National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Cemiplimab for treating cutaneous squamous cell carcinoma

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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 [sic]	Action
Wording	British Association of Dermatology (BAD). Endorsed by Royal College of Physicians (RCP).	Yes	Comment noted.
	Sanofi	The wording of the remit should be updated to reflect the expected licenced indication for cemiplimab as follows: *"To appraise the clinical and cost effectiveness of cemiplimab within its marketing authorisation for treating patients with metastatic cutaneous squamous cell carcinoma (mCSCC), or locally advanced cutaneous squamous cell carcinoma (laCSCC) who are not candidates for surgery"*	Comment noted. The remit has been kept broad to ensure that it captures possible wording of the marketing authorisation from the European Medicines Agency.

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Timing Issues	BAD. Endorsed by RCP.	This is a potentially effective new treatment for metastatic cutaneous squamous cell carcinoma where there is currently no consensus on treatment – therefore this should be considered relatively urgently	Comment noted. The dates of the expected marketing authorisation were taken into account when the topic was planned into the work programme.
	Sanofi	[redacted] There is a very high unmet need in the patient population for which we are seeking a recommendation for cemiplimab. There are currently no licenced treatment options available to these patients who have a poor prognosis with a median overall survival of less than 2 years.[1,2] A decision making process closely aligned with the above regulatory timings will ensure that patients who develop metastatic cutaneous squamous cell carcinoma and patients with locally advanced cutaneous squamous cell carcinoma who are not candidates for surgery will have access to an effective, licenced treatment option. [1]Stratigos A, Garbe C, Lebbe C, Malvehy J, del Marmol V, Pehamberger H et al. On behalf of the European Dermatology Forum (EDF) the European Association of Dermato-Oncology (EADO) and the European Organization for Research and Treatment of Cancer (EORTC), European Journal of Cancer (2015) Volume 51, Issue 14, Pages 1989–2007. [2]Jarkowski III A, Hare R, Loud P, Skitzki JJ, Kane III JM, May KS, Zeitouni NC, Nestico J, Vona KL, Groman A, Khushalani NI. Systemic therapy in advanced cutaneous squamous cell carcinoma (CSCC): The Roswell Park experience and a review of the literature. American journal of clinical oncology. 2016 Dec 1;39(6):545-8.	Comment noted. The dates of the expected marketing authorisation were taken into account when the topic was planned into the work programme.

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Additional comments on the draft remit	BAD. Endorsed by RCP.	The information on this treatment is limited to an initial Phase 1 trial of 26 patients (Kyriakos et al ascopbs.org from the 2018 annual meeting, Abstract 195) of which 3 patients at the time of the presentation were not evaluable and median PFS and OS had not been reached but it was ell tolerated and only one patient had experienced PD after initial response although follow up time was short. However there is no good alternative to treatment and these initial results look promising. A phase II study is underway.	Comment noted. The committee will consider all available evidence.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	BAD. Endorsed by RCP.	It is accurate. It does not discuss other treatments previously used including Gefitinib, Cetuximab (EGFR inhibitors), other antiPD1 agents such as Pembrolizumab, Nivolumab (case series/case report), cisplatin as this is not a head to head trial as there is no current recommended treatment.	Comment noted.
	Sanofi	Sanofi suggest updating the second and third paragraphs of the background section in order to increase the relevance of this scope to the indication under consideration as follows: *"Around 122,000 cases of non-melanoma skin cancer were registered in 2015 in England.[2]Cutaneous SCC accounts for about 20% of skin cancers[2] and 23% of non-melanoma skin cancers[3].* *Surgery is the main treatment for early stages of CSCC. It involves removing the cancerous tumour and some of the surrounding skin. Surgical removal provides very high rates of local control with cure rates of 95%.[4] Deaths from cutaneous SCC are rare, however the prognosis for patients who develop metastatic cutaneous squamous cell carcinoma or locally advanced*	Comments noted. The background section of the scope is only intended to provide a brief description of the condition and current treatment options. A detailed description of these aspects will be included in the company's evidence submission and will be

