# BTKi Treatment for CLL: A Patient Information Guide

This guide has been developed in collaboration with patient representatives from the CLL Advocates Network and with input from health care providers.

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This guide is intended for use by patients and caregivers outside of the United Kingdom. Patients in the UK are advised to consult their healthcare provider for information and guidance specific to their country.

# Content

This patient information guide has been developed by Johnson & Johnson and patient representatives from the CLL Advocates Network (CLLAN), Professor Patrick Thornton, Consultant Haematologist, Honorary Professor RCSI, and Clinical Director of Hermitage Medical Clinic and Beaumont Hospital Laboratory and Geraldine Walpole, Advanced Nurse Practitioner in Haematology, Sligo University Hospital.

If you experience any side effects or unusual symptoms while taking your medication, please contact your healthcare provider immediately. Your safety and wellbeing are top priority, and your clinician can provide the best guidance based on your individual health needs.

# Introduction

## About this guide

Chronic lymphocytic leukaemia (CLL) is a cancer that affects the blood and bone marrow and is characterised by the overproduction of abnormal white blood cells called lymphocytes.[1]

CLL typically develops slowly, meaning many patients may not need treatment straightaway (or ever).[1] However, when the time comes to start treatment, finding information about the different options available along with any possible side effects can be a difficult and overwhelming experience.

In fact, the global Leukaemia Patient Experience Survey conducted by the CLL Advocates Network (CLLAN) found that 42% of patients were not offered written information about their CLL without needing to ask for it and of those who were given resources, 52% do not fully understand it.[2] More than half (55%) of patients also reported that they were not offered or directed to any support.[2]

**42% of patients are not offered written information about their CLL at diagnosis[2]**

Developed with CLLAN and healthcare professionals (see Appendix for full list of contributors), this guide provides practical information and advice about living with and being treated for CLL. It also looks in detail at a widely used type of targeted therapy for CLL patients called Bruton's tyrosine kinase inhibitors (BTKis).

This includes:

- Information about how BTKis work
- What a typical BTKi treatment programme looks like
- Potential side effects and how they are managed
- How BTKis may interact with other medications
- Answers to common questions about why and when BTKis may be used

Ideally, you should read this guide from beginning to end to gain a full understanding of CLL, BTKi therapy and what you can expect during your treatment. But it has also been designed to be as interactive as possible, allowing you to quickly find and refer to individual sections as and when you need them.

Note also that the information contained in this guide was correct at the time of publishing (December, 2024). However, as the treatment landscape for CLL is continually evolving, it is important to always check with your healthcare team for the latest information. They should be your first point of contact for any other queries too as their personalised advice and support can help you make the best decisions about your care. Further, the information provided here is about BTKi therapy **generally** and does not replace reading the patient information leaflet (PIL) that comes with your specific medicine. You should refer to the PIL for important safety information about the medicine that you are taking.

However you choose to use this guide, we hope it helps you embark on your own CLL treatment path with knowledge and confidence.

### How to navigate this guide

The digital version of this guide is designed to be easy to navigate, even if you aren't very familiar with using online PDFs.

At the top of each page, there are links you can click on to take you directly to any of the eight main sections of the guide.

Throughout the guide, you will also find red and underlined links that can take you to specific sections within the guide or even to other websites with more information—just click, and you'll be taken directly to the information you want.

If you are reading the print version, you can scan the QR code to access the digital version of the guide.

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[1] NHS. What is chronic lymphocytic leukaemia? Available at: https://www.nhs.uk/conditions/chronic-lymphocytic-leukaemia/. Last accessed: December 2024.

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# About CLL

## What is CLL?

Chronic lymphocytic leukaemia (CLL) may be a rare form of blood cancer, but it is one of the most common types of leukaemia in adults.[3] It tends to occur during or after middle age and rarely affects children.[3]

CLL starts in the white blood cells (known as lymphocytes) found in the bone marrow and blood. It is referred to as 'chronic' because it tends to develop slowly,[4] with many individuals not requiring treatment for months or years after receiving a diagnosis.[4]

CLL causes abnormal white blood cells to be overproduced and, over time, crowd out the healthy blood cells, so that they are unable to do their usual job.[4] In CLL, high numbers of abnormal lymphocytes are found in the blood, lymph nodes (glands), spleen and bone marrow (the spongy tissue inside the large bones in the body, where blood cells are produced).[5] The term 'small lymphocytic lymphoma' (SLL) is used when the cancer cells are located mainly in the lymph nodes and the blood count is frequently normal.[4]

Despite advancements in both disease understanding and treatment options, CLL remains an incurable condition, underlining the importance of pursuing new therapies while at the same time improving support for those affected by it and their loved ones. Fortunately, over the past 30 years, the survival rate has increased, and many patients can now expect to live a normal life expectancy.[6]

## What causes CLL?

The precise cause of CLL is still undetermined but genetic predisposition is believed to be the primary contributor, with environmental factors playing a minimal role.[7]

### There are, however, some known risk factors, including:

- **Age:** CLL is more prevalent in older adults[8]
- **Sex:** CLL occurs more commonly in men than in women[8]
- **Race:** individuals of Caucasian descent may be more likely to develop CLL than other races[8]
- **Family history:** family history associated with cancers of the blood and bone marrow may increase risk of developing CLL[8]
- **Chemical exposure:** certain herbicides and insecticides have been linked to an increased risk of CLL[8]
- **Tobacco**: tobacco users and smokers face a significantly increased risk of CLL compared to non-tobacco users[8]
- **Monoclonal B-cell lymphocytosis:** this is a condition in which individuals have an increased number of B-cells in their blood, giving them a higher risk of developing CLL[9]

Notably, the progression of CLL can differ among individuals, while not everyone with genetic predispositions will necessarily develop the disease.[10]

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[5] UpToDate. Patient education: Chronic lymphocytic leukemia (CLL) in adults (Beyond the Basics). Available at: https://www.uptodate.com/contents/chronic-lymphocytic-leukemia-cll-in-adults-beyond-the-basics/. Last accessed: December 2024.

