**National Institute for Health and Care Excellence**

**Health Technology Evaluation**

# Cemiplimab for adjuvant treatment of high-risk cutaneous squamous cell carcinoma after surgery and radiotherapy ID6659

## 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 |
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| Appropriateness of an evaluation and proposed evaluation route | Regeneron (company) | No comments. | Thank you for your comment. |
| | British Dermatology Nursing Group (professional) | There is an unmet clinical need for adjuvant systemic therapy in high-risk cutaneous squamous cell carcinoma. Cemiplimab has the potential to significantly reduce recurrence and prevent progression to advanced disease. This is an appropriate STA for this treatment. | Thank you for your comment. This appraisal is being routed as a single technology appraisal. |
| Wording | Regeneron (company) | No comments. | Thank you for your comment. |
| | British Dermatology | Yes | Thank you for your comment. No action required. |

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| | Nursing Group (professional) | | |
| Timing Issues | Regeneron (company) | Following surgery and radiation therapy for their primary CSCC tumour, there are no current approved treatment options for a minority of patients at high risk of recurrence beyond routine clinical surveillance. Disease recurrence (both locoregional and distant recurrence) is associated with a substantial mortality risk; uncontrolled locoregional disease accounts for 81% of disease-specific deaths.**Error! Reference source not found.** There is an urgent unmet need for effective adjuvant treatment options that reduce the risk of recurrence at an earlier disease stage and prevent progression to advanced unresectable disease, which has a poor prognosis and is associated with a significant burden for patients.<br>As an adjuvant treatment for high-risk CSCC, cemiplimab has the potential to transform CSCC care and embodies the NHS's vision for the next decade to transform care from "sickness to prevention" via proactive prevention, rather than reactive treatment of locoregional and distant CSCC recurrences. | Thank you for your comment. No action required. |
| | British Dermatology Nursing Group (professional) | Not known | Thank you for your comment. |
| Additional comments on the draft remit | Regeneron (company) | None. | Thank you for your comment. |
| | British Dermatology Nursing Group (professional) | The epidemiology is confusing and not clear, do you need to talk about SCC and non-melanoma | Thank you for your comment. The epidemiology has been updated in the background section and |

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| | | | no longer includes figures on non-melanoma. |

**Comment 2: the draft scope**

| Section | Consultee/ Commentator | Comments [sic] | Action |
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| Background information | Regeneron (company) | Background<br>"High-risk cutaneous SCC is defined by stage node-negative (no regional lymph node metastasis) and has high-risk features associated with sub-clinical metastasis (cancer that has spread from the primary tumour to other sites but are not detectable by clinical examination or standard imaging)."<br>This is factually inaccurate. Regeneron suggests this is reworded to "*There is no standard definition of high-risk CSCC but high-risk CSCC is commonly identified in clinical guidelines by presence of nodal features (e.g. nodal disease with extracapsular extension [ECE]) and non-nodal features (e.g. perineural invasion [PNI], in-transit metastases, T4 tumours, and recurrent CSCC.*"**Error! Reference source not found.**,**Error! Reference source not found.**<br>*"Surgery is the main treatment for non-melanoma skin cancer. For cutaneous SCC tumours that recur, further surgery, with or without radiotherapy, may be used. There are currently no NICE-recommended adjuvant treatment options for people with high-risk cutaneous SCC after surgery and radiation therapy."*<br>Regeneron suggests clarifying that following completion of surgery and radiation therapy, patients are typically managed with routine clinical surveillance and are not offered further active anti-cancer treatment unless there is disease recurrence, as outlined in the British Association of | Thank you for your comment. The scope has been updated to more accurately reflect how high-risk cutaneous SCC is identified, and treatment options post-surgery and radiation therapy. |

