National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Lenalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma ID1449

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	UK Myeloma Forum	The wording of the remit is appropriate	Comment noted.
Timing Issues	UK Myeloma Forum	Myeloma is an incurable cancer. For most patients the longest remission/control is achieved with their 1st line therapy. This is also usually the time associated with best quality of life. Therefore any therapy which is associated with improved responses and durations of response requires urgent appraisal	Comment noted. NICE schedules technology appraisals so that guidance to the NHS is timely. For cancer drugs, NICE aims to publish final guidance within 90 days of marketing authorisation wherever possible.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	UK Myeloma Forum	The background wording is appropriate	Comment noted.
The technology/ intervention	Celgene	The text should clarify that; • "Lenalidomide with dexamethasone (without bortezomib) for treating 'adult patients with previously untreated multiple myeloma who are not eligible for transplant'" is subject to a separate ongoing NICE appraisal (ID474). • The marketing authorisation for lenalidomide as "monotherapy for 'adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation" is specifically for maintenance treatment and is subject to a separate ongoing NICE appraisal (ID475). • Lenalidomide in combination with dexamethasone for treating 'adult patients who have received at least one prior therapy' is subject to a separate ongoing NICE appraisal (ID667), which is a part-review of TA171 Guidance which recommends lenalidomide in combination with dexamethasone for the treatment of multiple myeloma only in people who have received two or more prior therapies.	Comment noted. The text has been amended to include ID numbers of ongoing appraisals.
Population	UK Myeloma Forum	Yes the population should be split into those who are eligible and those who are ineligible for stem cell transplant	Comment noted.
Comparators	Celgene	This section should specify the comparators as follows to reflect the marketing authorisation for bortezomib and NICE TA311 Guidance;	Comment noted. The comparators for people who

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		• Bortezomib with dexamethasone • Bortezomib with dexamethasone and thalidomide	are eligible for stem-cell transplantation have been updated to specify the 2 bortezomib combinations recommended in TA311.
	Janssen-Cilag	For people who are eligible for stem-cell transplantation, standard of care treatment in England is bortezomib in combination with thalidomide and dexamethasone (VTd). For people who are not eligible for stem-cell transplantation, NICE currently recommends thalidomide based regimens including cyclophosphamide, thalidomide & dexamethasone (CTd), and melphalan, prednisone & thalidomide (MPT); whereas bortezomib based regimens (including bortezomib, cyclophosphamide & dexamethasone [VCd] and bortezomib, melphalan & prednisone [VMP]) are reserved for patients unsuitable for thalidomide.	Comment noted. The comparators for people who are eligible for stem-cell transplantation have been updated to specify the 2 bortezomib combinations recommended in TA311.
	UK Myeloma Forum	Broadly yes. Transplant eligible – VTD (bortezomib / thalidomide / dex) or VD (bortezomib / dex) Transplant ineligible – VMP (bortezomib / melphalan / prednislone) or CTD (cyclophosphamide / thalidomide / dex) or Lenalidomide / dex (if approved by NICE). NB in this population VMP is the most commonly used- is has baseline commissioning	Comment noted.
Outcomes	Janssen-Cilag	In relation to response rates, MRD-negative status an important prognostic marker in the front line treatment of multiple myeloma.	Comment noted. The list of outcomes in the scope is not

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			intended to be exhaustive and includes only the principal outcome measures of interest; MRD-negativity is not considered one of those.
Economic analysis	UK Myeloma Forum	Overall survival time horizon of 5 years and 10 years would be appropriate economic parameters to examine	Comment noted.
Equality and Diversity	UK Myeloma Forum	There are no subgroups that should be considered – it is important to ensure equal access for all patients	Comment noted.
Innovation	Celgene	Despite currently available therapies, myeloma remains an incurable disease characterised by immune dysfunction and relatively high mortality rates. There is a lack of a lack of a singular initial therapy approach. Treatments aims to achieve a deep response and maintain low levels of residual disease, restore and stimulate immune function and maintain and improve quality of life. Providing the most efficacious frontline therapy helps to improve patient outcomes and minimise disease burden. Combination regimes such as lenalidomide with bortezomib and dexamethasone (LEN+BORT+DEX) enhance tumoricidal effects and can reduce the impact of high risk cytogenetics. LEN+BORT+DEX is recommended as an initial therapy option in national and international guidelines, despite not yet having regulatory approval. LEN+BORT+DEX as initial therapy builds on LEN+DEX with a fixed duration of bortezomib to extend survival, and the safety profile is	Innovation will be considered by the appraisal committee when formulating its recommendations. The company will have an opportunity to describe the innovative nature of its technology in its submission to NICE.

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		consistent with the well characterised profiles of the three drugs in the newly diagnosed setting.	
	UK Myeloma Forum	This is an improvement on the currently available therapies in both the populations described. Progression free survival is an important surrogate marker for overall survival in myeloma. It also recognised that quality of life is usually improved during prolonged progression free survival.	Innovation will be considered by the appraisal committee when formulating its recommendations. Consultees will have an opportunity to describe the innovative nature of the technology in their submission to NICE. No action required.
Questions for consultation	Celgene	**Where do you consider for lenalidomide with bortezomib and dexamethasone will fit into the existing NICE pathway, Myeloma?** In line with NICE TA311 and TA228 Guidance; • as induction treatment of adults with previously untreated multiple myeloma, who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation • as first-line treatment of multiple myeloma in people for whom high-dose chemotherapy with stem cell transplantation is considered inappropriate**.**	Comment noted.
	UK Myeloma Forum	Some of the questions for consultation have been answered above. We would suggest that this combination treatment would fit as a 1st line therapy in the current NICE pathway. There are no subgroups that need to be considered.	Comment noted.

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		The main evidence sources are for transplant eligible patients – Attal et al NEJM 2017 and transplant ineligible patients Durie et al Lancet 2017	
Additional comments on the draft scope	UK Myeloma Forum	This is an excellent combination therapy that combines drugs with complementary mechanisms of action. In both transplant eligible and ineligible patients this combination offers some of the best reported progression free and overall survival outcomes observed in a phase 3 setting for 1st line therapy. This is particularly the case for the transplant ineligible population with very impressive overall survival results. This is important as the older less medically fit population are less likely to be able to tolerate multiple lines of therapy making it even more important to treat with the best possible combinations as early in the disease course as possible.	Comment noted. Consultees are encouraged to describe the innovative nature of the technology in their submission to NICE.

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

Myeloma UK
Napp Pharmaceuticals
Department of Health and Social Care