[6] van der Straten L, Maas CCHM, Levin MD, Visser O, Posthuma EFM, Doorduijn JK, Langerak AW, Kater AP, Dinmohamed AG. Long-term trends in the loss in expectation of life after a diagnosis of chronic lymphocytic leukemia: a population-based study in the Netherlands, 1989-2018. Blood Cancer J. 2022 Apr 20;12(4):72. doi: 10.1038/s41408-022-00669-7.

[7] Montague AM, Pathak S. Chronic Lymphocytic Leukemia With Variant Genetics. StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK585059/. Last accessed: December 2024.

[8] Mayo Clinic. Chronic lymphocytic leukemia. Available at: https://www.mayoclinic.org/diseases-conditions/chronic-lymphocytic-leukemia/symptoms-causes/syc-20352428#:~:text=Doctors%20aren't%20certain%20what,the%20cell%20what%20to%20do. Last accessed: December 2024.

[9] Mukkamalla SKR et al. Chronic Lymphocytic Leukemia. StatPearls Publishing; 2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK470433/. Last accessed: December 2024.

[10] American Cancer Society. Chronic Lymphocytic Leukemia Causes, Risk Factors, and Prevention. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8680.00.pdf. Last accessed: December 2024.

## What are the symptoms of CLL?

Because CLL tends to progress slowly,[1] many individuals may not experience symptoms for years. CLL symptoms may not be easily noticeable and can resemble those of other conditions.[11]

### These symptoms can include:[12]

- Weakness
- Feeling more tired than usual
- Unintentional weight loss
- Chills
- Fever
- Bone pain and night sweats
- Bleeding or bruising more easily than normal
- Swollen glands (often felt as lumps under the skin that may cause pain from pressing on nearby tissues and nerves)
- Abdominal discomfort from an enlarged spleen
- Anaemia (which may include feeling breathless, persistent tiredness and pale skin)
- Frequent infections or infections that will not get better

## How is CLL diagnosed?

There are various tests doctors may use to diagnose CLL. Some of these tests might also be used to monitor its progression and help inform treatment decisions further down the line.

### Diagnosis tests include:

- **Blood tests:** your doctor may conduct a blood cell count to check the number of blood cells in your blood and your general health (this cannot diagnose CLL but may indicate the need for further, specialised testing).[11]
- **Immunophenotyping tests:** immunophenotyping examines the presence (or absence) of certain protein structures, called antigens, on or within your lymphocytes. The most common technique is flow cytometry in which a machine is used to check the number and characteristics of cells and whether the lymphocytes in your blood sample contain abnormal B-cell markers.[13]

### Monitoring/tests after a diagnosis include:

- **Ongoing blood tests:** your healthcare team will typically advise you to have blood tests at regular periods, whether you are in 'active surveillance' (see active surveillance section) or in remission. These tests can help monitor for changes in your blood count and initiate a change in your treatment schedule.[14]
- **Ultrasound scan:** this scan uses high frequency sound waves to assess a part of your body and may be used to look at the organs that are typically affected the most by CLL: the liver and spleen.[11]

**Genetic tests for symptomatic patients: sometimes called cytogenetics, genetic tests can be conducted on those who are symptomatic using samples of your blood or bone marrow to find out if genetic changes (abnormalities) are present in the CLL cells.[14] These tests can help inform doctors about the most appropriate treatment pathway for you, as well as whether your CLL is high- or low-risk. For more on the various types of genetic tests, you can read the 'Genetic Testing' information here.**

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[11] Cancer Research UK. Tests for CLL. Available at: https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/getting-diagnosed/tests. Last accessed: December 2024.

[12] Cancer Research UK. Symptoms of chronic lymphocytic leukaemia (CLL). Available at: https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/symptoms. Last accessed: December 2024.

[13] Leukaemia & Lymphoma Society. Chronic Lymphocytic Leukaemia. Diagnosis. Available at: https://www.lls.org/leukemia/chronic-lymphocytic-leukemia/diagnosis. Last accessed: December 2024.

[14] Blood Cancer UK; Tests after diagnosis. Available at: https://bloodcancer.org.uk/understanding-blood-cancer/leukaemia/chronic-lymphocytic-leukaemia-cll/cll-testing/cll-tests-after-diagnosis/. Last accessed: December 2024.

## CLL risk stratification, staging and indication for treatment

As with other types of cancer, CLL is categorised into different stages to indicate the severity of the disease. These stages also help doctors determine if or when you may need treatment.[4]

For CLL, there are two clinical staging systems: the Binet system and the Rai system.[15]

In Europe, the Binet system is the most widely used and sees CLL classified by the number of affected lymphoid tissue groups (neck lymph nodes, groin lymph nodes, underarm lymph nodes, spleen and liver) and by whether or not patients have anaemia (too few red blood cells) or thrombocytopenia (too few blood platelets).[16]

### The three Binet stages are A, B and C:[15]

| Stage A | Stage B | Stage C |
|---|---|---|
| You have enlarged lymph nodes in **fewer than three** areas (such as your neck, armpit or groin) and a high white blood cell count | You have enlarged lymph nodes in **three or more** areas and a high white blood cell count | You have enlarged lymph nodes or an enlarged spleen, a high white blood cell count and a low red blood cell or platelet count |

Only patients with active disease or those showing symptoms (symptomatic) with advanced Binet or Rai stages require treatment.[1,17]

These staging systems help doctors understand your disease by using information from physical exams and blood tests. However, with recent advances in our understanding of CLL and new treatments, staging alone is not enough to fully determine a patient's risk. More detailed tests, like genetic and molecular tests, are needed to give doctors a more complete picture of how the disease might behave, including whether the cancer might grow quickly or respond well to certain treatments:[18,19,20,21]

