

National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Carfilzomib in combination with lenalidomide and dexamethasone for previously treated multiple myeloma

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

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Amgen	We support the referral of this topic to the Institute for appraisal.	Comments noted. No action required.
	Janssen-Cilag	We consider this topic is appropriate for referral.	Comments noted. No action required.
	Leukaemia CARE	We consider it appropriate to refer this topic to NICE for appraisal.	Comments noted. No action required.
	Myeloma UK	Myeloma UK considers this to be an appropriate topic to be referred to the National Institute for Health and Care Excellence (NICE) for appraisal.	Comments noted. No action required.
	Royal College of Pathologists	Yes. Carfilzomib is a new generation proteasome inhibitor with a good toxicity profile and recently published phase 3 data indicate impressive activity in combination with Lenalidomide and Dexamethasone	Comments noted. No action required.
	UK Myeloma Forum	Yes. Carfilzomib is a new generation proteasome inhibitor with a good toxicity profile and recently published phase 3 data indicate impressive activity in combination with Lenalidomide and Dexamethasone	Comments noted. No action required.
Wording	Amgen	We believe the wording of the remit is appropriately defined.	Comments noted. No action required.
	Leukaemia CARE	We have no issues with the wording.	Comments noted. No action required.

Section	Consultees	Comments	Action
	Myeloma UK	The wording of the remit accurately reflects the issues of clinical and cost-effectiveness at this stage in the appraisal process and conforms to the European marketing licence application for carfilzomib.	Comments noted. No action required.
	Royal College of Pathologists	Yes, broadly	Comments noted. No action required.
	UK Myeloma Forum	Yes, broadly	Comments noted. No action required.
Timing Issues	Amgen	<p>We believe that this topic is an area of urgency for the NHS in England and Wales, as despite the availability of several therapies to treat relapsed multiple myeloma, the prognosis is poor and there is an ongoing unmet need for new, effective and tolerable therapies that further improve efficacy compared to existing therapies. During the course of disease, remissions are increasingly transient with disease eventually becoming refractory (defined as progression on or within 60 days of stopping most recent treatment), and patients ultimately die from myeloma-related complications.^{1,2}</p> <p>It is therefore important that relapsing patients have prompt access to new drugs, such as carfilzomib, to prolong survival and ensure the myeloma is kept at bay for as long as possible. This urgent need for new treatments in multiple myeloma is also reflected in the current NHS Outcomes Framework improvement area for reducing premature mortality from the major causes of death (1.4 Under 75 mortality rate from cancer)³ and we therefore recommend that the commencement of this topic occurs as soon as possible to ensure timely guidance for the NHS post marketing authorisation.</p> <p>References:</p> <ol style="list-style-type: none"> Richardson PG, Sonneveld P, Schuster M, et al. Extended follow-up of a phase 3 trial in relapsed multiple myeloma: final time-to-event results of the APEX trial. <i>Blood</i> 2007; 110: 3557–3560. Kumar SK, Therneau TM, Gertz MA, et al. Clinical course of patients with relapsed multiple myeloma. <i>Mayo Clin Proc.</i> 2004;79:867–74. Department of Health. NHS Outcomes Framework 2014/15. 2013. 	Comments noted. This topic has been added to the technology appraisals schedule with consideration of the need to provide timely guidance to the NHS.

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	Leukaemia CARE	<p>Myeloma is a relentless relapsing and remitting disease, which is currently incurable. With the average 5 year survival as low as 42%, patients need access to treatments which can offer them an improvement in their survival prospects.</p> <p>We consider this to be an area of unmet need, requiring urgent action.</p>	<p>Comments noted. This topic has been added to the technology appraisals schedule with consideration of the need to provide timely guidance to the NHS.</p>
	Myeloma UK	<p>We consider a NICE appraisal of carfilzomib to be very timely for relapsed myeloma patients, but whilst urgent, will depend on the timings of the ongoing European license application.</p> <p>As myeloma is a relapsing and remitting cancer, it is always important that clinicians have a range of treatments available to them to use flexibly in their patients and best according to their individual needs.</p> <p>Having new treatments available, with demonstrable evidence of prolonging progression free survival and with a reduced side-effect profile compared to already approved drugs, is important to ensure that patients are able to live longer with myeloma and with a better quality of life.</p> <p>Given the efficacy and effectiveness data on carfilzomib that has been published to-date from the Phase III ASPIRE trial, it is clear that patients gain considerable survival benefit from receiving carfilzomib, at all stages of relapse and in combination with already available myeloma treatments. This is a benefit that is likely to increase as the ASPIRE trial progresses and more data on patient survival is published.</p> <p>It is therefore important that carfilzomib is made available as soon as possible for patients following European marketing authorisation approval.</p>	<p>Comments noted. This topic has been added to the technology appraisals schedule with consideration of the need to provide timely guidance to the NHS.</p>

