

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Carfilzomib for previously treated multiple myeloma

The multiple myeloma treatment pathway in the NHS has changed since this guidance was published. So we have updated the recommendations in section 1 of the guidance and explained this change in section 4.25. We have also made sections 2 and 4 more accessible. No other sections of the guidance have been updated, so these are the same as in the original guidance.

1 Recommendations

1.1 Carfilzomib with dexamethasone is recommended as an option for treating multiple myeloma in adults, only if:

- they have had only 1 previous therapy and
- the company provides carfilzomib according to the commercial arrangement (see section 2). **[2020]**

1.2 These recommendations are not intended to affect treatment with carfilzomib that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. **[2017]**

2 The technology

Marketing authorisation indication

- 2.1 Kyprolis 'in combination with either lenalidomide and dexamethasone or dexamethasone alone, is indicated for the treatment of adult patients with multiple myeloma who have had at least 1 prior therapy'. [2017]

Adverse reactions

- 2.2 The most common adverse reactions (in more than 20% of patients) were: anaemia, fatigue, diarrhoea, thrombocytopenia, nausea, pyrexia, dyspnoea, respiratory tract infection, cough and peripheral oedema. For full details of adverse reactions and contraindications, see the summary of product characteristics. [2017]

Dosage in the marketing authorisation

One cycle of carfilzomib is 28 days. [2017]

In combination with lenalidomide and dexamethasone

- Carfilzomib is given on 2 consecutive days each week for 3 weeks (days 1, 2, 8, 9, 15, and 16), followed by a 12-day rest period (days 17 to 28) for the first 12 cycles.
- From cycle 13, the day 8 and 9 doses of carfilzomib are omitted.
- Carfilzomib is administered at a starting dose of 20 mg/m² (maximum dose 44 mg) in cycle 1 on days 1 and 2.
- If tolerated, the dose should be increased to 27 mg/m² (maximum dose 60 mg) from day 8 of cycle 1. [2017]

In combination with dexamethasone alone

- Carfilzomib is given on 2 consecutive days each week for 3 weeks (days 1, 2, 8, 9, 15, and 16) followed by a 12-day rest period (days 17 to 28).

- Carfilzomib is administered at a starting dose of 20 mg/m² (maximum dose 44 mg) in cycle 1 on days 1 and 2.
- If tolerated, the dose should be increased to 56 mg/m² (maximum dose 123 mg) from day 8 of cycle 1.

For further details, see the [summary of product characteristics](#). [2017]

Price

2.3 The list price of carfilzomib is £1,056 for a 60-mg vial (excluding VAT; MIMS online, accessed October 2016). [2017]

In combination with lenalidomide and dexamethasone

- From cycle 1 to 12: £5,127 (no wastage), £6,336 (wastage).
- From cycle 13: £3,418 (no wastage), £4,220 (wastage). [2017]

In combination with dexamethasone alone

- £10,644 (no wastage), £12,627 (wastage).

The company has a commercial arrangement (simple discount patient access scheme). This makes carfilzomib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount. [2017]

3 Evidence

The appraisal committee considered evidence submitted by Amgen, including new evidence submitted after responses to the consultation document and suspension of the initial final appraisal determination, and a review of these submissions by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence. [2017]

4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of carfilzomib, having considered evidence on the nature of multiple myeloma and the value placed on the benefits of carfilzomib by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