- For instance, changes in a specific part of chromosome 17 (otherwise called del[17p]) and mutations in the TP53 gene are associated with resistance to chemoimmunotherapy and a faster disease progression with most targeted therapies.[18,20]
- Another important factor doctors consider when assessing a patient's risk is IGHV gene mutational status. IGHV stands for immunoglobulin heavy chain variable region, which plays a role in how your immune system makes antibodies. In CLL, this gene can be either mutated or unmutated.[18,19,20]
  - » Mutated IGHV is generally considered a good sign. Patients with mutated IGHV tend to have slower-growing CLL, and they often respond better to treatment. They may not need treatment for many years after diagnosis.[20]
  - » Unmutated IGHV is considered higher-risk. Patients with unmutated IGHV usually have more aggressive CLL, and the disease tends to progress faster.[18] Doctors might consider starting treatment earlier or using more advanced therapies, like targeted drugs (e.g., BTK inhibitors or B-cell lymphoma 2 (Bcl-2) inhibitors), rather than traditional chemotherapy.[19]

Before selecting a recommended therapy, it is therefore essential to evaluate a patient's IGHV status and check for any 17p deletions [del(17p)] or TP53 mutations. Testing for IGHV is only needed once, but tests for del(17p) and TP53 need to be repeated before starting any new line of treatment.[18]

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[15] CancerResearchUK. Staging chronic lymphocytic leukaemia (CLL). Available at: https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/staging#:~:text=This%20has%203%20stages%20of. Last accessed: December 2024.

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[18] CLL Society | Prognostic Factors in CLL. Available at: https://cllsociety.org/2017/09/prognostic-factors-cll/. Last accessed: December 2024.

[19] Agathangelidis A, et al. Immunoglobulin gene sequence analysis in chronic lymphocytic leukemia: the 2022 update of the recommendations by ERIC, the European Research Initiative on CLL. Leukemia. 2022;36(8):1961-1968.

[20] CLL Society | Blood Testing in CLL/SLL. Available at: https://cllsociety.org/cll-sll-patient-education-toolkit/blood-testing/. Last accessed: December 2024.

[21] Galieni P, Troiani E, Picardi P, et al. Unmutated IGHV at diagnosis in patients with early-stage CLL independently predicts for shorter follow-up time to first treatment (TTFT). Leuk Res. 2024;143:106917.

# Managing CLL after diagnosis

## Preventing infections

Chronic lymphocytic leukaemia (CLL) affects your white blood cells, weakening your immune system. This makes you more susceptible to other infections, such as flu or pneumonia.[22]

It is therefore advisable to take as many preventative steps as you can to avoid infection. This includes washing your hands regularly, wearing a mask in crowded indoor spaces, and asking your doctor, oncology nurse or pharmacist about getting vaccinated. Vaccines such as (but not limited to) the flu shot and the pneumococcal vaccine can help keep you safe from serious illnesses like pneumonia and meningitis.[23,24] Vaccinations for shingles and COVID-19 are also recommended.[25,26]

## Cancer surveillance

As someone living with CLL, you may also face a higher risk of developing other types of cancer, particularly skin cancer, which is the most common secondary cancer diagnosed among people with CLL.[23] This is due to the immune system's decreased ability to detect and destroy cancer cells.[23] People with CLL are more than twice as likely to develop skin cancer compared to the general population.[27]

Regular surveillance or monitoring for skin cancer and other cancers is therefore crucial, either via routine check-ups, skin examinations by a dermatologist or other screenings. Your healthcare team can recommend the most suitable schedule for these check-ups, tailored to your specific needs. It is therefore also very important to be 'sun smart' all year round:[28]

- Try to avoid sun exposure during the hottest parts of the day (typically the sun is at its hottest between 11am-3pm)
- Wear the right suncream, sunglasses, loose-fitting clothes and a wide-brimmed hat to shade your face, neck and ears
- Stay hydrated

It is also important to be aware of and adhere to cancer screening programmes that test for cancers such as breast, colon and prostate. Screening tests are usually done via your GP.

## Active surveillance

CLL cannot currently be cured but treatments have greatly improved and many people with the disease go on to live a life expectancy that is similar to the general European population (i.e. those without CLL).[1,29] It does, though, affect every person differently, with some patients not requiring treatment right away, or ever, and others needing it immediately after diagnosis.

If your CLL is considered low-risk (slow-growing) and you have no symptoms or symptoms that are not affecting you greatly, your healthcare team may not recommend treatment. This approach is called active surveillance or active monitoring.[30]

Active surveillance includes regular medical check-ups and blood tests to assess whether the disease is stable or if it is beginning to progress. And while it can feel confusing or concerning to be diagnosed with cancer and not receive treatment, many studies have shown that there are no benefits in early treatment for people with low-risk asymptomatic CLL.[31,32] Active surveillance instead remains the recommended standard of care.[32]

Your healthcare team will support you in deciding whether or not you need treatment, depending on your stage of CLL and your symptoms.

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[22] Blood Cancer UK | CLL and infection. Available at: https://bloodcancer.org.uk/understanding-blood-cancer/leukaemia/chronic-lymphocytic-leukaemia/cll-infection/. Last accessed: December 2024.

[23] Leukaemia & Lymphoma Society. Chronic Lymphocytic Leukaemia. Treatment. Complications of CLL or CLL treatment. Available at: https://www.lls.org/leukemia/chronic-lymphocytic-leukemia/treatment/complications-cll-or-cll-treatment. Last accessed: December 2024.

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[25] CLL Support. Shingles. Available at: https://cllsupport.org.uk/information-support/diagnosis/shingles-2/ Last accessed: December 2024.

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[27] Turk T, et al. The risk of melanoma in patients with chronic lymphocytic leukemia; a population-based study. Curr Probl Cancer. 2020 Apr;44(2):100511.