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		cutaneous squamous cell carcinoma is poor, with a median overall survival of less than 2 years.[4,6] *For patients who develop metastatic or locally advanced CSCC who are not candidates for surgery, treatment options are limited. Currently there are no licenced treatments available for this population. Although there have been single arm studies of several systemic treatments, none of these studies clearly demonstrate a therapeutic benefit.* [7,8]" [2,3]Same references as provided in the draft scope [4]Stratigos A, Garbe C, Lebbe C, Malvehy J, del Marmol V, Pehamberger H et al. On behalf of the European Dermatology Forum (EDF) the European Association of Dermato-Oncology (EADO) and the European Organization for Research and Treatment of Cancer (EORTC), European Journal of Cancer (2015) Volume 51, Issue 14, Pages 1989–2007. [6]Jarkowski III A, Hare R, Loud P, Skitzki JJ, Kane III JM, May KS, Zeitouni NC, Nestico J, Vona KL, Groman A, Khushalani NI. Systemic therapy in advanced cutaneous squamous cell carcinoma (CSCC): The Roswell Park experience and a review of the literature. American journal of clinical oncology. 2016 Dec 1;39(6):545-8. [7]Maubec, E., P. Petrow, I. Scheer-Senyarich, P. Duvillard, L. Lacroix, J. Gelly, A. Certain, X. Duval, B. Crickx, V. Buffard, N. Basset-Seguin, P. Saez, A. B. Duval-Modeste, H. Adamski, S. Mansard, F. Grange, A. Dompmartin, S. Faivre, F. Mentre and M. F. Avril (2011). "Phase II study of cetuximab as first-line single-drug therapy in patients with unresectable squamous cell carcinoma of the skin." J Clin Oncol 29(25): 3419-3426. [8]Nakamura, K., R. Okuyama, T. Saida, and H. Uhara. 2013. Platinum and anthracycline therapy for advanced cutaneous squamous cell carcinoma. Int J Clin Oncol. 18:506-509.	considered during the appraisal.
The technology/ intervention	BAD. Endorsed by RCP.	Yes	Comment noted.
	Sanofi	Sanofi propose updating the last paragraph of the 'The technology' section as per below in order to correctly represent the trial programme and the proposed indication under review for cemiplimab. *"Cemiplimab does not currently have a marketing authorisation in the UK for treating locally advanced or metastatic cutaneous squamous cell carcinoma (SCC). Cemiplimab has been studied in two clinical trials (one phase I and one phase II trial) as monotherapy without an active comparator in adults with*	Comment noted. The description of the clinical trials was updated.

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		untreated metastatic cutaneous SCC or with locally advanced cutaneous squamous cell carcinoma who are not candidates for surgery."	
Population	BAD. Endorsed by RCP.	Yes the population is defined correctly	Comment noted.
	Sanofi	The population should be defined in line with our expected licenced indication as well as the anticipated use of cemiplimab in the UK. *"Adults with:* • *metastatic cutaneous squamous cell carcinoma or* • *locally advanced cutaneous squamous cell carcinoma in whom surgery is not appropriate"* In particular, "untreated" should be removed from the proposed population as in the cemiplimab trials there were no restrictions on the number of prior systemic treatments patients could have received before receiving cemiplimab.[1] In addition, Sanofi anticipate that in clinical practice cemiplimab will only be a treatment option for locally advanced patients who are not suitable for curative radiotherapy. This is based on initial discussions with UK clinical experts. This population is in line with the phase I and II trial populations for cemiplimab in which locally advanced patients were not eligible for surgery or radiotherapy. [1] https://clinicaltrials.gov/ct2/show/record/NCT02760498	Comments noted. The population definition has been updated and includes people with metastatic cutaneous squamous cell carcinoma or people with locally advanced cutaneous squamous cell carcinoma in whom there is no curative local therapy.
Comparators	BAD. Endorsed by RCP.	There is no established standard care for unresectable locally advanced or metastatic cutaneous squamous cell carcinoma however other treatment options are available.	Comment noted.

