NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Idelalisib in combination with bendamustine and rituximab for previously treated chronic lymphocytic leukaemia

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of idelalisib in combination with bendamustine and rituximab within its marketing authorisation for treating relapsed chronic lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). It causes anaemia, swollen lymph nodes, spleen enlargement, unexplained weight loss and increased susceptibility to infection.

In England around 3,000 people were diagnosed with CLL in 2013.[1] The risk of developing CLL increases with age and it is more common in men. Median survival ranges from about 3 to over 10 years depending on the genetic subtype and the stage at which the disease is diagnosed.[2]

Approximately 5% to 10% of people diagnosed with CLL are considered to have 'high-risk' disease characterised by the presence of cytogenetic mutation or abnormalities (that is, 17p deletion or TP53 mutation). The presence of 17p deletion or TP53 mutation influences the rate of cell growth as well as the resistance of the disease to treatment. People with the 17p deletion or TP53 mutation have a median survival of 2 to 3 years.

Treatment options for relapsed CLL vary depending on response to previous treatments and co-morbidities. The British Committee for Standards in Haematology defines relapse as disease progression at least 6 months after achieving a complete response or partial response[2].

NICE technology appraisal guidance 193 recommends rituximab only in combination with fludarabine and cyclophosphamide (FCR) as an option for people with relapsed or refractory CLL unless their disease is refractory to fludarabine or has been previously treated with rituximab. NICE technology appraisal guidance 359 recommends idelalisib, in combination with rituximab for CLL in adults when the disease has been treated but has relapsed within 24 months. NICE technology appraisal guidance TA429 recommends ibrutinib for people with CLL who have had at least 1 prior therapy or who have a 17p deletion or TP53 mutation and in whom chemo-immunotherapy is unsuitable. Before this guidance was issued, ibrutinib was used in clinical practice in England through the Cancer Drugs Fund for CLL only in people for whom

treatment with idelalisib plus rituximab was considered unsuitable. Chlorambucil has a UK marketing authorisation for treating chronic lymphocytic leukaemia and is used in clinical practice in England with or without rituximab in people with relapsed or refractory CLL for whom FCR is unsuitable.

The technology

Idelalisib (Zydelig, Gilead Sciences) inhibits the cellular pathway that regulates cell proliferation, death and migration. Idelalisib is administered orally.

Idelalisib in combination with bendamustine and rituximab for previously treated chronic lymphocytic leukaemia does not have a marketing authorisation in the UK. It has been studied in clinical trials compared with bendamustine and rituximab in adults with previously treated chronic lymphocytic leukaemia.

Idelalisib has a marketing authorisation in the UK in combination with rituximab for “the treatment of adults with chronic lymphocytic leukaemia who have received at least one prior therapy or, as first-line treatment in the presence of 17p deletion or TP53 mutation in people unsuitable for chemo-immunotherapy”.

Intervention(s)	Idelalisib in combination with bendamustine and rituximab
Population(s)	Adults with previously treated chronic lymphocytic leukaemia.
Comparators	• Fludarabine in combination with cyclophosphamide and rituximab • Idelalisib in combination with rituximab • Chlorambucil with or without rituximab • Ibrutinib
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any simple discount agreement for the intervention or comparator technologies will be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. If evidence allows the following subgroups will be considered: • the presence or absence of the 17p deletion or TP53 mutation • time since relapse
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Rituximab for the treatment of relapsed chronic lymphocytic leukaemia' (2010). NICE Technology Appraisal 193. Guidance on static list. 'Idelalisib for previously treated chronic lymphocytic leukaemia' (2015). NICE Technology Appraisal 359. Review date September 2018. 'Ibrutinib for treating chronic lymphocytic leukaemia' (2016) NICE Technology Appraisal TA429 Review date January 2020. Appraisals in development (including suspended appraisals) 'Ofatumumab for the maintenance treatment of relapsed chronic lymphocytic leukaemia'. Suspended NICE technology appraisal guidance [ID732]. 'Idelalisib in combination with ofatumumab for treating previously treated, relapsed chronic lymphocytic leukaemia'. Suspended NICE technology appraisal [ID817]. 'Ofatumumab in combination with chemotherapy for treating relapsed chronic lymphocytic leukaemia'. Suspended NICE technology appraisal [ID777]. Related NICE Pathways: Blood and bone marrow cancers
Related National Policy	NHS England (2015) National Cancer Drugs Fund List v.6.1: https://www.england.nhs.uk/wp-content/uploads/2016/02/ncdf-list-01-02-16.pdf Improving outcomes in haematological cancers – the manual' October 2003. NHS England Manual for prescribed specialised

	services 2016/17. Specialist cancer services (adults) [section 105, page 228]: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf NHS England 2013/14 NHS standard contract for cancer: chemotherapy (adult). Section B part 1- service specifications: http://www.england.nhs.uk/wp-content/uploads/2013/06/b15-cancr-chemoth.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1–5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

References

1. Office for National Statistics (2015). Cancer registration statistics. Accessed November 2015.

2. Cancer Research UK (2015). Statistics and outlook for chronic lymphocytic leukaemia. Accessed November 2015.