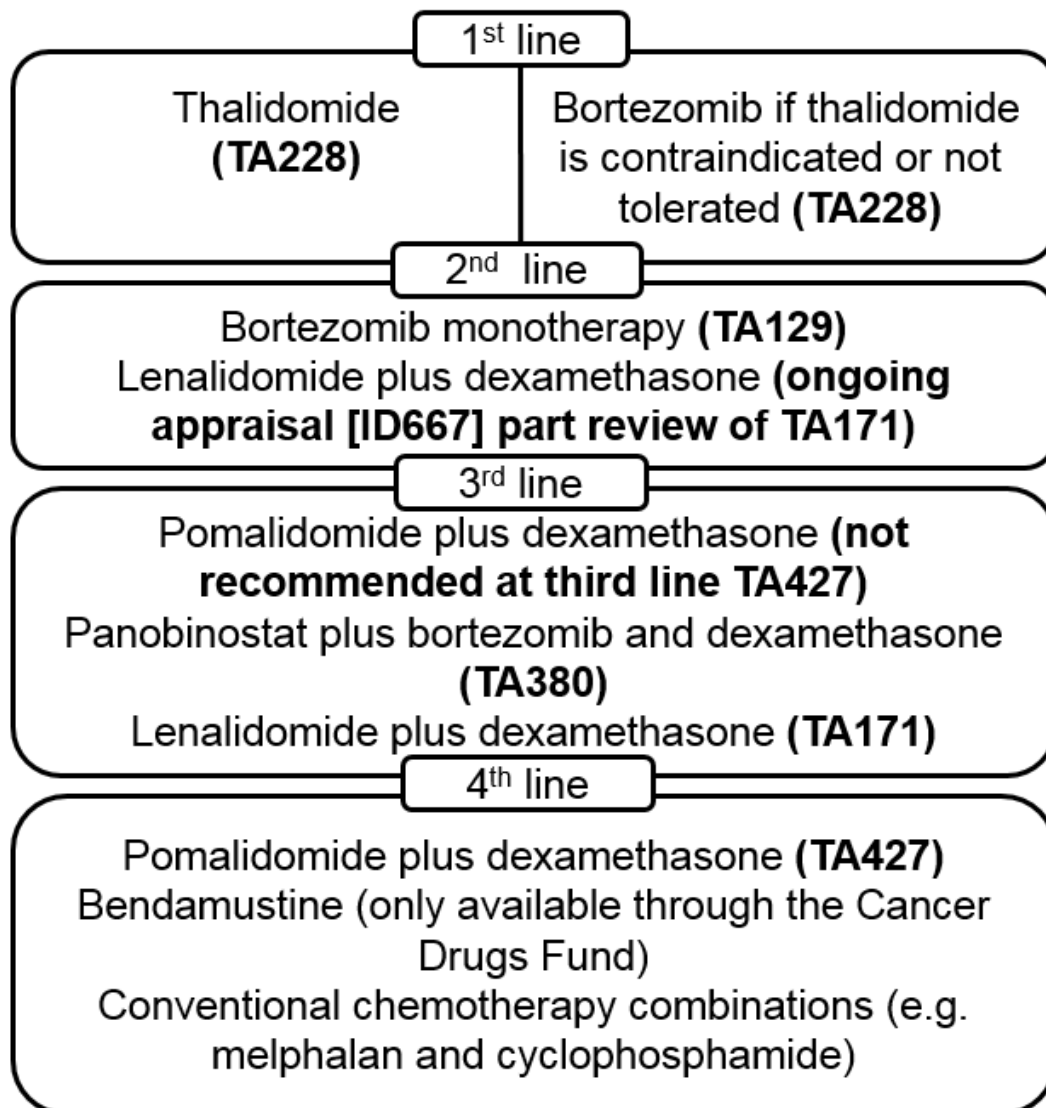
Clinical need

- 4.1 The committee noted the emotional impact and burden of disease on people with multiple myeloma, their families and carers, and the value of carfilzomib because it provides an additional treatment option that is well tolerated. The committee understood that there are effective treatments at earlier stages of the disease but there is a need for novel chemotherapeutic agents at later stages of the disease. The clinical experts emphasised the problem of emergent cells that are resistant to current treatment options; because of this, double and triple therapies are often used at later stages of the treatment pathway because a combination of different mechanisms is needed to control the resistant cells. The committee heard from the patient expert that although carfilzomib is given intravenously, which often deters patients, it offers important benefits over existing treatments. In particular, carfilzomib does not appear to be associated with neuropathic adverse reactions to the same extent as standard treatment and offers an increased remission time so patients are willing to have an intravenous administration. The committee concluded that patients and clinicians would welcome carfilzomib because there is a need for effective treatments after relapse and because it offers a number of quality-of-life improvements over current treatment options. **[2017]**