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	Sanofi	Based on UK clinical expert opinion, Sanofi believe the comparators for this appraisal should be: • Best supportive care • Chemotherapy It is our understanding that most patients would receive best supportive care constituting palliative care aimed at controlling the symptoms of the condition but that some patients (~25%) may be fit enough to tolerate chemotherapy (platinum based + 5 Fluorouracil).	Comments noted. Chemotherapy was added to the list of comparators.
Outcomes	BAD. Endorsed by RCP.	Yes	Comment noted.
	Sanofi	The outcome measures to be considered in this evaluation should be updated to reflect the primary and secondary endpoints included in the phase 2 registrational study of cemiplimab as follows: • overall response rate • duration of response • progression-free survival • overall survival • adverse effects of treatment • health-related quality of life.	Comments noted. Duration of response was added to the list of outcomes.
Economic analysis	BAD. Endorsed by RCP.	No additional comments	Comment noted.

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Equality and Diversity	BAD. Endorsed by RCP.	No foreseeable issues	Comment noted.
Innovation	BAD. Endorsed by RCP.	Yes	Comment noted.
	Sanofi	Cemiplimab is an innovative technology with the potential to significantly impact the health-related benefits, both in terms of quality of life and survival, for patients with metastatic or locally advanced CSCC, unsuitable for surgery, and if recommended will be a step-change in the management of these patients. Currently there are no licenced treatments available for this population. Although there have been single arm studies of several systemic treatments, none of these studies clearly demonstrate a therapeutic benefit.[1,2] Given there is a dearth of data to guide clinical decision making, there is a significant unmet medical need for new, effective treatments for this patient group. If recommended, cemiplimab will offer an effective treatment option for a patient group with a particularly poor prognosis for whom there are few alternatives. [1]Maubec, E., P. Petrow, I. Scheer-Senyarich, P. Duvillard, L. Lacroix, J. Gelly, A. Certain, X. Duval, B. Crickx, V. Buffard, N. Basset-Seguin, P. Saez, A. B. Duval-Modeste, H. Adamski, S. Mansard, F. Grange, A. Dompmartin, S. Faivre, F. Mentre and M. F. Avril (2011). "Phase II study of cetuximab as first-line single-drug therapy in patients with unresectable squamous cell carcinoma of the skin." J Clin Oncol 29(25): 3419-3426. [2]Nakamura, K., R. Okuyama, T. Saida, and H. Uhara. 2013. Platinum and anthracycline therapy for advanced cutaneous squamous cell carcinoma. Int J Clin Oncol. 18:506-509.	Comments noted. The innovative nature of cemiplimab will be considered by the committee during the appraisal.
Questions for consultation	Sanofi	*"Which treatments are considered to be established clinical practice in the NHS for unresectable locally advanced cutaneous squamous cell carcinoma (SCC)? Which treatments are considered to be established clinical practice in the NHS for metastatic cutaneous SCC?"*	Comments noted. Chemotherapy was

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		As discussed above based on clinical expert opinion standard of care for patients with metastatic SCC or locally advanced SCC who are not candidates for surgery is considered to be: • Best supportive care OR • Chemotherapy *"How should best supportive care be defined?"* According to UK clinical experts, best supportive care constitutes palliative care to control the symptoms of the condition. Palliative radiotherapy may be used for a proportion of patients for whom this would be appropriate. *"Are there any active treatments with which cemiplimab should be compared?"* There are currently no licenced treatments for patients with metastatic SCC or locally advanced SCC who are not candidates for surgery. According to UK clinical experts, chemotherapy (platinum based + 5-FU) is the only alternative option to best supportive care currently in use for the treatment of this patient population.	added to the list of comparators.
Additional comments on the draft scope	Sanofi	No further comments.	-

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

BASCSN (British Association of Skin Cancer Specialist Nurses): *BASCSN does not have any comment to make on this scop and are unable to attend the meeting. Experience with this drug is very limited in the UK.*