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	Royal College of Pathologists	Multiple myeloma remains an incurable cancer and hence new technologies that have shown benefit in phase 3 studies should be made available on the NHS as soon as possible.	Comments noted. This topic has been added to the technology appraisals schedule with consideration of the need to provide timely guidance to the NHS.
	UK Myeloma Forum	Multiple myeloma remains an incurable cancer and hence new technologies that have shown benefit in phase 3 studies should be made available on the NHS as soon as possible.	Comments noted. This topic has been added to the technology appraisals schedule with consideration of the need to provide timely guidance to the NHS.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Amgen	We agree that the background information is accurate however note that the data presented cover all patients with multiple myeloma and not specifically the adult patient population who have received at least one prior therapy, which is the remit of this scope	Comments noted. The background section is intended to provide a brief overview of the disease and its associated management. No action required.

Section	Consultees	Comments	Action
	Leukaemia CARE	We consider the information to be accurate.	Comments noted. No action required.
	Myeloma UK	As the background information covers the majority of treatment options for myeloma that are NICE approved, it would be beneficial to include all relevant NICE guidance. In particular, where the background information covers high-dose therapy and stem cell transplantation, NICE TA 311 makes Velcade® (bortezomib) induction therapy available for patients at this stage. In addition, whilst not NICE approved, patients will typically receive a thalidomide containing regimen in this setting.	Comments noted. The background section is intended to provide a brief overview of the disease and its associated management. Attendees at the scoping workshop agreed that most people eligible for carfilzomib would not be fit enough for stem cell transplantation, so the scope does not refer to TA311.
	Royal College of Pathologists	This is adequate.	Comments noted. No action required.
	UK Myeloma Forum	This is adequate.	Comments noted. No action required.
The technology/ intervention	Amgen	The branded spelling for carfilzomib is incorrect – the correct spelling is Kyprolis.	Comments noted. The brand name has been corrected.
	Leukaemia CARE	Yes.	Comments noted. No action required.
	Myeloma UK	Please note that the brand name of carfilzomib is Kyprolis®.	Comments noted. The brand name has been corrected.
	Royal College of Pathologists	Yes	Comments noted. No action required.
	UK Myeloma Forum	Yes	Comments noted. No action required.
Population	Amgen	We agree the population is appropriately defined.	Comments noted. No action required.

Section	Consultees	Comments	Action
	Leukaemia CARE	The population is defined widely as 'people with multiple myeloma who have received at least 1 prior therapy'. We would suggest that it might be more appropriate to consider it primarily as a third-line treatment option.	Comments noted. The wording of the scope reflects the indication that gained a positive opinion from the Committee for Medicinal Products for Human Use. No action required.
	Myeloma UK	We agree that the population is defined appropriately.	Comments noted. No action required.
	Royal College of Pathologists	Yes	Comments noted. No action required.
	UK Myeloma Forum	Yes	Comments noted. No action required.
Comparators	Amgen	<p>We believe the relevant comparator treatments for carfilzomib (in combination with lenalidomide and dexamethasone) are lenalidomide (in combination with dexamethasone) and bortezomib, (alone or in combination with dexamethasone).</p> <p>We recommend the removal of the following treatments listed in the draft scope:</p> <ul style="list-style-type: none"> • thalidomide, • chemotherapy regimens, <p>Both of the above treatments are most commonly used in the first line setting and would therefore be used before carfilzomib (in combination with lenalidomide and dexamethasone) in the treatment pathway given the anticipated marketing authorisation in adults who have received at least 1 prior therapy.</p> <ul style="list-style-type: none"> • bendamustine, • pomalidomide, <p>Both of the above treatments are most commonly used in the latter line settings. We therefore believe that these treatments would be used as options after carfilzomib (in combination</p>	<p>Comments noted. Following the scoping workshop, the comparators have been updated to:</p> <ul style="list-style-type: none"> • bortezomib containing regimens • lenalidomide in combination with dexamethasone • bendamustine • panobinostat in combination with bortezomib and dexamethasone (for people who have had at least 2 prior regimens) <p>Although the workshop attendees agreed that bortezomib and lenalidomide were the most appropriate comparators for carfilzomib, they also noted that the carfilzomib trial population included people who received 1 – 3 prior therapies. Therefore it was agreed that bendamustine could be a relevant comparator if the marketing authorisation for carfilzomib allows it to be used later in the treatment pathway. Pomalidomide is not recommended by NICE for this indication</p>