Decision problem and treatment pathway

- 4.2 The committee considered the current treatment pathway for people whose disease has relapsed after having 1 therapy, including current NICE-recommended treatments and other agents used in practice. [2017]

Figure 1 Treatment pathway for multiple myeloma in people who cannot have a stem cell transplant

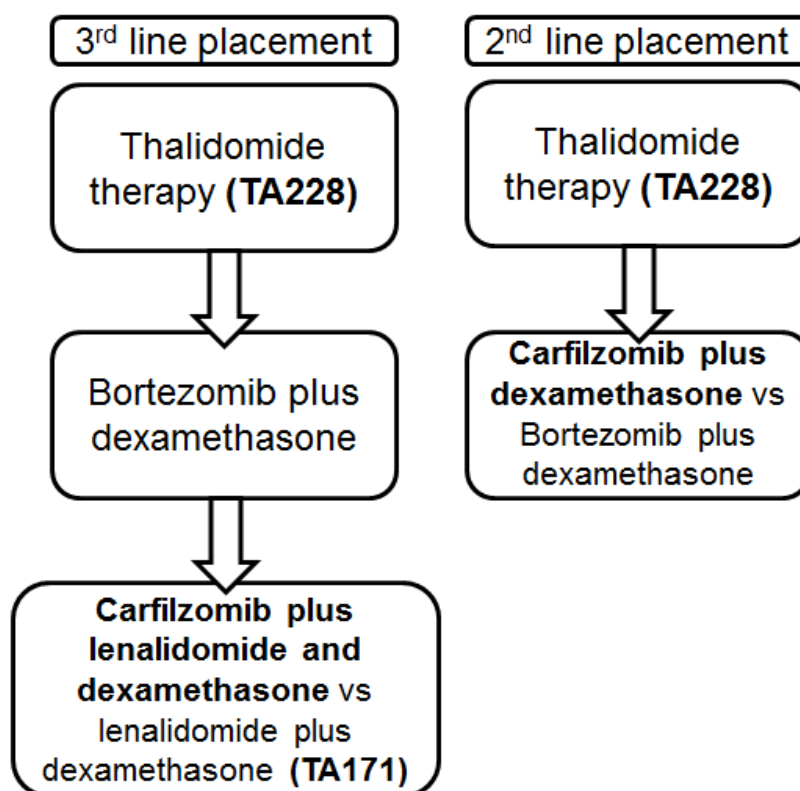


- 4.3 The NICE scope specified comparator treatments that are currently used at second, third and fourth line (see figure 1). The committee noted that the marketing authorisation for carfilzomib is for people who have had at

least 1 previous therapy (and therefore includes fourth line treatment). However the company's comparisons restricted placement to second and third line only, based on the previous treatments received (taking account of current NICE guidance and the most commonly used treatment regimens in practice; see figure 2). The committee heard from the clinical expert that the company's approach was clinically rational and carfilzomib would mainly be used at second and third line. Clinicians prefer to use a combination of chemotherapeutic agents, alternating between agents with different mechanisms of action (immunomodulators and proteasome inhibitors, such as thalidomide and bortezomib). The clinical expert also explained that there are several treatments newly recommended in NICE technology appraisals, which are not yet used routinely in practice (pomalidomide for treating multiple myeloma after 3 previous treatments which included both lenalidomide and bortezomib, panobinostat for treating multiple myeloma after at least 2 previous therapies and lenalidomide for treating multiple myeloma after at least 2 previous therapies). The committee accepted this opinion and concluded that the positioning and comparison rationale provided by the company for carfilzomib is appropriate, that is:

- carfilzomib and dexamethasone compared with bortezomib and dexamethasone at second line
- carfilzomib, lenalidomide and dexamethasone compared with lenalidomide and dexamethasone at third line. **[2017]**