[28] Blood Cancer UK. Keeping Safe in the Sun. Available at: https://bloodcancer.org.uk/news/keeping-safe-sun/. Last accessed: December 2024.

[29] Ghia, P., et al. First-line ibrutinib in patients with chronic lymphocytic leukemia demonstrates overall survival comparable to an age-matched European population. Presented at 2024 European Hematology Association Hybrid Congress. Poster #P664

[30] NCI. NCI Dictionary of Cancer Terms: active surveillance. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/active-surveillance. Last accessed: December 2024.

[31] Langerbeins P, et al. The CLL12 trial: ibrutinib vs placebo in treatment-naïve, early-stage chronic lymphocytic leukemia. Blood. 2022; 139(2): 177–87.

[32] Hoechstetter MA, et al. Early, risk-adapted treatment with fludarabine in Binet stage A chronic lymphocytic leukemia patients: results of the CLL1 trial of the German CLL study group. Leukemia. 2017; 31(12): 2833–7.

## Treatment options according to current guidelines

There is no one-size-fits-all approach to treating CLL. Instead, the decisions you and your healthcare team make are unique to you and will take into account various factors.

> “The way you navigate your treatment entirely depends on your own personal and individual lifestyle. What works for one individual, might not work for another.”
>
> CLL patient, 61, UK

### These include:

- Your personal preferences
- Other medications you are taking
- Other diseases or conditions you may have
- Whether you demonstrate certain genetic mutations
- The stage and status of your disease - i.e., if you have relapsed or become refractory to your prior treatment[33]
- Whether the medication and any potential side effects are safe and acceptable for your individual health needs
- The approval and availability of drugs (this can vary between countries)

Doctors may also use different treatment approaches, again based on your individual circumstances. However, at the time of this guide’s publication (CLL treatments are advancing all the time), the following are the most widely used:

**Targeted therapies** – these target the specific genes and proteins on or within cells that are helping the cancer to grow and survive.[34] This minimises damage to healthy cells and makes these therapies generally more tolerable than chemotherapy.[34] Targeted therapy may be administered alone, or in combination with another targeted therapy or immunotherapy drug.[34] Currently, the two main types of targeted therapies for CLL are BTKis and Bcl-2 inhibitors.[35]

**Chemoimmunotherapy** – although used less frequently with the rise of targeted therapies, chemotherapy combined with monoclonal antibodies may still be an option in certain cases (for example, in young and fit patients).[35] Chemoimmunotherapy treatment is administered either orally or intravenously (through a drip).

**Allogeneic stem cell transplantation (ASCT)** – while it is uncommon given the newer options that exist today, individuals with very high-risk CLL (as determined by specific factors that influence how quickly CLL will progress) may sometimes be recommended for a stem cell transplant early in their treatment. This procedure takes stem cells from a healthy donor and transplants them to people with relapsed high-risk CLL or CLL that is resistant to other treatments.[36] The donor’s cells replace the patient’s damaged, blood-forming cells and potentially treat the disease.[36] It is reserved for cases of CLL that are resistant to existing treatment methods.[36]

**Investigational immunotherapy treatments – such as CAR-T cell therapy, are being explored to boost the immune system's ability to fight CLL.**

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[33] EMA. BRUKINSA SMPC. Available at: https://www.ema.europa.eu/en/documents/product-information/brukinsa-epar-product-information_en.pdf. Last accessed: December 2024.

[34] Macmillan Cancer Support. Targeted therapies for chronic lymphocytic leukaemia (CLL). Available at: https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/targeted-therapies-for-cll. Last accessed: December 2024.

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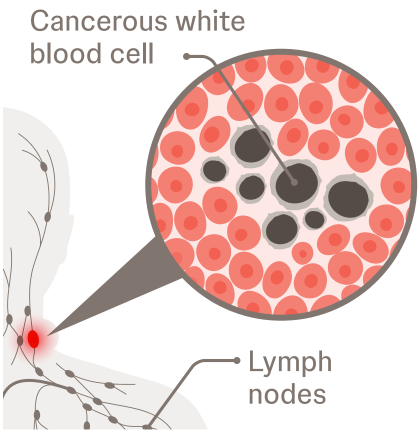
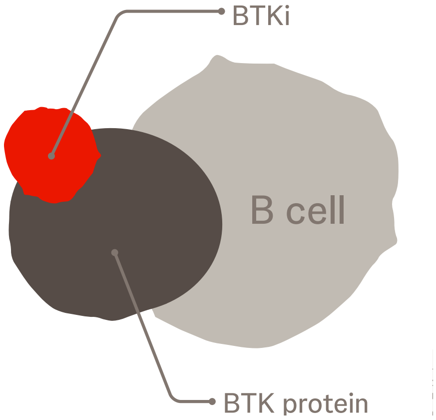
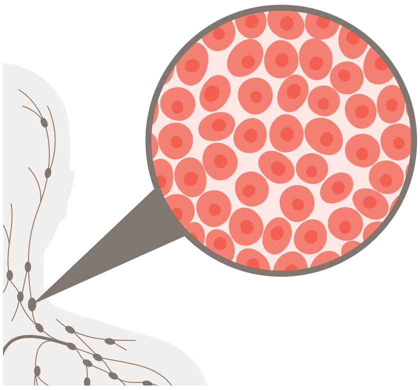
In the following sections of this guide, we look specifically at what to expect if you are prescribed a BTKi treatment.

# Treating CLL with continuous BTKis







## What are BTKis and how do they work?

Specific kinases, called BTKs, play a critical role in supporting the normal growth and survival of some white blood cells, called B-lymphocytes, including cancerous B-cells found in CLL.[38,39]

By binding to the BTK protein, BTKi's "turn off" their communication signals, preventing the survival and multiplication of the malignant B-lymphocytes.