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		with lenalidomide and dexamethasone for this indication) in the treatment pathway. For example, pomalidomide is specifically indicated for patients who have received prior therapy with lenalidomide.	and will be removed from the Cancer Drugs Fund in November 2015, so it is not an appropriate comparator.
	Leukaemia CARE	<p>The list of comparators appears to be very wide. We feel that it is probably inappropriate to compare carfilzomib to first-line treatments (which may include thalidomide or bortezomib).</p> <p>We feel that it may be more suitable to compare against 2nd or 3rd line (particularly 3rd line) treatment options only, which may include bortezomib, lenalidomide and possible bendamustine and pomalidomide.</p> <p>If carfilzomib is to be considered a second-line option then we would recommend the addition of Stem Cell/Bone Marrow transplants as a comparators option.</p>	<p>Comments noted. Following the scoping workshop, the comparators have been updated to:</p> <ul style="list-style-type: none"> • bortezomib containing regimens • lenalidomide in combination with dexamethasone • bendamustine • panobinostat in combination with bortezomib and dexamethasone (for people who have had at least 2 prior regimens) <p>Scoping workshop attendees agreed that, whilst stem cell transplantation may be given in some instances, most of the population covered by this scope would not be fit enough for stem cell transplantation, and therefore it was not an appropriate comparator.</p>
	Myeloma UK	<p>As the most likely approved indications of carfilzomib are likely to be at first (second line) and second relapse (third line), we consider the main comparators to be as follows:</p> <p>Bortezomib in combination with dexamethasone (NICE first relapse guidance).</p> <p>Lenalidomide (Revlimid®) in combination with dexamethasone (NICE second relapse guidance and subject to NICE assessment at first relapse).</p>	<p>Comments noted. Following the scoping workshop, the comparators have been updated to:</p> <ul style="list-style-type: none"> • bortezomib containing regimens • lenalidomide in combination with dexamethasone • bendamustine • panobinostat in combination with bortezomib and dexamethasone (for people who have had at least 2 prior regimens)

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		<p>We do not consider thalidomide containing regimens or standard chemotherapy to be major comparators in this appraisal as they are not used routinely in the appraisal setting.</p> <p>We also do not consider pomalidomide and dexamethasone to be an appropriate comparator. This is because pomalidomide is licensed and being assessed by NICE in patients who are relapsed and refractory to bortezomib and lenalidomide. Carfilzomib would be appraised in combination with lenalidomide and dexamethasone - so it wouldn't cover the same group of patients as pomalidomide. Carfilzomib would be used as a treatment before pomalidomide rather than instead of.</p> <p>Bendamustine is commonly used in myeloma clinical practice also likely to be used later on in the treatment pathway for myeloma patients (i.e. in very advanced patients).</p>	<p>Although the workshop attendees agreed that bortezomib and lenalidomide were the most appropriate comparators for carfilzomib, they also noted that the carfilzomib trial population included people who received 1 – 3 prior therapies.</p> <p>Therefore it was agreed that bendamustine could be a relevant comparator if the marketing authorisation for carfilzomib allows it to be used later in the treatment pathway. Pomalidomide is not recommended by NICE for this indication and will be removed from the Cancer Drugs Fund in November 2015, so it is not an appropriate comparator.</p>
	Royal College of Pathologists	The most appropriate comparator is lenalidomide and dexamethasone. Bortezomib (with dexamethasone), bendamustine and pomalidomide may also be comparators, but not in combination with Lenalidomide and Dexamethasone.	<p>Comments noted. Following the scoping workshop, the comparators have been updated to:</p> <ul style="list-style-type: none"> • bortezomib containing regimens • lenalidomide in combination with dexamethasone • bendamustine • panobinostat in combination with bortezomib and dexamethasone (for people who have had at least 2 prior regimens) <p>Pomalidomide is not recommended by NICE for this indication and will be removed from the</p>

