NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of 380; Panobinostat for treating multiple myeloma in people who have received at least one prior therapy

Original publication date:	27 January 2016
Review date	January 2019
Existing recommendations:	Recommended To see the complete existing recommendations and the original remit for TA380, see Appendix A.

1. Proposal

The guidance should be transferred to the 'static guidance list'.

2. Rationale

[redacted] There has been no additional evidence identified which addresses the uncertainties in the guidance. The clinical guideline on myeloma (NG35) has recently been updated (October 2018). If this guideline is updated in future, the incorporation of this appraisal could be considered (note: there is no scheduled review date on the NICE website).

3. Summary of new evidence and implications for review

No new evidence has been identified related to the identified uncertainties (notably, head-to-head evidence with the relevant comparator, lenalidomide + dexamethasone).

Has there been any change to the price of the technology(ies) since the guidance was published?
No.
Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?
No.

Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?
Main uncertainties identified in the original guidance: • The population from the trial that was applicable to the appraisal was based on a post-hoc subgroup analysis. • No direct trials with the comparator of interest (lenalidomide + dexamethasone) were identified, so a matched adjusted indirect treatment comparison was conducted. However, there were some concerns that the matching was not sufficient as several important predictors of survival were not used to match patients; also, the data on the comparator did not necessarily include bortezomib and an immunomodulatory agent in the previously used treatments. *No new direct, head-to-head evidence on the population and comparator of interest has been identified.* • Main QALY gains were after treatment discontinuation, costs of panobinostat plus bortezomib and dexamethasone were lower than for the comparator, lenalidomide plus dexamethasone. • Subsequent treatment (post‑progression) data was not available for the comparator, lenalidomide plus dexamethasone. *No new evidence identified.*
Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?
See Appendix C for a list of related NICE guidance.
Additional comments
None.

The search strategy from the original ERG report was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from December 2015 to November 2018 were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

4. Equality issues

No equality issues were raised in the original guidance.

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Confidential information has been removed.

Appendix A – Information from existing guidance

5. Original remit

To appraise the clinical and cost effectiveness of panobinostat within its marketing authorisation for treating multiple myeloma in people who have received at least 1 prior therapy.

6. Current guidance

Panobinostat in combination with bortezomib and dexamethasone is recommended, within its marketing authorisation, as an option for treating multiple myeloma, that is, for 'adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent' when the company provides panobinostat with the discount agreed in the patient access scheme.

7. Research recommendations from original guidance

N/A

8. Cost information from original guidance

Panobinostat costs £776 per 20 mg tablet. The recommended starting dose of panobinostat is 20 mg, taken orally once a day, on days 1, 3, 5, 8, 10 and 12 of a 21‑day cycle. Patients should have panobinostat for 8 cycles, after which it is recommended that patients showing clinical benefit continue the treatment for 4 additional cycles of 6 weeks each. The company has agreed a patient access scheme with the Department of Health.

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the Technology Appraisal process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to a specific date or trial.	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Appendix B

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	**Yes**
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Confidential information has been removed.

Appendix C – other relevant information

1. Relevant Institute work

Published

Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2018) NICE technology appraisal guidance 510

Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2018) NICE technology appraisal guidance 505

Myeloma: diagnosis and management (2016: updated 2018) NICE guideline 35

Carfilzomib for previously treated multiple myeloma (2017) NICE technology appraisal guidance 457

Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427

Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (2009) NICE technology appraisal guidance 171. Reviewed in 2012 and moved to static list.

Bortezomib monotherapy for relapsed multiple myeloma (2007) NICE technology appraisal guidance 129. Reviewed in 2012 and moved to static list.

2. Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
Panobinostat has received a marketing authorisation in combination with bortezomib and dexamethasone, for the treatment of 'adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent'.	No change to indication: 'Farydak, in combination with bortezomib and dexamethasone, is indicated for the treatment of adult patients with relapsed and/or refractory multiple myeloma who have received at least two prior regimens including bortezomib and an immunomodulatory agent.' https://www.medicines.org.uk/emc/product/7776/smpc The price is unchanged: £4656 for 6 20mg capsules = £776 per capsule. (BNF November 2018)