Figure 2 Company's comparators and treatment route to receive carfilzomib¹



4.4 The committee was aware that carfilzomib could theoretically be considered, within its marketing authorisation, in other positions within the treatment pathway (for example, as an alternative to lenalidomide plus dexamethasone at second line, for which the company provided a scenario analysis, and at subsequent lines after third line). However, it was not able to consider carfilzomib in these positions because not enough evidence was received from the company. The committee therefore focused its recommendations on the second and third line positions. [2017]

¹ The company also provided a scenario analysis in which carfilzomib plus lenalidomide and dexamethasone was proposed at second line, as an alternative to lenalidomide plus dexamethasone for people who have had bortezomib first line.

Clinical effectiveness

4.5 The committee noted that the company presented data from 2 trials:

- ENDEAVOR: carfilzomib plus dexamethasone, compared with bortezomib plus dexamethasone
- ASPIRE: carfilzomib plus lenalidomide and dexamethasone, compared with lenalidomide plus dexamethasone.

The committee noted that these trials were of good quality and included active comparators that are relevant to the appraisal, thereby providing direct head-to-head evidence. It noted the overall survival data had not yet matured, so considered in detail the progression-free survival estimates for the overall population. It agreed that the estimates were compelling in favour of carfilzomib over the comparator treatments. It noted that, compared with bortezomib and dexamethasone, carfilzomib and dexamethasone doubled the progression-free survival to 18.7 months. When compared with lenalidomide and dexamethasone, carfilzomib with lenalidomide and dexamethasone increased the progression-free survival to 26.3 months (a gain of 8.7 months). The committee concluded the trial evidence showed a progression-free survival benefit for carfilzomib combinations over the comparators in the overall population.

4.6 The committee understood that to estimate the efficacy of carfilzomib at second and third line, the company specified post hoc subgroups for:

- people who had 1 previous therapy, not bortezomib (second line compared with bortezomib and dexamethasone)
- people who had 2 previous therapies, not lenalidomide (or carfilzomib; third line compared with lenalidomide and dexamethasone).

The committee was aware of the limitations and the uncertain outcomes associated with subgroups that were not prespecified. It

recognised the company's attempt to counter the uncertainties by adjusting for imbalances in the baseline characteristics with additional covariates by using a Cox proportional hazards model to estimate efficacy (as hazard ratios) of carfilzomib and its comparators. But the committee heard from the evidence review group (ERG) that the choice of these covariates was unclear without sufficient justification. The committee noted that the choice of variables to adjust the model should be those that are prognostic of the outcome. In response to the appraisal consultation document the company presented a range of methods to adjust for covariates, including stepwise-selection and least absolute shrinkage and selection operator (LASSO) methods, to explore the plausibility of different combinations of covariates. The committee noted that the company preferred the stepwise-selection method, whereas the ERG considered that the LASSO method was more appropriate. The committee was satisfied that the company had sufficiently explored uncertainty around the choice of covariates and that the comparative efficacy estimates were reasonable to consider for decision-making for both comparisons of carfilzomib at second and third line. **[2017]**

- 4.7 The committee noted that the median age of people in ENDEAVOR (comparing carfilzomib and dexamethasone with bortezomib and dexamethasone) and ASPIRE (comparing carfilzomib, lenalidomide and dexamethasone with lenalidomide and dexamethasone) was 64 and 65 respectively. Patients had an average Eastern Cooperative Oncology Group (ECOG) status of 0 to 2. In comparison, data collected in the UK by the Haematological Malignancy Research Network (HMRN) from 2001 to 2012 showed that the median age at diagnosis was 73. The committee was therefore concerned that the results of the trials may not be generalisable to clinical practice in England. The committee understood from the clinical expert that patients in myeloma trials are generally younger because they are more willing and able to travel to the treatment

centre. It also understood that patients are being diagnosed earlier and, as a result, the average age at diagnosis in England is younger than that recorded by the HMRN. The committee concluded that the patient characteristics in the trials could be generalised to UK clinical practice.

