NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA135: Pemetrexed disodium for the treatment of mesothelioma

This guidance was issued in January 2008
The review date for this guidance is September 2010

Recommendation

- The guidance should be transferred to the 'static guidance list'. That we consult on the proposal.

Consideration of options for recommendation:

Options	Comment
A review of the guidance should be planned into the appraisal work programme.	No substantive new evidence or ongoing trials which would be likely to change the conclusions of this Appraisal has been identified.
The decision to review the guidance should be deferred [to a specified date].	No substantive new evidence or ongoing trials which would be likely to change the conclusions of this Appraisal has been identified.
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	There are no related appraisals
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	There are no new, related appraisals
A review of the guidance should be incorporated into an on-going clinical guideline.	There are no related guidelines
A review of the guidance should be updated into an on-going clinical guideline.	There are no related guidelines
A review of the guidance should be transferred to the 'static guidance list'.	NICE is not aware of any substantive new evidence or ongoing trials which would be likely to change the conclusions of this Appraisal. The guidance should therefore be added to the list of static guidance, where it will still be monitored in case new

	evidence emerges.

Original remit(s)

"To appraise the clinical and cost effectiveness of pemetrexed disodium for mesothelioma".

Because pemetrexed disodium is licensed only for malignant pleural mesothelioma, the appraisal objective was amended accordingly. The final scope for TA135 was:

"To appraise the clinical and cost effectiveness of pemetrexed disodium for the treatment of unresectable malignant pleural mesothelioma in chemo-naïve patients, and to provide guidance to the NHS in England and Wales".

Current guidance

1.1 Pemetrexed is recommended as a treatment option for malignant pleural mesothelioma only in people who have a World Health Organization (WHO) performance status of 0 or 1, who are considered to have advanced disease and for whom surgical resection is considered inappropriate.

1.2 Patients currently receiving pemetrexed who do not fall into the patient population defined in section 1.1 should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

Relevant Institute work

The Institute has no other guidance, either published or in development, on mesothelioma.

Safety information

In June 2008 the FDA highlighted:

> *"reports of radiation recall associated with pemetrexed. Radiation recall is an inflammatory reaction limited to previously irradiated areas of the body that occurs following the subsequent administration of a drug"* (source: NeLM).

Details of changes to the indications of the technology

Drug (manufacturer)	Details
Pemetrexed (Eli Lilly)	Since the publication of TA135 pemetrexed has been subject to license extensions covering various stages of non-small cell lung cancer.

	These have been covered on the NICE work programme. There have been no changes to the indication for mesothelioma.

Details of new products

Drug (manufacturer)	Details
Ranpirnase (Alfacell)	Ranpirnase is being investigated in phase III studies for the treatment of malignant mesothelioma. UK launch is planned for 2013.

On-going trials

Trial name	Details
A Study Comparing Pemetrexed Plus Best Supportive Care Versus Best Supportive Care Alone in the Treatment of Mesothelioma	Completed
Mesothelioma Avastin Plus Pemetrexed-cisplatin Study	Currently recruiting Estimated completion date: November 2012.

Proposal for updating the guidance

If the guidance is to be updated as an appraisal, it would be scheduled into the work programme accordingly.

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from May 2005 onwards were reviewed. The results of the literature search are discussed in the 'Appraisals comment' section below.

Implementation

No submission was received from Implementation.

Equality and diversity issues

No equality and diversity issues were explicitly raised in the original guidance. However, it may be relevant to consider equality and diversity issues related

to the criterion for performance status of 0 or 1 specified in the recommendations of TA135 (section 1.1).

Appraisals comment:

The indication for malignant pleural mesothelioma remains unchanged.

No new interventions or comparators for malignant pleural mesothelioma have come to market since the original guidance was issued.

Two studies were identified that assessed pemetrexed plus platinum analogues in chemotherapy-naïve patients, and two studies included both chemotherapy-naïve and pre-treated patients. Overall, the outcomes of these studies suggest support for the recommendations of TA135.

One phase III randomised study was identified that compared overall survival and tumour response of pemetrexed plus best supportive care versus best supportive care alone in previously treated patients with advanced malignant pleural mesothelioma (Jassem et al, 2008). Pemetrexed is licensed only in chemotherapy-naive patients and this study is outside of the marketing authorisation.

An on-going phase II/III randomised controlled study due to report in November 2012 was identified which is comparing bevacizumab in combination with pemetrexed-cisplatin chemotherapy with pemetrexed-cisplatin alone (Avastin, Roche) for malignant pleural mesothelioma. The study is anticipated to include 445 chemotherapy-naive patients. As pemetrexed-cisplatin chemotherapy is included in both arms of the trial, this trial is not relevant to the appraisal of pemetrexed within its licensed indication, which is in combination with cisplatin.

The recommendation for further research in the original guidance stated that trials should be conducted in which pemetrexed plus cisplatin is compared with treatments that are currently commonly used in clinical practice in England and Wales to determine relative effectiveness. However, no published studies were identified that compared pemetrexed in combination with cisplatin with such treatments (for example, the mitomycin C, vinbalstine and cisplatin combination (MVP) or vinorelbine).

The inclusion criteria of the studies mentioned above typically specify a Karnofsky performance status of 70 to 100, which is equivalent to WHO scores of 0 to 1. This is consistent with the recommendations of the original NICE guidance.

Key issues

No new evidence or ongoing trials which would be likely to change the conclusions of this appraisal have been identified. Therefore it would be appropriate for the guidance to be transferred to the 'static guidance list'.

However, it may be relevant to consider equality and diversity issues related to the criterion for performance status of 0 or 1 specified in the recommendations of TA135 (section 1.1). In more recently published guidance, a statement has been added about being mindful of equalities issues when using performance status measures. CHTE proposes that TA135 be transferred to the static list without change, but that a statement could be added to the Quick Reference Guide and/or webpage for this appraisal.

GE is asked to consider whether a statement should be added to the Quick Reference Guide and/or to the webpage of the appraisal. Suggested text is as follows:

When using the World Health Organization (WHO) performance status score, clinicians should be mindful of the need to secure equality of access to treatment for patients with disabilities. Clinicians should bear in mind that people with disabilities may have difficulties with activities of daily living that are unrelated to their prognosis with respect to malignant pleural mesothelioma. In such cases clinicians should make appropriate judgements of performance status taking into account the person's usual functional capacity and requirement for assistance with activities of daily living.

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