# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

**Technology Appraisals and Guidance Information Services**

**Static List Review (SLR)**

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| **Title and TA publication number of static topic:** | **TA119; Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia** |
| **Final decision:** | The guidance will remain on the 'static guidance list' |

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| **1. Publication date:** | February 2007 |
| **2. Date added to static list:** | May 2010 |
| **3. Date the last searches were run:** | August 2009 |
| **4. Current guidance:** | 1.1 Fludarabine monotherapy, within its licensed indication, is not recommended for the first-line treatment of chronic lymphocytic leukaemia. |
| **5. Research recommendations from original guidance:** | 6.1 The Committee recommended using data from all clinical trials comparing fludarabine monotherapy, fludarabine plus cyclophosphamide and chlorambucil to provide definitive information on treatment effects including retreatment response rates, overall survival outcomes, incidence and severity of adverse events.<br>6.2 The Committee recommended further research to identify prognostic markers that would allow better characterisation of subgroups of patients who would benefit the most from fludarabine-containing regimens. |

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| **6. Current cost of technology:** | **Tablet**<br>Fludara (Sanofi): net price 10 mg 15-tab pack = £302.48; 10 mg 20-tab pack = £403.31<br><br>**Solution for injection**<br>Fludarabine phosphate (Actavis) = £155.00<br>Fludarabine phosphate (Teva) = £156.00<br>Fludarabine phosphate (AAH Pharmaceuticals) = £117.75<br><br>**Powder for solution for injection**<br>Fludara (Sanofi) = £735.34<br>Fludarabine phosphate (AAH Pharmaceuticals) = £155.00<br>Fludarabine phosphate (Actavis) = £155.00<br>Fludarabine phosphate (Hospira) = £735.35<br><br>Source: BNF (November 2015) |
| **7. Cost information from the TA:** | The unit cost of fludarabine is £156 for a 50-mg vial, and £18.60 per 10-mg tablet, available in packs of 15 and 20 tablets (excluding VAT; 'British national formulary', edition 52). |
| **8. Alternative company(ies):** | **Fludara (solution for injection/infusion or tablet)**<br>Sanofi-Aventis |

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| | **Non-proprietary (solution for injection/infusion)**<br>Accord Healthcare<br>Actavis<br>Hospira<br>Sandoz<br>Teva |
| **9. Changes to the original indication:** | No change |
| **10. New relevant trials:** | No ongoing, relevant trials identified. |
| **11. Relevant NICE guidance (published or in progress):** | **Fludarabine**<br>Fludarabine for the treatment of B-cell chronic lymphocytic leukaemia (2001) NICE technology appraisal guidance 29. Review date: December 2013. Review decision: static list.<br><br>**Chronic lymphocytic leukaemia (1st line) - published**<br>Blood and bone marrow cancers (2015) NICE Pathway.<br><br>Improving outcomes in haemotological cancer (2003) NICE guideline CGHSO.<br><br>Idelalisib for treating chronic lymphocytic leukaemia (2015) NICE technology appraisal guidance 359. Review date: September 2018.<br><br>Ofatumumab for treating previously untreated chronic lymphocytic leukaemia. (2015) NICE technology appraisal guidance 344. Review date: 3 years after publication. |

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| | Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia. (2015) NICE technology appraisal guidance 343. Review date: 3 years after publication.<br><br>Bendamustine for the treatment of chronic lymphocytic leukaemia (2011) NICE technology appraisal guidance 216. Review date: December 2013. Review decision: static list.<br><br>Rituximab for the first line treatment of chronic lymphocytic leukaemia (2009) NICE technology appraisal guidance 174. Review date: 2012. Review decision: static list.<br><br>**Chronic lymphocytic leukaemia (1st line) - in development**<br>Ibrutinib for treating chronic lymphocytic leukaemia. NICE technology appraisal guidance [ID749]. Publication expected June 2016.<br><br>Idelalisib in combination with ofatumumab for chronic lymphocytic leukaemia NICE technology appraisal guidance [ID817]. Publication date to be confirmed. |
| **12. Relevant safety issues:** | None identified. |
| **13. Any other additional relevant information or comments:** | British Committee for Standards in Haematology (2015) Interim statement from the BCSH CLL Guidelines Panel<br><br>British Committee for Standards in Haematology (2013) Guidelines on the diagnosis, investigation and management of chronic lymphocytic leukaemia<br><br>European Society for Medical Oncology (2015) Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up |
| **14. Technical Lead comments and** | Fludarabine monotherapy was not recommended for first-line treatment of chronic |

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| **recommendation:** | lymphocytic leukaemia in NICE technology appraisal guidance 119. The marketing authorisation for fludarabine for the first-line treatment of chronic lymphocytic leukaemia has not changed since, nor have any ongoing and relevant trials been identified. Additionally no relevant safety issues have been identified.<br><br>NICE has published several technology appraisal guidance for treating first-line chronic lymphocytic leukaemia. The most appropriate treatment option depends on factors such as stage of chronic lymphocytic leukaemia, performance status and co-morbidities. In general, fludarabine combination therapy is the standard of care for people whom need immediate treatment (fludarabine, cyclophosphamide plus rituximab [FCR], NICE technology appraisal guidance 174). In NICE technology appraisal guidance 174, FCR was recommended in people for whom fludarabine in combination with cyclophosphamide is considered appropriate, because the evidence suggested it was clinically and cost-effective compared with fludarabine in combination with cyclophosphamide. Since March 2014, NICE technology appraisal 174 has also been on the 'static guidance list'. It is understood that fludarabine combination therapy may not be suitable for about half the people needing immediate treatment, for example, people who are older or have comorbidities such as impaired renal function, hypertension or diabetes. In these circumstances, other treatment options are preferred (for further information, see published 'Relevant NICE guidance').<br><br>Since the publication of NICE technology appraisal guidance 119, further research has been undertaken that has identified prognostic markers that allow better characterisation of subgroups of patients who would benefit the most from fludarabine-containing regimens (for example, people without 17p deletion and without TP53 mutation). The treatment effect of fludarabine-containing regimens is also better understood relative to other treatment options.<br><br>No new clinical evidence for fludarabine monotherapy that may impact the current recommendation has been highlighted, and NICE guidance, clinical guidelines and the available evidence suggest that FCR has become embedded as the standard of care in |

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| | people who need immediate first-line treatment and for whom it is an appropriate option. Since NICE technology appraisal 119 was published, fludarabine has become generic. This change in price will also impact FCR as well as fludarabine given as a monotherapy, and therefore this change in price is unlikely to have an impact on the recommendations of technology appraisal guidance 119.<br><br>Overall, no new evidence has been identified that would impact on the current recommendations in technology appraisal guidance 119. It is therefore appropriate for the guidance to remain on the 'static guidance list'. |

**SLR paper sign off:** Janet Robertson – Associate Director, Technology Appraisals

**Contributors to this paper:**

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Date of IS searching: 22 October 2015

## Appendix 1 – explanation of options

| Options | Consequence | Selected – 'Yes/No' |
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| **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. 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 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 |