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| | | Dermatologists clinical guidelines on management of CSCC (2020).**Error! Reference source not found.**<br><br>See also comments on the draft scope comparator.<br><br><u>The technology</u><br>The wording should be updated to reflect the UK marketing authorisation status (approved by MHRA on 27 January 2026). The approved indication is: *<u>as monotherapy for the adjuvant treatment of adult patients with CSCC at high risk of recurrence after surgery and radiation</u>*. | The technology section has been updated to reflect the approved marketing authorisation wording. |
| | British Dermatology Nursing Group (professional) | • The epidemiology is slightly confusing, do you need to give figures for SCC and NMSC, are they relevant to each other.<br>• There is no mention of perineural invasion, tumour size, immunosuppression, or margin status, all of which are relevant in MDT decisions. Is the population clearly identifiable in clinical practice?<br>• It implies radiotherapy always used, but this is not the case.<br>• Is chemotherapy used for node-negative SCC? | Thank you for your comment. The figure for NMSC has been removed from the scope. The background is intended to give a brief overview of the condition and treatment options. The treatment pathway for cutaneous SCC will be discussed during the course of the appraisal. |
| Population | Regeneron (company) | The population is defined appropriately. | Thank you for your comment. No action required. |
| | British Dermatology | Will all patients have had radiotherapy? | Thank you for your comment. The marketing authorisation |

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| | Nursing Group (professional) | | indicates that this technology is intended for use in the population with cutaneous squamous cell carcinoma at high risk of recurrence **after surgery and radiation.** The intended population will be discussed during the course of the appraisal. No action required. |
| Subgroups | Regeneron (company) | In the registrational C-POST study, disease-free survival (DFS) benefit was demonstrated with cemiplimab compared to placebo in all clinically relevant subgroups.**Error! Reference source not found.**<br>Regeneron considers there to be no specific subgroups that should be considered separately in this appraisal. | Thank you for your comment. No action required. |
| | British Dermatology Nursing Group (professional) | No comment made. | Thank you for your comment. |
| Comparators | Regeneron (company) | Radiation therapy is not a relevant comparator for this appraisal. To be eligible to receive adjuvant cemiplimab per its approved MHRA indication statement, registrational C-POST study, and the NICE draft scope population, patients must have already received **both** surgery and radiation therapy. | Thank you for your comment. The comparators section has been updated to |

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| | | The wording should be updated to: *'Established clinical management without cemiplimab **i.e., routine clinical surveillance.'*** This is consistent with the British Association of Dermatologists clinical guidelines on management of CSCC (2020).**Error! Reference source not found.** | reflect the proposed changes. |
| | British Dermatology Nursing Group (professional) | Can radiotherapy be described as a comparator if the population has already received it, patients entering the adjuvant setting will already have completed definitive local treatment. Would active surveillance be the comparator, or does this require rewording as it's not clear? | Thank you for your comment. The comparator section has been updated to include routine clinical surveillance as the comparator rather than radiotherapy. |
| Outcomes | Regeneron (company) | The outcomes listed are appropriate. | Thank you for your comment. No action required. |
| | British Dermatology Nursing Group (professional) | Is 'response rate' relevant in the adjuvant setting? | Thank you for your comment. The outcomes section of the scope is not exhaustive. Additional outcomes to those listed on the scope can be reported. No action needed. |
| Equality | Regeneron (company) | CSCC disproportionally affects the elderly and older patients may be frail and/or have a number of comorbidities and/or disabilities, all of which can negatively impact CSCC outcomes (note that age and disability are protected characteristics under the Equality Act 2010). | Thank you for your comment. This has been noted in the accompanying equality |