During the past decade, the clinical use of BTKis in treating B-cell malignancies such as CLL has grown rapidly.[38] Currently, the EU and UK regulatory authorities have approved three different BTKis for CLL.[38,40] Several other new inhibitors are also under development.[29]

BTKis have traditionally been approved as a continuous therapy, meaning the treatment is administered for an indefinite period, continuing for as long as your disease is responding to it.[33,41,42]

Some BTKis have been found to significantly improve outcomes for many people living with CLL who require treatment, extending survival, relieving or even resolving cancer symptoms and ensuring patients can enjoy a better quality of life.[43,44]

## What does a typical BTKi treatment programme look like?

The goal of treatment with a continuous BTKi is to control cancer growth and reduce your symptoms; it is not a cure.

[37] Todorovic Z, et al. CAR T Cell Therapy for Chronic Lymphocytic Leukemia: Successes and Shortcomings. Curr Oncol. 2022;29(5):3647-3657.

[38] Palma M, et al. BTK Inhibitors in Chronic Lymphocytic Leukemia: Biological Activity and Immune Effects. Front Immunol. 2021 Jul;12:686768.

[39] NCI. Zanubrutinib's Approval Improves Targeted Treatment for CLL. Available at: https://www.cancer.gov/news-events/cancer-currents-blog/2023/fda-zanubrutinib-cll-sll#:~:text=BTK%20plays%20a%20critical%20role,blood%20cells%20found%20in%20CLL. Last accessed: December 2024.

[40] Cancer Research UK. How you have targeted drugs and other cancer drugs for chronic lymphocytic leukaemia (CLL). Available at: https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/treatment/how-you-have#. Last accessed: December 2024.

[41] EMA. IMBRUVICA SMPC. Available at: https://www.ema.europa.eu/en/documents/product-information/imbruvica-epar-product-information_en.pdf. Last accessed: December 2024.

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[44] Moninger J, et al. BTK Inhibitors Offer a Revolutionary Treatment of Relapsed CLL/SLL. Cure. 2023 Mar; 1(22):23-27.

[45] National Comprehensive Cancer Network. NCCN Guidelines for Patients Chronic Lymphocytic Leukaemia. Available at: https://www.nccn.org/patients/guidelines/content/PDF/cll-patient.pdf. Last accessed: December 2024.

[46] Nixon S, et al. How We Manage Patients with Indolent B-Cell Malignancies on Bruton's Tyrosine Kinase Inhibitors: Practical Considerations for Nurses and Pharmacists. Curr Oncol. 2023 Apr;30(4):4222-4245.

[47] Jiang R, et al. Time-limited, Combined Regimen in Chronic Lymphocytic Leukemia: A Promising Strategy to Achieve a Drug Holiday. Curr Med Sci. 2021;41(3):431-442.

[48] clinicaltrials.gov. (n.d.). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT06333262?cond=fixed%20duration&rank=2. Last accessed: December 2024.

[49] clinicaltrials.gov. (n.d.). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT04523428?term=acalabrutinib. Last accessed: December 2024.

Also, not everyone responds the same way to treatment, so it is important to enter any treatment programme with the right expectations.[45]

The presence of genetic changes (mutations) found within leukaemia cells can help inform your doctor about the most appropriate treatment pathway for you.[45] And as we saw in Section 3, they may run a series of genetic tests before making a final decision on whether to recommend a BTKi.[45]

If you are prescribed a BTKi, the treatment will be administered orally, requiring less frequent clinic visits than if you were prescribed chemotherapy.[33,41,42] This makes BTKis a good option for people who have difficulty travelling to cancer centres for treatment and/or who wish to reduce public exposure to reduce the risk of other infections.[46]

BTKis may be used in the first-line or relapsed setting and can be given on their own or in combination with other anti-cancer medicines.[33,41,42] They are usually taken once or twice daily as tablets for as long as you are responding to the treatment.[33,41,42]

Newer treatment options include BTKis as a 'fixed duration' (also called 'time-limited') option, approved for use in combination with other novel agents (additionally, several other fixed duration options are under investigation using both BTKi-based combinations and BCL2 inhibitor-based combinations).[47]

In a fixed duration approach, the treatment is administered for a specific, predetermined period of time before being paused.[48,49] This method is designed to manage the disease effectively while potentially reducing long-term side effects and improving quality of life thanks to 'treatment-free windows'.

According to the ESMO treatment guidelines, time-limited therapies may be preferred for patients with CLL regardless of the cytogenetic profile. Time-limited chemoimmunotherapy combinations may also be offered to patients with CLL, but only to those with a favourable genetic risk profile.[50]

A favourable genetic risk profile may be defined by:

- Mutated IGHV status and no TP53 mutations
- A non-complex karyotype

A non-complex karyotype is defined by having fewer than five mutations.[50] Additionally, chemoimmunotherapy should only be an option if targeted therapies are not covered for by healthcare systems in a given country.[50]

For more detailed information, please refer to the ESMO clinical practice treatment guidelines for CLL.

## Understanding your BTKi treatment and how you are responding to it

Learn as much as possible about your CLL, the recommended treatment, any potential side effects and discuss your personal preferences as well as any pre-existing conditions with your doctor. This will help you and your doctor make shared decisions about your care that best suit your needs and supports your quality of life.[51] Discussing possible side effects in advance can also help you and your healthcare team come up with ways to best mitigate or manage them.

One important thing to remember is that the impact of a BTKi treatment on controlling your CLL typically increases over time.[52] This means it can often take around three to six months for you to feel better after starting therapy, and years to achieve the best response.

### Learn more

**Here are five steps you can take to help get the best outcome when starting BTKi treatment:**

1 Try to learn about the different options available. Your doctors will recommend what pathway to follow but doing your own research can help you have a more informed discussion about what may best suit you, your health status and your lifestyle.