[2017]

4.8 The committee noted a discrepancy between the length of carfilzomib treatment stipulated in the marketing authorisation and the stopping rule applied in ASPIRE. It understood that in ASPIRE, carfilzomib was stopped after 18 cycles whereas the marketing authorisation allows for treatment until progression or unacceptable toxicity. The committee heard from the company that no stopping rule was applied in ENDEAVOR and the average length of treatment was 16.5 cycles, which the clinical experts stated would be reflective of clinical practice. The committee concluded that the length of treatment in the trials was reflective of clinical practice in the UK. **[2017]**

4.9 The committee noted the adverse reactions listed in the summary of product characteristics. It heard that in practice, serious adverse reactions and toxicity are managed through dose reduction and concomitant medication. It also heard that people taking carfilzomib find it tolerable and that neuropathic adverse reactions are less evident than with bortezomib. The committee was satisfied that although carfilzomib is associated with serious adverse reactions, these are not any more significant than those experienced with other chemotherapeutic agents and are manageable in practice. **[2017]**

Cost effectiveness

4.10 The committee had concerns about the company's initial approach to survival modelling. It stated in the appraisal consultation document that it would have liked to see the effect of fitting different covariate-adjusted parametric models, using different extrapolation techniques and assessing the plausibility of the resulting predictions. The committee recognised that

the company provided revised analyses to address these concerns in response to the appraisal consultation document but was still uncertain on the cost-effectiveness results due to immature survival data. The committee was subsequently made aware that more mature overall survival data was available from the ENDEAVOR trial after the meeting had concluded. Therefore, the initial final appraisal determination was suspended to allow the committee to consider the new data and analysis. It considered in detail the most appropriate extrapolation function and the validity of the proportional hazards assumption. [2017]

4.11 The committee considered the validity of the proportional hazards assumption and noted that this assumes the hazards are constant over time (that is, the benefits of treatment continue until the end of the time horizon or death). The committee was aware that the company presented a model with jointly-fitted survival curves in its revised base case, which requires the assumption of proportional hazards. The company also presented a detailed exploration of the appropriateness of the proportional hazards assumption, including a scenario analysis comparing the effect of using jointly or independently fitted curves (no proportional hazards assumption required) on the cost-effectiveness results. The committee heard from the ERG that in the extrapolation of overall survival for carfilzomib plus lenalidomide and dexamethasone compared with lenalidomide plus dexamethasone (third line), the convergence of curves in the log-log plots suggested that the proportional hazards assumption was not valid. The committee recognised that the company had thoroughly explored the proportional hazards assumption in response to the appraisal consultation document but it was not convinced by the company's interpretation that the proportional hazards assumption was valid for the comparison of carfilzomib at third line. The independently fitted model had a substantially higher incremental cost-effectiveness ratio (ICER) for carfilzomib plus lenalidomide and dexamethasone compared with lenalidomide plus dexamethasone (third line). The committee

acknowledged that when comparing joint and independently fitted models in the company's revised scenario analysis there was very little difference in the cost-effectiveness results for carfilzomib plus dexamethasone compared with bortezomib plus dexamethasone at second line. For these reasons, the committee concluded that the proportional hazards assumption was acceptable for consideration in decision-making for the comparison of carfilzomib at second line but not third line. **[2017]**

