National Institute for Health and Clinical Excellence

Single Technology Appraisal (STA)

Ipilimumab for previously untreated unresectable malignant melanoma

Response to consultee and commentator comments on the draft scope

Section	Consultees	Comments	Action
Background information	Bristol-Myers Squibb	"first line standard care normally involves the administration of dacarbazine." Note, treatment decisions are increasingly likely to be based on BRAF mutation status.	Noted. BRAF gene mutation status has been added to the background section of the scope as a decision-making factor for people with melanoma.
	Cochrane Skin Group	The background section might be enriched by describing in some detail the recent progress made with ipilimumab and vemurafenib in the treatment of patients with metastatic melanoma	Noted. The background sections of NICE scopes are meant to be very brief. As a result, detailed information cannot be included.
	Melanoma Study Group and National Cancer Research Institute	Accurate	Noted. No action required.
The technology/ intervention	Bristol-Myers Squibb	The description of the technology is accurate.	Noted. No action required.
	Cochrane Skin Group	This section is fine	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	Yes	Noted. No action required.

Section	Consultees	Comments	Action
Population	Bristol-Myers Squibb	The population would be more accurately defined as 'Adults with previously untreated advanced (unresectable or metastatic) malignant melanoma.	Noted. It is NICE's preference to refer to the population as "people" rather than "adults". However, the appraisal will be conducted using the population indicated by the marketing authorisation.
	Cochrane Skin Group	This section is fine	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	Yes	Noted. No action required.
Comparators	Bristol-Myers Squibb	Carboplatin-based chemotherapy is not a relevant comparator in this setting. Dacarbazine is the standard treatment currently used in this setting in the NHS. As noted, subject to the on-going technology appraisal, for people with BRAF V600 mutation-positive malignant melanoma, vemurafenib is a relevant comparator.	Noted. Carboplatin-based chemotherapy has been removed from the draft scope.
	Cochrane Skin Group	This section is fine	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	Carboplatin-based chemotherapy is not a UK standard first line treatment. First line chemotherapy would be dacarbazine. In England, for patients with BRAF mutant melanoma, vemurafenib is a standard first line treatment, accessed via the regional cancer drug funds (irrespective of the NICE appraisal)	Noted. Carboplatin-based chemotherapy has been removed from the draft scope.

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Outcomes	Bristol-Myers Squibb	As ipilimumab is an immunotherapy, progression free survival and response rate are not optimal outcome measures. Overall survival, adverse effects of treatment and health-related quality of life are appropriate outcomes measures.	Noted. Progression free survival and response rate are normally included as outcome measures, but NICE recognises that certain outcome measures are more appropriate for demonstrating the efficacy of immunotherapies. As a result, progression free survival and response rate have been removed from this scope.
	Cochrane Skin Group	This section is fine	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	Note, it is now recognised that objective response assessments may not provide accurate information when evaluating immunotherapy. Immune response criteria have been established which may also be considered in order to capture the most important treatment benefits.	Noted. Progression free survival and response rate are normally included as outcome measures, but NICE recognises that certain outcome measures are more appropriate for demonstrating the efficacy of immunotherapies. As a result, progression free survival and response rate have been removed from this scope.
Economic analysis	Cochrane Skin Group	We have no expertise in this field	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	Appropriate	Noted. No action required.

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Equality	Cochrane Skin Group	No equality issues are expected	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	This technology is pertinent to all metastatic melanoma patients, irrespective of BRAF mutation status.	Noted. No action required.
Other considerations	Melanoma Study Group and National Cancer Research Institute	It is likely that in clinical practice, ipilimumab may be offered alone, without DTIC as a first line treatment. The US license permits this, the EU license for first line use is not yet established. It is not clear what contribution DTIC makes to the activity of the combination regimen, but compared with the use of ipilimumab in previously treated patients, it is difficult to conceive that it is contributing significantly to efficacy, but may be contributing to additional hepatotoxicity. For these reasons clinicians may favour using ipilimumab single agent and this needs to be considered in this appraisal.	Noted. The scope has been changed to reflect the possibility of ipilimumab use as monotherapy in first line treatment.
Innovation			
Questions for consultation	Cochrane Skin Group	Definitely yes No Not applicable	Noted. No action required.
	Melanoma Study Group and National Cancer Research Institute	Development of ipilimumab as a treatment for metastatic melanoma is a step change in management of this disease. Data is from the published randomised trial: C Robert et al, NEJM 2011;364: 3517-26	Noted. No action required.
Additional comments on the draft scope	Bristol-Myers Squibb	The most appropriate comparators are included in the scope. At this time, there are no identified sub-groups of patients in whom the technology is expected to be more clinically effective or cost effective. It would be appropriate to appraise this topic via the Single Technology	Noted. No action required.

Section	Consultees	Comments	Action
		Appraisal process.	
	Cochrane Skin Group	none	

The Melanoma Study Group and National Cancer Research Institute response was supported by Melanoma Clinical Studies Group, the Royal College of Physicians, the Royal College of Radiologists, the Association of Cancer Physicians and the Joint Collegiate Council for Oncology

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

Department of Health
Roche Products Ltd
Royal College of Pathologists
The Royal College of Nursing