2 Never hesitate to bring up any concerns and ask your doctor as many questions about side effects as possible, ideally prior to starting any treatment so you can identify them early and best mitigate or manage them.

3 Keep telling your doctor about what is working and what is not; your quality of life and living well with CLL are the priority.

4 Always attend your scheduled follow-up appointments. This ensures your healthcare team can address your concerns and conduct regular examinations/tests to monitor for signs of cancer recurrence or treatment-related side effects.

5 Stay as positive as you can. CLL and the side effects of a BTKi treatment are manageable if you have a treatment plan that is tailored to your unique situation.

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[50] Eichhorst B, et al. ESMO Clinical Practice Guideline interim update on new targeted therapies in the first line and at relapse of chronic lymphocytic leukaemia. Ann Oncol. 2024;35(9):762-768.

[51] NHS England (2019). NHS England: Shared Decision Making. [online] www.england.nhs.uk. Available at: https://www.england.nhs.uk/personalisedcare/shared-decision-making/.

[52] ASCO Daily News. Managing Adverse Events in Chronic Lymphocytic Leukemia While Achieving Durable Remission: Strategies and Solutions. Available at: https://dailynews.ascopubs.org/do/managing-adverse-events-chronic-lymphocytic-leukemia-while-achieving-durable-remission. Last accessed: December 2024.

Your healthcare team will meet with you regularly to check how you are responding to the treatment, assess your general health and monitor for any signs of your CLL becoming more active again.[53]

Of course, undergoing tests can be a very anxious experience, so always talk to your healthcare team about any concerns you have and ask your doctor as many questions as you need to. They can help you understand what to expect as well as discuss any results and what they mean for you.

### Blood tests

You will have regular blood tests during BTKi treatment to check your levels of red blood cells, white blood cells and platelets, as well as tests to check your kidney and liver function.[54] In particular, your doctor will want to calculate how long it takes for the number of lymphocytes in your blood to double as this helps to assess how/if your CLL is progressing.[14]

The results of these tests should not be considered in isolation. For example, your first blood test results after starting therapy may show a rise in white blood cell count. This is called lymphocytosis.[55] Lymphocytosis is expected and may last for a few months, but it does not necessarily mean that your condition is getting worse.[55] Instead, discuss the findings with your healthcare team. It is the pattern of these blood counts over time that most interests your doctor.

### Sticking to your BTKi treatment

Taking your BTKi as prescribed is critical to how well it works.[56] In fact, high adherence to treatment has been linked to longer remission times, fewer side effects and an overall improved quality of life.[57]

## Top tips

### Four ways to help you remember to take your BTKi treatment

| | |
|---|---|
| **Link it** | Take your medicine at the same time as something else you do every day, like walking the dog or preparing for bed. |
| **See it** | Use reminder notes or put your tablet/capsule container in a place where you will easily see it. It is helpful to keep your medication in one obvious place (i.e. beside your bed or on the kitchen counter). |
| **Hear it** | Set a daily alarm on your phone, watch or clock to go off when you need to take your tablet/capsule. |
| **Tool it** | Use tools, such as an app on your smartphone or a calendar, to set reminders for yourself and/or track your progress. |

As part of your treatment, you will need to take your tablet(s) or capsule(s) every day.[33,41,42] It can be helpful to take the treatment at approximately the same time(s) each day. [33,41,42] Do not stop unless told to by your doctor, even when you are feeling well or worrying about side effects.

***If you have concerns about your treatment or wish to discontinue it, always speak to your healthcare team before taking any action.***

### Combining other medicines and supplements with your BTKi treatment

BTKis can interact with other medicines[46] so always let your pharmacist and/or healthcare team know about any medicine you are taking before starting treatment. Taking antibiotics may be more complicated. Some are contra-indicated with BTKis (e.g., clarithromycin).[41,42] You may receive a medical alert card stating that you are on a specific BTKi to show to healthcare professionals and it is good practice to keep this on you at all times. Similarly, if you are prescribed a new treatment while already on a BTKi, always discuss it with your doctor to confirm it is suitable to take.[58]

All BTKis are associated with an increased risk of bleeding, so it is important to be aware whether any other medicines you are taking can increase bleeding risk too, such as aspirin, anti-inflammatory drugs, anticoagulants and antiplatelets.[58] Certain supplements may also increase your risk of bleeding and should be avoided, for example fish oil, flaxseed, vitamin E, omega-3 fatty acids and ginkgo biloba.[59]

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[53] Lymphoma Action. Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL). Available at: https://lymphoma-action.org.uk/types-lymphoma/chronic-lymphocytic-leukaemia-cll-and-small-lymphocytic-lymphoma-sll#:~:text=As%20part%20of%20your%20follow,or%20new%20swollen%20lymph%20nodes. Last accessed: December 2024.

[54] CancerResearchUK. Blood tests. Available at: https://www.cancerresearchuk.org/about-cancer/tests-and-scans/blood-tests. Last accessed: December 2024.

[55] Herman SE, et al. Ibrutinib-induced lymphocytosis in patients with chronic lymphocytic leukemia: correlative analyses from a phase II study. Leukemia. 2014 Nov;28(11):2188-96.

[56] Lu X, et al. Real-World Comparison of First-Line Treatment Adherence Between Single-Agent Ibrutinib and Acalabrutinib in Patients with Chronic Lymphocytic Leukemia. Patient Prefer Adherence. 2023 Aug;17:2073-2084.

[57] Alu, Aqu et al. BTK inhibitors in the treatment of hematological malignancies and inflammatory diseases: mechanisms and clinical studies. Journal of Hematology & Oncology. 2022 Oct;15:138.

[58] DrugBank Online. Warfarin. Available at: https://go.drugbank.com/drugs/DB00682. Last accessed: December 2024.

[59] Hatfield J, et al. Dietary supplements and bleeding. Proc. 2022 Sep 15; 802-807.

