National Institute for Health and Care Excellence

Health Technology Evaluation

Zolbetuximab with chemotherapy within its marketing authorisation for untreated claudin 18.2 positive HER2-negative locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma ID5123

Response to stakeholder organisation comments on the draft remit and draft scope

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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Astellas Pharma Ltd	The evaluation and the proposed route are appropriate.	Thank you for your comment. No action required.
Wording	Astellas Pharma Ltd	Suggest changing the wording regarding the draft remit/evaluation objective as follows in line with the expected indication: To appraise the clinical and cost effectiveness of zolbetuximab with chemotherapy within its marketing authorisation for claudin 18.2 positive HER2-negative locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma. The wording of the remit reflects the issues about the appraisal.	Thank you for your comment. The remit has been updated in line with the expected indication.

Section	Stakeholder	Comments [sic]	Action
Timing Issues	Astellas Pharma Ltd	There is a high unmet need in this patient population, therefore scheduling the appraisal in line with the expected regulatory timeline is appropriate.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.
Additional comments on the draft remit	Astellas Pharma Ltd	No comments	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Astellas Pharma Ltd	Suggest adding: The most common histological subtype of gastric and gastro-oesophageal junction cancer is adenocarcinoma, with 95% of gastric cancers being adenocarcinomas. In the first paragraph under “Background”, the sentence about oesophageal cancer is not relevant to this appraisal, as zolbetuximab was not studied in this condition and is not expected to receive marketing authorisation for oesophageal cancer. Therefore, Astellas suggests deleting the sentences: “*Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus.*”	Thank you for your comment. The background section has been updated to remove the details about oesophageal cancer. No further action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		"*Oesophageal cancer is also more common in men than women, with 5,349 cases diagnosed in men, and 2,332 cases in women in England on average per year from 2016 to 2018*[2]*. Around 41% of all new cases of oesophageal cancer in the UK are diagnosed in people aged 75 and over*[2]*.*" Additionally, to remove the references to oesophageal cancer in the paragraph about symptoms (3rd paragraph below Background).	
Population	Astellas Pharma Ltd	Suggest the population wording is amended as follows in line with the expected licence indication: People with locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma whose tumours are claudin 18.2 positive.	Thank you for your comment. Population description has been amended as suggested in line the expected licence indication. However, given the trial was carried out in people who had not had previous treatment the population states the population as 'people with untreated locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma whose tumours are claudin

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			18.2 positive**.**No further action required
Subgroups	Astellas Pharma Ltd	Subgroup by tumour location (gastric and gastroesophageal junction cancer) data will be included in the submission. However, it is not expected to inform the cost effectiveness analysis as the trials were powered to investigate the relative efficacy in the entire population but not in subgroups, and the number of patients with gastroesophageal junction cancer in the trials is too small to enable robust inference. Furthermore, most of the characteristics investigated in the subgroup analysis were not stratification factors for randomisation. Additionally, clinical feedback to Astellas is that tumour location has little relevance to how patients are treated in clinical practice, and treatment is similar irrespective of whether it is gastric or gastroesophageal junction cancer.	Thank you for your comment. Subgroup by tumour location have been removed. However, the committee will consider any relevant subgroups if the evidence allows. No further action required.
Comparators	Astellas Pharma Ltd	Astellas assumes that pembrolizumab with chemotherapy is referring to the currently ongoing appraisal of pembrolizumab for HER2-negative advance gastric or gastroesophageal junction adenocarcinoma (ID4030). Astellas does consider not pembrolizumab in this indication to be a relevant comparator as it will not be recommended or considered established practice in the NHS (in line with NICE Methods paragraph 1.2.2.12) at the point of evidence submission. Furthermore, as the NICE appraisal is ongoing, it is not known yet if and in whom pembrolizumab will eventually be recommended (beyond the currently existing recommendation via TA737). Hence there is uncertainty regarding: a) extent of overlap with the population expected to be eligible for zolbetuximab; and b) the relevant evidence on clinical efficacy to inform a comparison to zolbetuximab.	The scope includes all possible comparators and are kept broad at this stage of the evaluation. The company can propose to exclude comparators in its evidence submission. The most appropriate comparator will be discussed by the appraisal committee during the development

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		Astellas notes that PD-L1 CPS and tumour location are not the only considerations for whether patients are eligible for immune checkpoint inhibitors, as the contra-indications and cautions regarding immune checkpoint inhibitors do not fully overlap with those of zolbetuximab (e.g., clinically significant autoimmune disease, liver transplant recipients). Therefore, some patients whose CPS would deem them eligible for immune checkpoint inhibitors may not receive them in clinical practice, and currently receive chemotherapy.	of this appraisal. No further action required.
Outcomes	Astellas Pharma Ltd	Astesllas considers the listed outcomes as appropriate.	Thank you for your comment. No action required.
Equality	Astellas Pharma Ltd	Astellas is not aware of any additional equality considerations.	Thank you for your comment. No action required.
Other considerations	Astellas Pharma Ltd	No additional comments.	Thank you for your comment. No action required.
Questions for consultation	Astellas Pharma Ltd	**Where do you consider zolbetuximab with chemotherapy will fit into the existing care pathway for untreated HER2-negative advanced gastric or gastro-oesophageal junction cancer?** Astellas expects that zolbetuximab with chemotherapy will be used in line with its expected marketing authorisation.	Thank you for your comment. No action required.

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		Would zolbetuximab with chemotherapy be a candidate for managed access? At this time, Astellas does not consider zolbetuximab to be a candidate for managed access. **Are the biomarker tests to establish the correct diagnosis of claudin 18.2 positive standard practice in the NHS?** Testing for claudin 18.2 is not standard practice in the NHS. **Do you consider that the use of zolbetuximab and chemotherapy can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Astellas does not consider that the use of zolbetuximab with chemotherapy will result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation. **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:** • **could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which zolbetuximab will be licensed;**	

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		• **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** Astellas has not identified any equality issues.	
Additional comments on the draft scope	Astellas Pharma Ltd	Please replace the reference to “Claudiximab” in the paragraph headed “The technology” with IMAB362. The proposed brand name ([redacted]) is still subject to approval by the MHRA during the Marketing Authorisation Assessment. It is suggested that this paragraph is updated as follows in line with the expected market authorisation: Zolbetuximab (IMAB362, Astellas Pharma) with chemotherapy does not currently have a marketing authorisation in the UK for claudin 18.2 positive HER2-negative locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma. It has been studied in clinical trials in people with claudin 18.2 positive HER2-negative locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma.	Thank you for your comment. The brand name has been amended. Thank you for your comment. The wording name has been amended in line expected indication. No further action required.

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

N/A