4.12 The committee considered the survival model used in the company's revised base case in response to the appraisal consultation document. It noted that the company used a Weibull distribution to estimate long-term survival whereas the ERG's exploratory base case used a Gompertz distribution. The committee also considered the company's revised scenario analysis to assess the effect of several different parametric distributions on the cost-effectiveness results. The company justified its choice of parametric curve by analysis of statistical fit, eliciting expert opinion and validating the curves externally. The committee considered the validation, plausibility and maturity of the overall survival data used to inform the Weibull and Gompertz parametric curves. It noted that the company presented new data in which the ENDEAVOR trial had reached its clinical endpoint for overall survival and the data were more mature than the ASPIRE trial, but it recalled its earlier conclusion on the lack of reliability of the proportional hazards assumptions for the comparison of carfilzomib at third line (see section 4.11). Therefore the committee focused on the comparison of carfilzomib at second line from the ENDEAVOR trial. The committee noted that the use of the Weibull or Gompertz distribution had a considerable effect on the ICER estimates, and that they had similar statistical fits. It also considered the external validity of both extrapolations; the company presented evidence that further validated the Weibull curve using data from Orlowski et al. (2016) trial (which compared bortezomib monotherapy to bortezomib combination therapy up to 9 years). The committee noted that the Kaplan–Meier curve

for the bortezomib monotherapy arm from Orłowski et al. showed a greater percentage of people surviving with multiple myeloma at 9 years than predicted by the Gompertz curve. It also heard from the ERG that it agreed with the validation evidence presented by the company. The committee concluded that the new overall survival data and external validation supported the Weibull distribution for extrapolation for the comparison of carfilzomib at second line. It further concluded that the trial data was too immature to inform on the most appropriate parametric curve for extrapolation for the comparison of carfilzomib at third line. [2017]

- 4.13 For comparison of carfilzomib at second line, the committee noted that there were discrepancies between the company's initial model and clinical practice in the dosing schedule and length of treatment for bortezomib. It noted that the marketing authorisation for bortezomib states that it can be given twice weekly for 8 cycles (21-day cycles equal to a total of 32 doses), whereas the model assumed bortezomib would be given twice weekly as an intravenous infusion until progression (consistent with the duration of treatment in ENDEAVOR). The clinical experts clarified that in practice they prefer to give bortezomib once weekly and subcutaneously, because this is associated with fewer adverse reactions, and to give the full 32 doses. In response to the appraisal consultation document, the company provided a scenario analysis in which the duration of bortezomib was limited to 8 cycles and its efficacy adjusted accordingly. The committee noted that the company estimated this reduction in efficacy using a matched-adjusted indirect comparison (MAIC). The committee heard that the ERG agreed with this approach in principle. However, the ERG noted that key adjustments in the MAIC may have been missed and it considered that the results may be unreliable. It therefore presented an exploratory analysis in which it assumed no reduction in efficacy for bortezomib, while capping the costs to 8 cycles. The committee considered that it was appropriate to limit the duration of bortezomib therapy to 8 cycles in the model, consistent with NHS clinical practice, and

that it was plausible that this approach would reduce the efficacy of bortezomib compared with continuing treatment until progression. The committee therefore concluded that the ERG's assumption was very conservative. In the absence of a more robust analysis the committee accepted that the company's approach was suitable for decision-making. **[2017]**

4.14 For the comparison of carfilzomib at second line, the committee noted that bortezomib has a complex patient access scheme (PAS), in which the price paid for bortezomib is reimbursed by the company if there is not at least a partial response after a maximum of 4 cycles. It noted that this PAS was not included in the company's new base case received in response to the appraisal consultation document, although it was included in a scenario analysis. The committee was aware that the company had approximated the price of bortezomib to be equivalent to a 15% discount and heard from the ERG that this was a reasonable approximation. The committee concluded that this was an appropriate approximation and that it was appropriate for it to be included in the analysis. **[2017]**

4.15 The committee was aware that the company presented a scenario analysis in response to the appraisal consultation document, in which it made a case for excluding the extra costs of lenalidomide and dexamethasone associated with long-term carfilzomib therapy. The committee acknowledged that treatments that extend the use of other high costs drugs (such as lenalidomide) can lead to additional cost associated with those other drugs. However, it was not convinced that the company's approach is valid because lenalidomide is part of the regimen in which carfilzomib is given. The committee concluded that the costs of lenalidomide are relevant because the NHS would incur those costs in practice, so they should be included in the model. **[2017]**