The following medicines, foods and supplements are not recommended to be used alongside a BTKi without the approval of your doctor:

- Warfarin and other vitamin K antagonists[58] (these are anticoagulant medicines used to prevent and treat blood clotting disorders and are sometimes described more commonly as 'blood thinners.' These medicines are typically prescribed to treat venous thromboembolism, pulmonary embolism, thromboembolism with atrial fibrillation, thromboembolism with cardiac valve replacement and thromboembolic events post myocardial infarction).[58]
- Grapefruit, Seville oranges and anything containing the herbal supplement St John's Wort, as these also contain moderate inhibitors of CYP3A and can impact the way your treatment works.[59]
- For some BTK inhibitors, the use of proton pump inhibitors (a group of medicines that decrease the production of stomach acid).[60]

***In each case, always speak to your haematology healthcare team about your specific BTKi treatment and what to avoid.***

> **“Understanding and managing side effects is important and they shouldn't be ignored. Many side effects can be managed with the assistance of your clinician or with lifestyle changes. It is also helpful to know what the side effects are, so that you can report any that might be severe and need attention. The key is talking to somebody. There are now options such as dose reductions or interruptions, but these should be done with medical assistance. Talking to others can really help you get through it.”**
>
> CLL patient, 61, UK

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[60] O'Brien SM, et al. Monitoring and Managing BTK Inhibitor Treatment-Related Adverse Events in Clinical Practice. Front Oncol. 2021 Nov;11:720704.

# Possible BTKi side effects

BTKis have been shown to have a positive benefit-risk profile in CLL and, in many cases, are the preferred first-line option.[43,50]

Like most medicines, BTKis can have side effects for those who take them, ranging in both commonality and severity.[60] For those on continuous BTKi treatment, the possibility of experiencing side effects can be an area of concern for patients.

The most important thing to remember is that every patient is different and every BTKi has a different side effect profile too. ***Therefore, the first step is always to speak to your healthcare team about what to expect.***

In this section, we explain some of the most common side effects of being treated with a BTKi, along with some practical suggestions for how to manage them.

Different side effects also require slightly different responses when it comes to reporting them:

**Tell your doctor immediately**: chest pain, shortness of breath, ankle swelling, heart palpitations and major bleeding/bruising that will not stop.

**Note down and discuss at your next appointment or with your primary care provider:** minor bruising and bleeding, diarrhoea, arthralgia (joint and bone pain), hair loss, memory issues, headaches and fatigue.

**Understand which side-effects are largely self managed:** flaking/breaking nails, dry skin, dehydration, mouth sores, vertigo, vision spots and cramping can all be self-managed using the guidance below.

Most importantly, trust your instincts. You know your own body better than anyone, so if any side effects you experience (no matter where they appear in the list below) feel severe, are debilitating or will not resolve, contact your doctor straightaway. Even with self-managed side effects, always let your healthcare team know you are experiencing them too.


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# Infections

CLL weakens your immunity, increasing the possibility of infectious complications with pneumonia being the most common.[61] While BTKis are effective at treating CLL, they do not address the underlying immune dysfunction.[60] Infection (of any severity) occurs in more than half of patients on BTKis, particularly during the period soon after starting treatment.[60] Those with relapsed and refractory CLL are at greater risk of infections.[60]

Symptoms to look out for include a change in body temperature, aching muscles, headaches, feeling cold and shivery and generally feeling unwell.[22] You may experience other symptoms depending on where the infection is.[60]

There can be an increased risk of fungal infections.[62] Early recognition of these and prompt treatment are important to prevent from life-threatening complications. Preventative steps may be necessary if you are at higher risk of fungal infections (i.e. you have a previous history of fungal infections, you are taking chronic steroid therapy, your age and fitness).[63] Any treatment given should be under medical supervision, as it is important to remember that some drugs are contra-indicated with BTKis.[33,41,42]

> **“I’ve learned to be extra cautious when handling my compost heap. I always make sure to water it down to keep it moist and wear a face mask to avoid inhaling any fungal spores, especially since I’m immunocompromised. This simple step helps prevent spores from getting into the air and keeps me safer.”**
>
> CLL patient, 61, UK

## What can you do?

- Follow good hygiene practices, like regularly washing your hands, bathing or showering every day and wearing a mask in high-risk environments.[64]
- Ensure where possible that spaces you share with others are well ventilated.
- Avoid crowds and close contact with people who are sick.[63]
- Drink plenty of clear fluids (non-caffeinated, non-alcoholic and non-carbonated options are best).[45]
- Do not keep fresh flowers or live plants in your home or living space.[65]
- Take precautions when cleaning up droppings from your pets or ask someone else to do it for you.[66]
- Talk to your healthcare team about vaccines, including any preventative vaccines you could have prior to starting treatment with a BTKi.
- If you experience multiple infections, such as serious lung infections, you may need extra help, including immunoglobulin infusions that give you extra antibodies from donors to help reduce the risk of future infections.
- Contact your healthcare team immediately if you have any signs or symptoms of an infection, especially if you suddenly become breathless or develop a cough.[22]

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[61] Lipsky A, et al. Managing toxicities of Bruton tyrosine kinase inhibitors. *Hematology Am Soc Hematol Educ Program*. 2020 Dec;2020(1):336-345.

[62] Agudelo Higuita NI, et al. Risk of Invasive Fungal Infections in Patients With Chronic Lymphocytic Leukemia Treated With Bruton Tyrosine Kinase Inhibitors: A Case-Control Propensity Score-Matched Analysis. Open Forum Infect Dis. 2024;11(6):ofae115.

[63] Rajapakse P, et al. Invasive Fungal Infection Complicating Treatment With Ibrutinib. Cureus. 2021 Jun 29;13(6):e16009.