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			Cancer Drugs Fund in November 2015, so it is not an appropriate comparator.
	UK Myeloma Forum	The most appropriate comparator is lenalidomide and dexamethasone. Bortezomib (with dexamethasone), bendamustine and pomalidomide may also be comparators, but not in combination with Lenalidomide and Dexamethasone.	<p>Comments noted. Following the scoping workshop, the comparators have been updated to:</p> <ul style="list-style-type: none"> • bortezomib containing regimens • lenalidomide in combination with dexamethasone • bendamustine • panobinostat in combination with bortezomib and dexamethasone (for people who have had at least 2 prior regimens) <p>Pomalidomide is not recommended by NICE for this indication and will be removed from the Cancer Drugs Fund in November 2015, so it is not an appropriate comparator.</p>
Outcomes	Amgen	We would like to confirm that the response rates in the list of outcomes in the draft scope encompass a range of response outcomes (e.g. complete response, progressive disease, duration of response, time to response etc.).	Comments noted. Scoping workshop attendees agreed that 'response rates' included the various response outcomes, and that 'complete response' was a particularly important outcome to note because of a correlation with length of survival. It therefore agreed to reword the outcome to "response rates (for example, complete response)"
	Leukaemia CARE	We agree that these are appropriate.	Comments noted. No action required.
	Myeloma UK	We agree that these are appropriate outcome measures.	Comments noted. No action required.

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	Royal College of Pathologists	We would suggest that, in addition to the response rate, complete response should also be included. This indicates a deep response, and is an indication of the quality of response. Thus the deeper the response, the greater the benefit in terms of disease free and overall survival	Comments noted. Scoping workshop attendees agreed that 'complete response' was a particularly important outcome to note because of a correlation with length of survival. It therefore agreed to reword the outcome to "response rates (for example, complete response)"
	UK Myeloma Forum	We would suggest that, in addition to the response rate, complete response should also be included. This indicates a deep response, and is an indication of the quality of response. Thus the deeper the response, the greater the benefit in terms of disease free and overall survival	Comments noted. Scoping workshop attendees agreed that 'complete response' was a particularly important outcome to note because of a correlation with length of survival. It therefore agreed to reword the outcome to "response rates (for example, complete response)"
Economic analysis	Amgen	We acknowledge that some of the comparators listed in the scope (bortezomib monotherapy [NICE TA129] and lenalidomide [NICE TA171]) have been recommended with Patient Access Schemes (complex schemes) that we will consider accordingly in our evidence submission	Comments noted. No action required.
	Leukaemia CARE	We have no comments to make.	Comments noted. No action required.
	Myeloma UK	As the comparators in the appraisal, particularly bortezomib (first relapse) and lenalidomide (second relapse) have patient access schemes attached to them, it is important that this is addressed at both the scoping workshop and also within the health economic analysis. In addition, if carfilzomib is approved in combination with lenalidomide and dexamethasone this has implications for the currently available patient access scheme on NICE TA171. This is something that should also be discussed in the scoping workshop.	Comments noted. The Appraisal Committee will discuss the health-economic modelling and the inclusion of patient access schemes.

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	Royal College of Pathologists	no comment	No action required.
	UK Myeloma Forum	no comment	No action required.
Equality and Diversity	Amgen	No comments.	No action required.
	Leukaemia CARE	No comment	No action required.
	Myeloma UK	We do not anticipate that there are any issues with equalities in this appraisal.	Comments noted. No action required.
	Royal College of Pathologists	we do not believe there are such considerations here.	Comments noted. No action required.
	UK Myeloma Forum	we do not believe there are such considerations here.	Comments noted. No action required.
Other considerations	Amgen	No comments.	No action required.
	Leukaemia CARE	N/A	No action required.
	Myeloma UK	No comments.	No action required.
	Royal College of Pathologists	Nil	No action required.
	UK Myeloma Forum	Nil	No action required.
Innovation	Amgen	Carfilzomib is an irreversible, highly specific, and rapidly acting proteasome inhibitor which is not reactive against non-proteasomal targets. Treatment with carfilzomib (in combination with lenalidomide	Comments noted. The potentially innovative nature of the drug will be considered by the Appraisal Committee.