4.16 The committee discussed how the company had derived the health state utility values used in the model. It noted that the company had used a

mixed method, using published utility values from Agthoven et al. (2004) and mapped utility values from the trials. The committee heard that the ERG considered it more appropriate to derive utility values straight from trial data, using a mapping algorithm from Proskorovsky et al. (2014). In response to the appraisal consultation document, the company presented a revised base case using utility estimates mapped straight from trial data. The committee considered that the approach in the revised base case was appropriate and consistent with its preferred assumptions. [2017]

Most plausible incremental cost-effectiveness ratio

- 4.17 Having considered the key issues in the economic modelling, the committee considered the most plausible estimates for the cost-effective results. It considered separately the ICERs for carfilzomib in the 2 treatment-pathway positions proposed by the company (see [section 4.4](#)) and the new overall survival evidence submitted after the initial final appraisal determination was suspended (see [section 4.10](#)). [2017]
- 4.18 Carfilzomib in combination with lenalidomide and dexamethasone, compared with lenalidomide in combination with dexamethasone (third line): The committee considered the range of ICERs presented by the company in its base-case and scenario analyses where they explored the effect of different parametric distributions for extrapolation and the effect of non-proportional hazards on the cost-effective results. It noted the company's revised base-case ICER, presented in response to the appraisal consultation document, was £41,429 per quality-adjusted life year (QALY) gained (with the Weibull distribution and proportional hazards) and the ERG's exploratory analysis ICER was £52,439 per QALY gained (Gompertz distribution and proportional hazards). The committee noted that this difference was driven by the choice of parametric extrapolation curve, which was highly uncertain due to immature overall survival data (see [section 4.12](#)). It also recalled there was doubt over the proportional hazards assumption in the model (see

[section 4.11](#)), and that using the independent-fit model (non-proportional hazards) further increases the ICER above £52,439. Therefore the committee reasoned that there was uncertainty in the cost-effective estimate for the comparison of carfilzomib at third line but the most plausible ICER is very likely to be in a range above the company's estimate of £41,429 per QALY gained and one that could be substantially higher. [2017]

- 4.19 Carfilzomib in combination with dexamethasone, compared with bortezomib in combination with dexamethasone (second line): The committee noted that the company's new analysis, received after the initial final appraisal determination was suspended, included the committee's preferred assumptions (with the new overall survival data, Weibull extrapolation, including the PAS for bortezomib, and capping the cost of bortezomib to 8 cycles and reducing its efficacy) and resulted in an ICER of £27,629 per QALY gained. The committee also noted that the ERG's exploratory analysis in response to the new evidence (which used the Weibull extrapolation, included the PAS for bortezomib and capped the cost to 8 cycles without adjusting bortezomib's efficacy) resulted in an ICER of £40,744 per QALY gained. The committee recalled its earlier decisions on adjusting for bortezomib efficacy, if capping its cost to 8 cycles (see [section 4.13](#)) and concluded that the most plausible ICER is the company's estimate of £27,629 per QALY gained and that carfilzomib with dexamethasone is a cost-effective use of NHS resources for people with multiple myeloma who have had only 1 previous therapy, which did not include bortezomib. [2017]

End-of-life considerations

- 4.20 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's [final Cancer Drugs Fund technology appraisal process and methods](#). [2017]

- 4.21 The committee considered whether survival after a second relapse (third line) was less than 24 months while on current treatment. It noted that the company presented data from the HMRN showing that median survival on lenalidomide and dexamethasone at third line is 1.3 years. The committee concluded that it is preferable to have mean estimates for survival over the entire expected lifetime horizon. It noted that the modelled mean overall survival for lenalidomide and dexamethasone was 4.93 years. In considering the overall survival with bortezomib after first relapse (second line) the committee noted the modelled survival was 4.26 years. The committee was aware this was contradictory as survival is expected to be lower at second relapse than after first relapse, but recalled that the overall survival data was immature (see [section 4.5](#)). Therefore, the committee concluded that even though the mean estimates for the model were uncertain, carfilzomib most likely did not meet the first end-of-life criterion for the comparison of carfilzomib at second and third line. **[2017]**
- 4.22 The committee discussed whether carfilzomib with lenalidomide and dexamethasone increases survival by 3 months compared with lenalidomide and dexamethasone. It noted the mean estimates from the model were uncertain and that the trial data was immature but reasoned that in the overall trial population there was a median gain in progression-free survival of more than 3 months (see [section 4.5](#)) and therefore it was highly likely that overall survival would also be greater than 3 months. The committee therefore concluded carfilzomib therapy meets the second end-of-life criterion for the comparison of carfilzomib at second and third line. **[2017]**

