NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of TA457; Carfilzomib for previously treated multiple myeloma

Original publication date:	July 2017
Review date	July 2020
Existing recommendations:	Optimised To see the complete existing recommendations and the original remit for TA457, see Appendix A.

1. Proposal

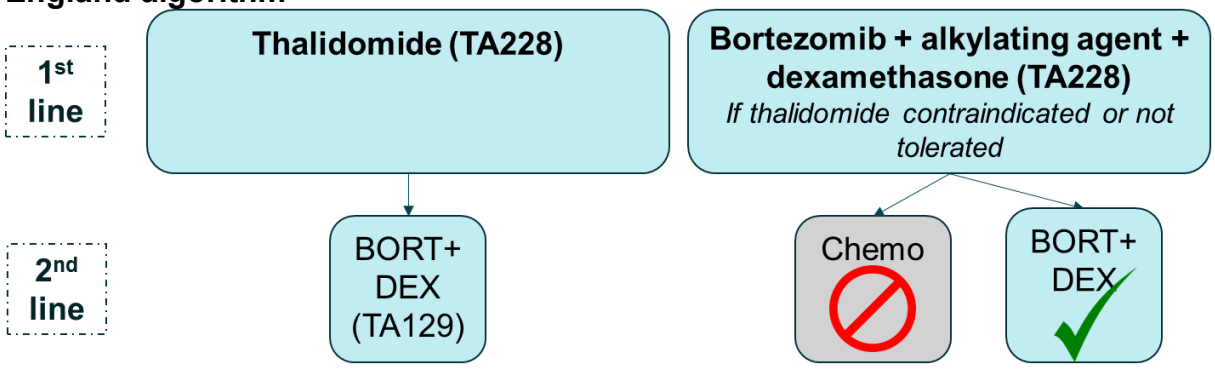
To re-issue the guidance, expanding the recommendation. To consult on this proposal.

2. Rationale

Since TA457 was conducted, NHS England have developed a treatment algorithm for multiple myeloma. This treatment algorithm changes the multiple myeloma treatment pathway in clinical practice (see figure 1).

During TA457, the committee understood that patients at first line could have thalidomide or bortezomib. At second line, for those who had thalidomide the comparator was bortezomib. The comparator for those who had bortezomib first line was chemotherapy, but this has since changed to bortezomib (re-treatment).

Figure 1. Changes to multiple myeloma treatment pathway as a result of NHS England algorithm



In TA457 the committee was unable to consider the group who had bortezomib first line because evidence was not available to compare the clinical effectiveness of carfilzomib with chemotherapy. Instead it focused its considerations on the comparison with bortezomib to make a recommendation for the population who had had thalidomide first line only.

The change to the multiple myeloma treatment pathway means that this comparison to bortezomib is now relevant in considering the population who received bortezomib first line. It is therefore suggested that the recommendation for this subgroup is reviewed.

The majority of patients are now treated with bortezomib first line, and so the stipulation in TA457 that patients must not have previously received bortezomib is limiting treatment options at second line.

3. Proposal

The Committee's judgement on the cost effectiveness of carfilzomib plus dexamethasone compared with bortezomib has already been established (in TA457).

During a recent appraisal of daratumumab (TA573), at the same position in the treatment pathway, the committee used one comparison of daratumumab with bortezomib to inform decision making across the whole second line setting (irrespective of first line treatment).

It is therefore proposed that it would be inconsistent not to take the same approach here, unless bortezomib at first line has a treatment modification effect on carfilzomib efficacy at second line, in which case the cost effectiveness of the populations would need to be considered independently.

- If no treatment modification effect is anticipated, the cost effectiveness of carfilzomib compared with bortezomib would be the same for both populations, so the recommendation should be expanded to include the population who received bortezomib first line.

- If a treatment modification effect is anticipated, the cost effectiveness of this population should be considered through a full appraisal review process.

Please note that during TA457 the committee also considered carfilzomib in combination with lenalidomide and dexamethasone, which was not recommended. This combination is being reviewed in the STA process and is not relevant to this proposal.

4. Process for the update

The recommendations could be updated without going through a full appraisal review process and would involve the following steps:

- To seek opinion from the stakeholders about whether a treatment modification effect is anticipated (that is, ask whether using bortezomib first line would be expected to impact the treatment effect of carfilzomib at second line)
    a. If stakeholder opinion suggests there is a likely treatment modification effect, an appraisal review of this population should be considered.
    b. If stakeholder opinion suggests that there is no clinical rationale to support a treatment modification effect, the stakeholder views would be shared with committee.
- In parallel, share the proposed draft recommendations (see section 5) with stakeholders, and clinical, patient, and NHS commissioning experts.
- Stakeholder responses would be shared with committee, to consider broadening the recommendation, and to seek ratification of the new recommendation wording.
- Issue an ACD or FAD:
    - If committee ratifies the new wording, either unchanged or in line with suggestions made by stakeholders during consultation, we will issue the new recommendations as an update to TA457, in a FAD for appeal.
    - Should the committee diverge substantively from the draft wording or the suggestions made by stakeholders during the consultation, we will consult on the committee's preliminary new recommendations in an ACD.

5. Proposed updated recommendations

The proposed wording is:

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

- they have had only 1 previous therapy, ~~which did not include bortezomib~~ and
- the company provides carfilzomib with the discount agreed in the patient access scheme

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.

GE paper sign off:

Helen Knight – Programme Director

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Appendix A – Information from existing guidance

6. Original remit

To appraise the clinical and cost effectiveness of carfilzomib in combination with lenalidomide and dexamethasone and carfilzomib in combination with dexamethasone within their marketing authorisation for treating multiple myeloma in people who have received at least 1 prior therapy.

7. Current guidance

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

- they have had only 1 previous therapy, which did not include bortezomib and
- the company provides carfilzomib with the discount agreed in the patient access scheme.

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.

8. Research recommendations from original guidance

N/A.

9. Cost information from original guidance

N/A