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		<p>and dexamethasone (CRd)) has led to significantly improved outcomes in patients with relapsed multiple myeloma. There are currently no other treatment regimens that have been associated with an equivalent duration of median progression-free survival, in the absence of transplantation to that observed with CRd. In the recently published ASPIRE study (NCT01080391), CRd demonstrated a clinically relevant 31% decrease in the risk of disease progression or death and an increase of 8.7 months in the median progression-free survival (26.3 months in the CRd group vs. 17.6 months in the lenalidomide and dexamethasone (Rd) control group). Since the primary objective in ASPIRE was met, an interim analysis of overall survival was conducted and while it was not reached in either group (hazard ratio of 0.79 (95% CI, 0.63 to 0.99; P = 0.04), it is trending in favour of the CRd group.</p> <p>The finding that the rate of complete response or better in the CRd group was more than three times the rate in the Rd group (31.8% and 9.3% of patients, respectively (P<0.001)) is also particularly notable, because studies have shown an association between more robust responses and improved survival in patients with multiple myeloma. Patients in the CRd group also reported superior health-related quality of life (according to the score on the QLQ-C30 Global Health Status and Quality of Life scale) than those in the Rd group during 18 cycles of treatment.</p> <p>Available non-clinical pharmacology data demonstrate the selectivity of carfilzomib for the N-terminal threonine-containing active sites of the 20S proteasome, the proteolytic core particle within the 26S proteasome, which is attributable for the lack of neurotoxic effects compared with other</p>	

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		<p>proteasome inhibitors, contributing to an acceptable safety and tolerability profile for CRd.</p> <p>We therefore believe that carfilzomib (in combination with lenalidomide and dexamethasone) represents a significant new advance in the treatment of adults with multiple myeloma who have received at least 1 prior therapy, fulfilling the current unmet need in these patients and representing a medical step-change in the management of the condition.</p> <p>The nature of the data is published literature regarding the aspects described above.</p>	
	Leukaemia CARE	<p>We are familiar with the ASPIRE study and its outcome, in particular the significance of the progression-free survival data and the combination of CRd, which demonstrated a clinically relevant decrease in the progression or death. We feel that this combination represents a significant advance in the treatment of patients with myeloma.</p> <p>We will defer to any submissions made by the marketing company, who we feel are in a better position to provide a more comprehensive review of the innovation.</p>	Comments noted. The potentially innovative nature of the drug will be considered by the Appraisal Committee.

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	Myeloma UK	<p>Carfilzomib produces effective and durable responses in relapsed patients, even in those refractory to two or more treatments. Results from the ongoing Phase III ASPIRE trial have shown adding carfilzomib, lenalidomide and dexamethasone can increase progression free survival by nearly nine months.</p> <p>Unlike other proteasome inhibitors such as bortezomib which is commonly associated with peripheral neuropathy, carfilzomib has been demonstrated to cause very low rates of peripheral neuropathy (in less than 1% of patients).</p> <p>In general, myeloma patients report that peripheral neuropathy is one of the most debilitating side-effects of myeloma treatments and one that impacts hugely on their quality of life and ability to carry out day-to-day tasks such as washing and walking.</p> <p>Patients report having trouble going to sleep at night due to tingling and pain in their hands and feet. Any treatment that reduces the likelihood and incidence of peripheral neuropathy and/or does not lead to any worsening of already present neuropathy, can be considered a step-change innovation.</p>	Comments noted. The potentially innovative nature of the drug will be considered by the Appraisal Committee.

Section	Consultees	Comments	Action
	Royal College of Pathologists	- Yes, carfilzomib is a proteasome inhibitor with improved target specificity and hence tolerability, compared to existing licensed PI Bortezomib. Given the central importance of PI-based therapy in the treatment of myeloma, the availability of this new generation agent is a 'step-change'. Improved safety profile means that patients can receive treatment on protocol in a timely fashion, with less discontinuations for adverse events, thus increasing overall response rates and duration of response.	Comments noted. The potentially innovative nature of the drug will be considered by the Appraisal Committee.
	UK Myeloma Forum	- Yes, carfilzomib is a proteasome inhibitor with improved target specificity and hence tolerability, compared to existing licensed PI Bortezomib. Given the central importance of PI-based therapy in the treatment of myeloma, the availability of this new generation agent is a 'step-change'. Improved safety profile means that patients can receive treatment on protocol in a timely fashion, with less discontinuations for adverse events, thus increasing overall response rates and duration of response.	Comments noted. The potentially innovative nature of the drug will be considered by the Appraisal Committee.
Questions for consultation	Amgen	<p>Have all relevant comparators for carfilzomib in combination with lenalidomide and dexamethasone been included in the scope?</p> <p>Yes. Please refer to our comments regarding comparators (Section 1).</p> <p>Which treatments are considered to be established clinical practice in the NHS for multiple myeloma following at least 1 prior therapy?</p> <p>In the second line setting, treatments considered to be established clinical practice are:</p> <ul style="list-style-type: none"> • bortezomib (in combination with dexamethasone). <p>In the third line setting, treatments considered to be</p>	Comments noted. No action required.

