NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Evaluation

Pirtobrutinib for untreated chronic lymphocytic leukaemia or small lymphocytic lymphoma

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of pirtobrutinib for untreated chronic lymphocytic leukaemia or small lymphocytic lymphoma.

Background

Chronic lymphocytic leukaemia (CLL) is the most common type of chronic leukaemia and is a type of cancer that affects the white blood cells. CLL occurs when the material found inside some bones (bone marrow) produces too many white blood cells, called lymphocytes, that aren't fully developed and don't work properly. It tends to progress slowly over many years.

CLL mostly affects people 60 years of age and over and is rare in people 40 years of age and younger[1,2]. The risk of developing CLL increases with age, is more common in men, those of white ethnicity, and have a family history of CLL[2]. There were 4,074 new cases of CLL (ICD-10 code C91.1: CLL of B-cell type) in England in 2023. Of these, 2,526 were male and 1,548 were female[3].

CLL usually progresses slowly, but some people may have rapidly progressive disease[2]. Over time people can develop anaemia, swollen lymph nodes, spleen enlargement and unexplained weight loss. People with CLL may live with a considerable burden of symptoms and an increased susceptibility to infection impacting on their quality of life, whether or not they have had treatment. Small lymphocytic lymphoma (SLL) is considered the same condition as CLL, as most people with CLL or SLL have abnormal white blood cells in locations that overlap, including lymph nodes, spleen, blood and bone marrow.[4]

The British Society of Haematology defines people with ‘high risk’ CLL as those with previously untreated CLL associated with a 17p deletion or TP53 mutation. The presence of 17p deletion or TP53 mutation influences the rate of cell growth and is associated with resistance of the disease to conventional chemotherapy treatments[5]. The presence of 17p deletion or TP53 mutation can be used as markers to predict the prognosis of people with CLL. The presence of an immunoglobulin heavy chain gene (IgHV) mutation and complex karyotypes (defined as more than 3-5 chromosome aberrations) may also impact treatment decisions and affect clinical outcomes[6].

Treatment of CLL is complex and depends on several factors such as stage of disease, previous treatment, patient’s age, symptoms, and general state of health. Many people with CLL will not have symptoms when they are first diagnosed and will have a period of active surveillance. The disease is monitored for progression and treatment is initiated upon progression. Targeted therapies such as zanubrutinib, acalabrutinib, ibrutinib, and venetoclax are the first choice of treatment across risk

groups where eligible. The British Society of Haematology guideline recommends universal testing for deletion 17p or TP53 mutation and IgHV gene status to inform first-line choice. Treatments may be for a fixed duration (also called time-limited) , or continuous therapy for as long as appropriate[7].

The technology

Pirtobrutinib (Jaypirca, Eli Lilly) does not currently have a marketing authorisation in the UK for treating untreated chronic lymphocytic leukaemia. It being studied in a clinical trial compared with Ibrutinib in adults with chronic lymphocytic leukaemia or small lymphocytic lymphoma.

Pirtobrutinib has a marketing authorisation, as monotherapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor. Pirtobrutinib has a marketing authorisation, as a monotherapy for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a BTK inhibitor.

Intervention(s)	Pirtobrutinib
Subgroups	If evidence allows the following subgroups will be considered: • People with and without a 17p deletion or TP53 mutation • According to IgHV mutation status (mutated or unmutated) • People for whom BTKi is or isn't suitable • ECOG performance status • Renal function • People with complex or high-complex karyotype (those with more than 3 or more than 5 chromosomal aberrations respectively).
Population(s)	Adults with chronic lymphocytic leukaemia or small lymphocytic leukaemia who are BTKi-treatment naïve
Comparators	• acalabrutinib • zanubrutinib • ibrutinib with venetoclax • venetoclax monotherapy • venetoclax with obinutuzumab • venetoclax with rituximab • acalabrutinib and venetoclax with/ without obinutuzumab (ID6232, subject to NICE evaluation)

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • minimal residual disease levels • overall and complete response rate • time to treatment failure • duration of response • time to next treatment • 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should 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.
Related NICE recommendations	Venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia (January 2026). NICE technology appraisal guidance 1119. Review date not stated Zanubrutinib for treating chronic lymphocytic leukaemia (2023) NICE Technology appraisal guidance 931. Review date not stated Ibrutinib with venetoclax for untreated chronic lymphocytic leukaemia (May 2023) NICE technology appraisal guidance 891. Review date not stated

	Venetoclax for treating chronic lymphocytic leukaemia (2022). NICE Technology appraisal guidance 796. Review date 2025. Acalabrutinib for treating chronic lymphocytic leukaemia (2021). NICE Technology appraisal guidance 689. Review date 2024 Venetoclax with rituximab for previously treated chronic lymphocytic leukaemia (2019). NICE technology appraisal guidance 561. Review date 2022 **Related technology appraisals in development:** Acalabrutinib and venetoclax with or without obinutuzumab for untreated chronic lymphocytic leukaemia NICE technology appraisal guidance ID6232. Publication date 22 April 2026 Venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia when there is no 17p deletion or TP53 mutation and FCR (fludarabine, cyclophosphamide, rituximab) or BR (bendamustine, rituximab) are suitable. NICE technology appraisal guidance ID6291. Publication date 18 March 2026 **Related NICE guidelines:** Haematological cancers: improving outcomes (May 2016) NICE guideline NG47. Suspected cancer: recognition and referral (June 2015, updated October 2023) NICE guideline NG12 **Related quality standards:** Haematological cancers (2017). NICE quality standard 150.

References

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2. What is chronic lymphocytic leukaemia (CLL)? (2024). Cancer Research UK. Accessed: December 2025
3. NHS Digital. Cancer Registration Statistics, England, 2023. Accessed: December 2025
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