NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Evaluation

Pirtobrutinib for untreated chronic lymphocytic leukaemia or small lymphocytic lymphoma ID6397

Draft scope

Draft 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 are often the first choice of treatment. Targeted therapies, such as zanubrutinib, acalabrutinib, ibrutinib, and

© National Institute for Health and Care Excellence 2026. All rights reserved.

venetoclax are particularly useful in people with a poor prognosis, such as those with 17p deletion or TP53 mutation. Treatments may be for a fixed duration (also called time-limited) with scheduled treatment breaks, or continuous therapy for as long as appropriate[7].

Table 1. Treatment options for untreated CLL in NHS practice

NICE technology appraisal	Date	Treatment option for untreated CLL
For adults with untreated CLL where mutation is not specified		
TA891	May 2023	ibrutinib with venetoclax
No TA published	TBC	acalabrutinib and venetoclax with/ without obinutuzumab
Adults with untreated CLL without a 17p deletion or TP53 mutation		
TA931	November 2023	zanubrutinib
TA689	April 2021	acalabrutinib
TA1119	Jan 2026	venetoclax with obinutuzumab
Adults with untreated CLL with a 17p deletion or TP53 mutation		
TA931	November 2023	zanubrutinib
TA796	June 2022	venetoclax
TA689	April 2021	acalabrutinib
TA1119	Jan 2026	venetoclax with obintuzumab

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.

© National Institute for Health and Care Excellence 2026. All rights reserved.

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) • 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)	People with untreated chronic lymphocytic leukaemia or small lymphocytic lymphoma.
Comparators	• zanubrutinib (TA931) • ibrutinib with venetoclax (TA891) • venetoclax monotherapy (TA796) • acalabrutinib (TA689) • venetoclax with obinutuzumab (TA1119) • 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.

© National Institute for Health and Care Excellence 2026. All rights reserved.

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	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 obinutuzumab for untreated chronic lymphocytic leukaemia (2020). NICE technology appraisal guidance 663. Review date 2023 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

© National Institute for Health and Care Excellence 2026. All rights reserved.

	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.

Questions for consultation

Where do you consider pirtobrutinib will fit into the existing care pathway for chronic lymphocytic leukaemia or small lymphocytic lymphoma?

Have all relevant comparators been included in the draft scope?

Which of the listed comparators would pirtobrutinib be most likely to displace if it were recommended?

Could you estimate what proportions of people with untreated CLL have the listed comparators in NHS clinical practice?

Have all relevant subgroups been included in the draft scope?

What is the distinction between chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL)? Does the anticipated marketing authorisation for pirtobrutinib for this appraisal cover SLL?

Is the clinical trial evidence that could inform this evaluation generalisable to the NHS clinical practice population? If not, could you explain why?

Please select from the following, will pirtobrutinib be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would pirtobrutinib be a candidate for managed access?

Do you consider that the use of pirtobrutinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

© National Institute for Health and Care Excellence 2026. All rights reserved.

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which pirtobrutinib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Chronic lymphocytic leukaemia (2023) NHS Choices. Accessed December 2025
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
4. Small lymphocytic lymphoma (SLL) (2021). Macmillan Cancer Support. Accessed December 2025
5. Walewska R, Parry-Jones N, Eyre TA et al. (2022) Guideline for the treatment of chronic lymphocytic leukaemia. British Journal of Haematology. 197 (5), 544-557
6. Eichhorst B, Robat T, Montserrat E et al. (2020). Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up on behalf of the ESMO Guidelines Committee. Annals of Oncology. 32 (1), 23-33
7. Chronic lymphocytic leukaemia: management approach (2024) BMJ Best Practice. Accessed: December 2025

© National Institute for Health and Care Excellence 2026. All rights reserved.