

Quick reference guide

Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia

1 Guidance

This technology appraisal considers the clinical and cost effectiveness of fludarabine monotherapy only. No recommendations have been made with respect to fludarabine plus cyclophosphamide combination therapy because the current marketing authorisation does not specifically provide a recommendation that fludarabine should be used concurrently with other drugs for the treatment of chronic lymphocytic leukaemia.

Clarification was sought with the MHRA on the issue of the inclusion of the combination of fludarabine and cyclophosphamide in the marketing authorisation of fludarabine. In all correspondence received from the MHRA, including that shared with NICE by Schering Health Care Limited, it has been made clear that 'the MHRA does not consider that the current marketing authorisations for oral and intravenous (i/v) Fludara (PL/0053/0239 and /0290) specifically provide a recommendation that fludarabine should be used concurrently with other drugs for the treatment of chronic lymphocytic leukaemia'.

The MHRA has further clarified that, in general, it would expect a manufacturer or sponsor to request a variation in the marketing authorisation when: 1. The summary of product characteristics (SPC) in general, and specifically the 'therapeutic indications' section, does not contain references to the combination therapy and the

company wishes to promote the use of combination therapy, and 2. The use of the combination has implications for the dosage specifications in the 'posology and method of administration' section of the SPC.

In the case of fludarabine, the SPCs do not contain references to the combination therapy. With reference to the second point, the dosage of fludarabine (i/v 25 mg/m² for 3 days and oral 24 mg/m² for 5 days) in the evidence base for the combination therapy that was submitted by the manufacturer (the CLL4 trial) is different from the fludarabine dosage specified in its SPCs (i/v 25 mg/m² for 5 days and oral 40 mg/m² for 5 days).

- 1.1 Fludarabine monotherapy, within its licensed indication, is not recommended for the first-line treatment of chronic lymphocytic leukaemia.

2 Implementation

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TA119).

- A costing statement explaining the resource impact of this guidance.
- Audit criteria to monitor local practice.

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This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Further information

Quick reference guide

This has been distributed to healthcare professionals working in the NHS in England and Wales (see www.nice.org.uk/TA119distributionlist). It is available from www.nice.org.uk/TA119quickrefguide

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1203).

Full guidance

This contains the following sections:

- 1 Guidance
- 2 The technology
- 3 The manufacturer's submission
- 4 Consideration of the evidence
- 5 Implementation
- 6 Recommendations for further research
- 7 Related NICE guidance
- 8 Review of guidance.

The full guidance also gives details of the Appraisal Committee and the sources of evidence considered. It is available from www.nice.org.uk/TA119guidance

'Understanding NICE guidance'

Information for patients with chronic lymphocytic leukaemia and their carers is available from www.nice.org.uk/TA119publicinfo

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1204).

Related NICE guidance

- Improving outcomes in haematological cancers. NICE cancer service guidance (2003). Available from: www.nice.org.uk/csgho
- Guidance on the use of fludarabine for B-cell chronic lymphocytic leukaemia. NICE technology appraisal guidance 29 (2001). Available from: www.nice.org.uk/TA029