**National Institute for Health and Care Excellence**

**Single Technology Appraisal (STA)**

**Nivolumab for previously treated unresectable advanced oesophageal cancer**

**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 |
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| Appropriateness | Bristol–Myers Squibb Pharmaceuticals Ltd | None. | Noted, thank you. |
| Wording | Bristol–Myers Squibb Pharmaceuticals Ltd | This is an appropriate topic for NICE to consider. | Comment noted, thank you. Taking into account treatment history and current treatment options for this indication, the wording of the appraisal remit has been changed. The remit no longer includes 'when standard chemotherapy has failed' but instead |

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| | | | reads 'for previously treated unresectable, advanced oesophageal cancer'. The same change has been made to topic title. |
| Timing Issues | Bristol–Myers Squibb Pharmaceuticals Ltd | It is important for NICE to provide a recommendation for the use of nivolumab within the NHS as close to marketing authorisation as possible, given the limited effective treatment options currently available to these patients.<br>Patients with advanced or recurrent oesophageal cancer which have received previous treatment with chemotherapy have a very poor prognosis - less than 5% of patients with metastatic oesophageal cancer survive to five years.[1]<br><br>Besides chemotherapy and best supportive care, there are currently no other systemic anti-cancer treatment options for patients in this second line setting, in which only about 25% of patients receive chemotherapy in the UK.<br><br>**[1] National Cancer Institute Cancer Stat Facts: Esophageal Cancer. Survival by Stage. 2013 September 2017. Available from: https://seer.cancer.gov/statfacts/html/esoph.html.** | Comment noted, thank you. NICE aims to ensure the timely production of guidance and has scheduled this topic into its work programme. |
| Additional comments on the draft remit | Bristol–Myers Squibb Pharmaceuticals Ltd | None | Noted, thank you |

**Comment 2: the draft scope**

| Section | Consultee/ Commentator | Comments [sic] | Action |
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| Background information | Bristol–Myers Squibb Pharmaceuticals Ltd | No comments. | Noted, thank you. |
| The technology/ intervention | Bristol–Myers Squibb Pharmaceuticals Ltd | Nivolumab is a human monoclonal antibody<br><br>Although the description in the draft scope is correct, it does not include or reference the ONO-4538-07 or ONO-4538-24/CA209-473 study.<br>• **ONO-4538-07** (JapicCTI-142422) is an open-label, uncontrolled, multi-centre phase II study to investigate efficacy and safety of ONO-4538 in oesophageal cancer patients.<br>• **ONO-4538-24/CA209-473** (NCT02569242) is a phase III randomised, double-blind, placebo-controlled study clinical trial of nivolumab in unresectable advanced or recurrent oesophageal cancer. | Comments noted, thank you. The technology section of the scope is intended to give an overview of the main trial evidence (NCT02569242). Additional supporting evidence will be considered by the committee at the time of the appraisal. No action required. |
| Population | Bristol–Myers Squibb Pharmaceuticals Ltd | No comments. | Noted, thank you. The population section of the scope has been updated to better reflect previous treatment options; it is 'Adults with previously treated advanced or recurrent unresectable oesophageal cancer that is refractory or |

| Section | Consultee/ Commentator | Comments [sic] | Action |
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| | | | intolerant to standard therapy'. |
| Comparators | Bristol–Myers Squibb Pharmaceuticals Ltd | In the UK, patients who receive active treatment in the second line setting receive a taxane. Patients who do not receive active therapy receive best supportive care (BSC).<br><br>BSC is not an effective anti-cancer therapy, it is mainly focussed on alleviating symptoms and complications from the advanced disease. It usually has very limited impact on survival.<br><br>Irinotecan is not used in clinical practice and therefore should not be considered a relevant comparator in the UK. This is based on evidence gathered at an advisory board and a questionnaire completed by clinicians. | Comments noted. The comparators included in the scope reflect those that are relevant to the proposed licensed indication. The appraisal committee will further discuss the most relevant comparators during the development of this appraisal. No action required. |
| Outcomes | Bristol–Myers Squibb Pharmaceuticals Ltd | No comments. | Noted, thank you |
| Economic analysis | Bristol–Myers Squibb Pharmaceuticals Ltd | No comments. | Noted, thank you. |
| Equality and Diversity | Bristol–Myers Squibb Pharmaceuticals Ltd | No equality issues have been identified. | Comment noted, thank you. |

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| Other considerations | Bristol–Myers Squibb Pharmaceuticals Ltd | No comments. | Noted, thank you. |

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| Innovation | Bristol–Myers Squibb Pharmaceuticals Ltd | BMS clinical trials have demonstrated that nivolumab is an innovative medicine for the treatment of multiple indications, and considers it innovative in the treatment of advanced oesophageal cancer, due to its novel mechanism of action in this therapeutic area. It also offers the potential to make a significant impact on the substantial unmet need, including a long term survival impact in a proportion of the target population.<br><br>Nivolumab is a novel immunotherapy agent for the treatment of cancer, with a new mechanism of action as a highly specific programmed death-1 (PD-1) immune checkpoint inhibitor. It specifically binds to PD-1 receptor on the surface of immune cells and restores T-cell activity by blocking the binding of the PD-L1 and PD-L2 ligands found at the tumour site to PD-1 receptors on immune cells. This approach, enabling the body's own immune system to target cancer, is novel in gastro-oesophageal cancer and is viewed by physicians and patient interest groups as a 'step-change' in its management.<br><br>In patients with advanced or recurrent oesophageal cancer, outcomes are poor, with very short survival and few recommended treatment options, so that there is significant unmet need in this patient population.<br><br>[redacted]<br><br>Based on available data relating to nivolumab, this is of major interest for public health, in particular from the view point of therapeutic innovation, as it has the potential to offer an alternative therapeutic option with an expected improved significant benefit over management of patients in the absence of nivolumab, including significantly improved long term survival in a proportion of patients. | Comment noted. The company submission can expand on the potential innovative nature of the technology, in particular its potential to make a significant and substantial impact on health-related benefits that are unlikely to be included in the QALY calculation during the assessment. No action required. |

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| Questions for consultation | Bristol–Myers Squibb Pharmaceuticals Ltd | No comments. | Noted, thank you. |
| Additional comments on the draft scope | Bristol–Myers Squibb Pharmaceuticals Ltd | None. | Noted, thank you. |

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

Department of Health and Social Care