Section	Consultees	Comments	Action
		<p>established clinical practice are:</p> <ul style="list-style-type: none"> • lenalidomide (in combination with dexamethasone). <p>Are the subgroups suggested in ‘other considerations appropriate? Are there any other subgroups of people in whom carfilzomib in combination with lenalidomide and dexamethasone is expected to be more clinically effective and cost effective or other groups that should be examined separately?</p> <p>An assessment of the pre-defined subgroups or any other subgroups in which carfilzomib may be expected to be more clinically and cost effective is currently under evaluation.</p> <p>Where do you consider carfilzomib in combination with lenalidomide and dexamethasone will fit into the existing NICE pathway, blood and bone marrow cancers?</p> <p>We consider carfilzomib to be potentially incorporated into the existing pathway based on the scope of this appraisal as an option alongside:</p> <ul style="list-style-type: none"> • Treatment after 1 prior therapy at first relapse (alongside bortezomib); and • Treatment after 2 or more prior therapies (alongside lenalidomide) <p>NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process.</p> <p>We support the appraisal of carfilzomib through the STA process to enable the Institute to provide timely guidance to the NHS following marketing authorisation due to the current</p>	

Section	Consultees	Comments	Action
		unmet need.	
	Leukaemia CARE	Any comments we may wish to make have already been mentioned in our submission.	Comments noted. No action required.
	Myeloma UK	<p>Q. Have all relevant comparators for carfilzomib in combination with lenalidomide and dexamethasone been included in the scope? Which treatments are considered to be established clinical practice in the NHS for multiple myeloma following at least one prior therapy.</p> <p>See section on comparators.</p> <p>Q. Where do you consider carfilzomib in combination with lenalidomide and dexamethasone will fit into the existing NICE pathway, blood and bone marrow cancers?</p> <p>We would expect carfilzomib to be made available to myeloma patients, after one or more prior therapies. More specifically in combination with lenalidomide and dexamethasone for myeloma patients either at first relapse (second line) or at second relapse (third line).</p>	Comments noted. No action required.

Section	Consultees	Comments	Action
	Royal College of Pathologists	<p>Question: Are the subgroups suggested in 'other considerations appropriate?</p> <p>Answer:- Based on published evidence use of Carfilzomib as set out in the current remit will not benefit any particular sub groups of myeloma patients</p> <p>Question: Do you consider that the use of carfilzomib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?</p> <p>Answer:- the improved safety profile, compared with currently available regimens, will lead to improved health related quality of life</p> <p>Question: Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.</p> <p>Answer:- measurement of HR-QoL using the EORTC QLQ-C30 tool confirmed superior benefit to patients receiving carfilzomib (with lenalidomide and dexamethasone) compared to those on the control arm (lenalidomide and dexamethasone only). These data are contained in the publication on the Phase 3 study in the New England Journal of Medicine (DOI: 10.1056/NEJMoa1411321)</p>	Comments noted. No action required.

Section	Consultees	Comments	Action
	UK Myeloma Forum	<p>Question: Are the subgroups suggested in 'other considerations appropriate?</p> <p>Answer:- Based on published evidence use of Carfilzomib as set out in the current remit will not benefit any particular sub groups of myeloma patients</p> <p>Question: Do you consider that the use of carfilzomib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?</p> <p>Answer:- the improved safety profile, compared with currently available regimens, will lead to improved health related quality of life</p> <p>Question: Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.</p> <p>Answer:- measurement of HR-QoL using the EORTC QLQ-C30 tool confirmed superior benefit to patients receiving carfilzomib (with lenalidomide and dexamethasone) compared to those on the control arm (lenalidomide and dexamethasone only). These data are contained in the publication on the Phase 3 study in the New England Journal of Medicine (DOI: 10.1056/NEJMoa1411321)</p>	Comments noted. No action required.
Additional comments on the draft scope.	Myeloma UK	N/A	No action required.
	Royal College of Pathologists	We agree the technology should be appraised through the STA process.	Comments noted. No action required.
	UK Myeloma Forum	We agree the technology should be appraised through the STA process.	Comments noted. No action required.

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

Department of Health

Merck Sharp & Dohme (no longer manufacture dexamethasone)

Napp Pharmaceuticals

National Collaborating Centre for Cancer