression free survival remains a relevant endpoint in this indication. **Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?** *EQRx Response*: We do not believe there are ongoing trials to report.	

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	Novartis Pharmaceuticals UK	How are treatment decisions made where multiple options exist for tumours with the same biological marker and histology? Have all relevant comparators for sugemalimab with chemotherapy been included in the scope? Yes Are the outcomes listed appropriate? Yes Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom sugemalimab with chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately? The subgroups are appropriate, where the evidence permits Where do you consider sugemalimab with chemotherapy will fit into the existing NICE pathway, non-small-cell lung cancer? sugemalimab should be considered alongside the other NICE approved therapies for advanced NSCLC in the existing pathway for the management of lung cancer. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:	Comments noted. No action required.

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		• could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sugemalimab with chemotherapy will be licensed; • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts. No comment Do you consider sugemalimab with chemotherapy to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? No comment Do you consider that the use of sugemalimab with chemotherapy can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? No comment Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. Not Applicable	

Section	Consultee/ Commentator	Comments [sic]	Action
		To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction). No comment NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. • Would it be appropriate to use the cost comparison methodology for this topic? • Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? • Is the primary outcome that was measured in the trial or used to drive the model for the comparators still clinically relevant?	

Section	Consultee/ Commentator	Comments [sic]	Action
		• Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year? No comment	
	AstraZeneca	No comments.	Comment noted. No action required.
Additional comments on the draft scope	EQRx (company)	We recommend removing the TA appraisals which are not relevant to this assessment: 670, 654, 643, 529, 310, Aumolertinib, and Tepotinib.	Comment noted. The scope has been updated to remove the suggested appraisals.
	Novartis Pharmaceuticals UK	None	Comment noted. No action required.
	AstraZeneca	No comments received.	Comment noted. No action required.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Pierre Fabre Ltd
Roy Castle Lung Cancer Foundation