NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology Appraisals and Guidance Information Services

Static List Review (SLR)

Title and TA publication number of static topic:	**TA135; Pemetrexed for the treatment of malignant pleural mesothelioma**
Final decision:	The guidance will remain on the 'static guidance list'

1. Publication date:	January 2008
2. Date added to static list:	December 2010
3. Date the last searches were run:	August 2010
4. 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.

5. Research recommendations from original guidance:	The Committee identified a need for RCTs comparing alternative chemotherapy regimens in MPM. Specifically, the Committee recommended that trials be conducted in which pemetrexed plus cisplatin is compared with treatments that are currently commonly used in clinical practice in England and Wales in order to determine its relative effectiveness. The Committee also recommended that comparative trials of pemetrexed plus cisplatin versus other promising treatments be conducted.
6. Current cost of technology/ technologies:	1 vial 100mg = £140 1 vial 500mg = £700 Source: BNF (June 2017)
7. Cost information from the TA	Pemetrexed costs £700 for a 500-mg vial (excluding VAT, 'British national formulary' [BNF]53rd edition). The cost per patient, assuming an average of five treatment cycles and a body surface area of 1.8 m2, is approximately £7000.
8. Alternative company(ies):	Generic drugs - date of European Medicines Agency marketing authorisation Pemetrexed Hospira - 20 Nov 2015 Pemetrexed Lilly - 14 Sept 2015 Pemetrexed Medac - 27 Nov 2015 Pemetrexed Sandoz - 18 Sept 2015
9. Changes to the original indication:	No change ALIMTA in combination with cisplatin is indicated for the treatment of chemotherapy naive patients with unresectable malignant pleural mesothelioma. Source: SPC (November 2012)

10. New relevant trials:	Phase 2 Pharmacological Study of Pemetrexed Administered With Cisplatin and a Vitamin Supplement in Patients With Nonresectable Pleural Mesothelioma NCT00541073 Completion date: May 2011 Enrollment: 60 Four Versus Six Cycles of Pemetrexed/Platinum as a First Line Treatment of Malignant Pleural Mesothelioma; a Randomized Phase II Study NCT02497053 Expected completion date: June 2016 Enrollment: 70 Phase II Toxicity Study Using Chemotherapy +/- Pleurectomy/Decortication Followed By Intensity Modulated Radiation Therapy to the Pleura in Patients With Locally Advanced Malignant Pleural Mesothelioma NCT00715611 Expected completion date: July 2016 Enrollment: 40 Randomized Phase II Study of Pleurectomy/ Decortication (P/D) Preceded or Followed by Chemotherapy in Patients With Early Stage Malignant Pleural Mesothelioma NCT02436733 Expected completion date: June 2019 Enrollment: 64

11. Relevant NICE guidance (published or in progress):	[redacted]
12. Relevant safety issues:	None identified
13. Any other additional relevant information or comments:	**NHS England** • NHS England commissions services for mesothelioma except malignant pleural mesothelioma. • Clinical Commissioning Groups commission services for lung cancer (including pleural mesothelioma). Source: NHS England (2014) Manual for prescribed specialised services 2013/14 (pp235-7) NHS England (2013) 2013/14 standard contract for cancer: malignant mesothelioma (adult) **Related guidance** British Thoracic Society (2010) Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010 European Society for Medical Oncology (2015) Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up European Respiratory Society, European Society of Thoracic Surgeons (2009) Guidelines of the European Respiratory Society and the European Society of Thoracic Surgeons for the management of malignant pleural mesothelioma

14. Technical Lead comments and recommendation:	A key research recommendation from TA135 was for trials comparing pemetrexed plus cisplatin with treatments that are most commonly used in the England and Wales, to determine its relative effectiveness. Since the review of TA135 in 2010 there have been a number of studies identified. None of these attempt to answer the research question and most are outside of the marketing authorisation for pemetrexed. 1 of these is within the MA and may inform of use at earlier stages of disease and could make use of the full license rather than limiting use at the advanced stage only. This trial (NCT02436733) is currently recruiting patient for pleuroectomy/decortication preceded by or followed by pemetrexed-cisplatin in patients with early-stage MPM. But again may be outside the license of pemetrexed. This trial is due to inform in 2019. 2 other trials identified are currently outside the MA and 1 other (NCT02497053) is a phase II trial looking at the efficacy of a 4 –cycle treatment against a 6-cycle treatment in a treatment naïve patients. This trial is completed but has not yet reported results. It is unlikely the trial results would have a bearing on the current recommendations. There is no planned extension to the MA for pemetrexed and several generics have now become available. The pemetrexed-cisplatin combination is still an important treatment option for patients and cited in European and British thoracic guidelines therefore this guidance is still relevant, but there are unlikely to be any trial results published in the near future that will change guidance. There are no new licensed products that have come into the market since the review in 2010 and there are no new potential comparators which are waiting to be appraised by NICE ([redacted])

	Conclusion – keep in the 'static guidance list'

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Appendix 1 – explanation of options

Options	Consequence	Selected – 'Yes/No'
The guidance will remain on 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. 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 decision to review the guidance will be deferred to specify date or trial	NICE will consider whether a review is necessary at the specified date. NICE will actively monitor the evidence available to ascertain when a consideration of a review is more suitable.	No
A full consideration of a review will be carried out through the Review Proposal Process	There is evidence that could warrant a review of the guidance. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No
The guidance will be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No

The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No