Conclusion

- 4.23 The committee concluded that the end-of-life criteria were not met for the comparison of carfilzomib at third line. Therefore, recalling that the most plausible ICERs were very likely above a range of £41,429 (and one that is substantially higher) and the important remaining uncertainties over

proportional hazards and the parametric distribution for extrapolation (see [section 4.18](#)), the committee concluded that carfilzomib in combination with lenalidomide and dexamethasone at third line is not recommended as a cost-effective use of NHS resources. **[2017]**

- 4.24 The committee also concluded that the end-of-life criteria was not met for the comparison of carfilzomib at second line but recalling its conclusion on the most plausible ICER (see [section 4.19](#)), the committee concluded that carfilzomib in combination with dexamethasone at second line was a cost-effective use of NHS resources. **[2017]**

2020 update to guidance

- 4.25 Since this guidance was first published in 2017, NHS England has developed a treatment algorithm for multiple myeloma, which changes the treatment pathway in clinical practice. Specifically, during development of the original guidance, the committee understood that patients could have thalidomide or bortezomib plus dexamethasone as their first treatment for multiple myeloma. The next treatment for those who had thalidomide was bortezomib plus dexamethasone. The next treatment for those who had bortezomib plus dexamethasone first was chemotherapy, but this has since changed to bortezomib plus dexamethasone (that is, re-treatment with bortezomib). **[2020]**
- 4.26 This change to the treatment pathway means that the comparator relevant to current NHS practice is bortezomib plus dexamethasone, regardless of what people have as their first treatment. The committee was aware that a post-hoc subgroup analysis from the ENDEAVOR trial was based on whether patients had previously had bortezomib (Mateos et al. 2017). The results suggested that the gain in progression-free survival and the overall response rate with carfilzomib plus dexamethasone compared with bortezomib plus dexamethasone was similar whether patients had previous bortezomib or not. A clinical expert explained that when bortezomib is used as the first treatment, it is often limited to 4 to 6 cycles.

They added that they did not expect that using bortezomib first would have a treatment modifying effect on carfilzomib. They acknowledged that although the data supporting this were from a post-hoc subgroup, the clinical community felt that this was based on a sufficiently large number of patients to be able to draw a robust conclusion. The committee therefore concluded that it could broaden the original recommendation to allow carfilzomib to be used after either thalidomide or bortezomib. [2020]

5 Implementation

- 5.1 Section 7(6) of the [National Institute for Health and Care Excellence \(Constitution and Functions\) and the Health and Social Care Information Centre \(Functions\) Regulations 2013](#) requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- 5.2 The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- 5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has multiple myeloma and the doctor responsible for their care thinks that carfilzomib is the right treatment, it should be available for use, in line with NICE's recommendations.

6 Review of guidance

- 6.1 The guidance on this technology will be considered for review 3 years after publication. The guidance executive will decide whether the

technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators

Professor Eugene Milne
Vice Chair, appraisal committee C
July 2017

Professor Andrew Stevens
Chair, appraisal committee C
July 2017

Stephen O'Brien
Chair, appraisal committee C
September 2020

7 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The [minutes](#) of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Hamish Lunagaria

Technical lead (2017)

Joanne Holden and Ian Watson

Technical advisers (2017)

Stephanie Yates

Project manager (2017)

Louise Jafferally

Project manager (2020)

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