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| | | Further, whilst not a protected characteristic under the Equality Act, it should also be noted that occupational exposure (e.g. agricultural workers) to ultraviolet radiation is a major risk factor for the development of CSCC. | impact assessment (EIA) form. The committee will consider equalities issues where evidence is presented. No change to scope required. |
| | British Dermatology Nursing Group (professional) | Treatment should be initiated and monitored in specialist secondary care settings (dermatology and/or oncology), with access to immunotherapy expertise and toxicity management. This is consistent with existing arrangements for cemiplimab in locally advanced or metastatic SCC and other immune checkpoint inhibitors.<br><br>SCC disproportionately affects older people<br>Immunosuppressed patients (e.g. transplant recipients) are at higher risk of aggressive disease and recurrence. Clear guidance will be needed to ensure equitable access and appropriate risk–benefit assessment for these populations. | Thank you for your comment. This has been noted in the accompanying equality impact assessment (EIA) form. The committee will consider equalities issues where evidence is presented. No change to scope required. |
| Other considerations | Regeneron (company) | No comments. | Thank you for your comment. |
| | British Dermatology Nursing Group (professional) | None | Thank you for your comment. |
| Questions for consultation | Regeneron (company) | **Please select from the following, will cemiplimab be:**<br>**A. Prescribed in primary care with routine follow-up in primary care**<br>**B. Prescribed in secondary care with routine follow-up in primary care** | Thank you for your comment. The |

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| | | **C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details)?**<br>C. Cemiplimab will be prescribed in secondary care with routine follow-up in secondary care.<br><br>**For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.**<br>For comparators and subsequent treatment, prescribing and routine follow-up will also be in secondary care.<br><br>**Would cemiplimab be a candidate for managed access?**<br>Regeneron considers cemiplimab to be a potentially suitable candidate for inclusion in the Cancer Drugs Fund if the committee agrees that further data collection would help to address any remaining uncertainty in the clinical and cost effectiveness evidence.<br><br>**Do you consider that the use of cemiplimab can result in any potential 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 committee to take account of these benefits.**<br>UK clinical experts have provided feedback to Regeneron that the additional monitoring of patients receiving adjuvant cemiplimab (which is included as costs within the economic model per the C-POST registrational study) may be associated with earlier detection of disease recurrence. This potential clinical benefit is not captured in the economic model since, within the clinical study setting, all monitoring was protocolised. | committee will consider the potential uncaptured benefits of cemiplimab during the course of the appraisal. No action required. |

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| | | Caregiver burden is also not captured in the QALY calculation. Caregivers of patients with high-risk CSCC experience a substantial physical and psychosocial burden. NICE TA802 specifically acknowledges that *"caring for a person with CSCC can be physically and emotionally draining"*. Patients with CSCC are often elderly and may be frail, with a number of comorbidities and/or disabilities. UK clinical experts consulted by Regeneron have provided feedback that early treatment to prevent recurrences may reduce the burden on family caregivers and informal support networks.<br><br>**Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice.**<br>In the SmPC, the recommended dose for cemiplimab in the adjuvant setting is<br>• 350 mg every 3 weeks (Q3W) for 12 weeks followed by 700 mg Q6W, *or*<br>• 350 mg Q3W<br>In the registrational C-POST trial, cemiplimab was initially administered Q3W. However, in a protocol amendment, this was revised to 350 mg Q3W for 12 weeks followed by 700 mg Q6W for an additional 36 weeks. The rationale for this change was based on the concept that after 12 weeks of treatment, immune responses can be maintained with a less frequent treatment schedule. The updated regimen was also supported by pharmacokinetic modelling.<br>Of the 209 patients who received cemiplimab in C-POST, 171 (82%) received 350 mg Q3W for 12 weeks followed by 700 mg Q6W; this is expected to be the preferred dosing regimen in clinical practice. | |
| | British Dermatology | None | Thank you for your comment. |

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| | Nursing Group (professional) | | |
| Additional comments on the draft scope | Regeneron (company) | No further comments. | Thank you for your comment. |
| | British Dermatology Nursing Group (professional) | The use of cemiplimab in the adjuvant setting may confer substantial benefits that are not fully captured in QALY calculations, including:<br><br>• Reduced anxiety and psychological burden associated with high recurrence risk<br>• Avoidance or delay of metastatic disease, which is associated with significant morbidity<br>• Reduced need for disfiguring surgery or high-dose radiotherapy at recurrence<br>• Preservation of function and appearance, particularly for head and neck primaries<br><br>These benefits are clinically meaningful and highly valued by patients but may not be fully reflected in standard utility measures | Thank you for your comment. The committee will consider the potential uncaptured benefits of cemiplimab during the course of the appraisal. No action required. |