[64] American Cancer Society. Watching for and Preventing Infections. Available at: https://www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/infections/preventing-infections-in-people-with-cancer.html. Last accessed: December 2024.

[65] Roswell Park Comprehensive Cancer Center. Gift Ideas for Cancer Patients: What to Avoid. Available at: https://www.roswellpark.org/cancertalk/202112/gift-ideas-cancer-patients-what-avoid#:~:text=Plants%20and%20flowers%20harbor%20fungal,at%20higher%20risk%20for%20infection.. Last accessed: December 2024.

[66] LLS. Pets and Cancer: How to Care for Yourself and Your Furry Friends During Treatment. Available at: https://www.lls.org/article/pets-and-cancer-how-care-yourself-your-furry-friends-during-treatment. Last accessed: December 2024.

# Bleeding risk (haemorrhage)

Taking BTKis puts you at increased risk of minor bleeding and bruising due to a drop in the number of platelets in your blood.[67] You may find you have nosebleeds, experience bleeding gums after brushing your teeth or find lots of tiny red spots or bruises on your arms and/or legs (known as petechiae).[68]

Severe bleeding complications (major haemorrhaging) associated with BTKi therapy are less common but can occur in some people.[69] Remember, experiencing mild bleeding does not mean it will progress or lead to major haemorrhage.[60]

Some women with leukaemia, including CLL, may also notice changes in their menstrual cycle (period), such as heavy menstrual bleeding and/or uncharacteristic bleeds midway through the menstrual cycle (menorrhagia).[70] This may be caused by low levels of platelets – a reduced ability of your platelets to help with blood clotting – or your BTKi treatment.[69] There are some gynaecological options that may help with this but it requires medical management and may contribute to iron/ferritin deficiency which may have serious side effects.[71] Some women may also develop menopausal symptoms or enter early menopause during treatment.[69]

## What can you do?

- Tell your healthcare team immediately if you experience:
  - blood in your stools
  - black stools (looking like tar)
  - pink or brown urine
  - unexpected bleeding
  - bleeding that is severe or that you cannot control
  - vomiting blood or vomit that looks like coffee grounds
  - coughing up blood or blood clots
  - increased bruising
  - dizziness
  - weakness
  - confusion
  - changes in your speech
  - a headache that lasts a long time or is severe
  - changes to your menstrual cycle
- Your doctor may advise you to pause treatment with your BTKi if you are having any elective procedure or surgery – this includes dental work or the need for a medical scope, such as a colonoscopy.[72] It is important to be aware of this as you may need to stop treatment for a certain period of time, before such a procedure.[71]
- Never make any changes to your treatment plan without first getting advice from a medical professional. With medical supervision, a dose reduction is possible to manage side effects.[33,41,42]
- For bruising, use ice and apply moisturisers to the affected area to reduce any swelling and ease tenderness.[73] Natural remedies that may provide relief include the use of topical creams and gel containing arnica.[74]
- For minor bleeds, such as cuts, scratches and abrasions, apply gentle pressure with a sterile bandage or clean cloth. Keep the wound elevated above the level of the heart to help reduce bleeding. It is useful to have a good supply of bandages and plasters to hand.
- If bleeding does not stop, seek medical attention promptly.[75]

> “I’ve learned to always wear gloves and long sleeves if I’m gardening to help protect my skin from small cuts, especially when dealing with thorns. It’s also important to be mindful of your legs and cover them up as well.”
>
> CLL patient, 61, UK

## Top tip

**You may receive a medical alert card when starting treatment with a BTKi. Remember to show this card in all interactions with healthcare professionals, including dentists.**

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[67] Cancer Research UK. Ibrutinib (Imbruvica). Available at: https://www.cancerresearchuk.org/about-cancer/treatment/drugs/ibrutinib. Last accessed: December 2024.

[68] Macmillan Cancer Support. Ibrutinib (Imbruvica®). Available at: https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/ibrutinib#. Last accessed: December 2024.

[69] Chen J, et al. The effect of Bruton's tyrosine kinase (BTK) inhibitors on collagen-induced platelet aggregation, BTK, and tyrosine kinase expressed in hepatocellular carcinoma (TEC). Eur J Haematol. 2018; 101: 604–612.

[70] LeukaemiaCare.org. Blood cancer and womens issues. Available at: https://www.leukaemiacare.org.uk/support-and-information/latest-from-leukaemia-care/blog/blood-cancer-and-womens-issues/. Last accessed: December 2024.

[71] Hedenus M, et al. Intravenous iron alone resolves anemia in patients with functional iron deficiency and lymphoid malignancies undergoing chemotherapy. Med Oncol. 2014;31(12):302.

# Diarrhoea

Diarrhoea means passing three or more loose or liquid stools per day, or more frequently than is usually normal for you.[76] It is a common side effect of BTKi therapy, typically occurring in early treatment (before month six).[60]

Diarrhoea can resolve quickly without the need for further intervention.[77] However, if it persists, consult your healthcare team. They can assess you and suggest the most appropriate course of action to help.[75]

## What can you do?

- Stay hydrated by drinking plenty of clear fluids (non-caffeinated, non-alcoholic and non-carbonated options are best).[45]
- Try a store bought oral rehydration solution.[75]
- Try to eat smaller meals throughout the day.[45]
- Avoid high-fat and high-fibre foods, raw fruits and vegetables and foods that are very spicy.
- Use over the counter antidiarrhoeic medicine if recommended by your doctor or pharmacist.

# Fatigue

This is among the most common symptoms reported at diagnosis in many cancer types and is also a common side effect of BTKis.[77] If fatigue persists, speak to your healthcare team who can evaluate the cause and recommend the most appropriate approach to overcoming it.

## What can you do?[78,79]

- Prioritise your energy and plan your day to ensure you do not overload yourself and can rest when you need to.
- Balance periods of light movement with periods of rest.
- Try to practice good sleep habits, like going to bed at the same time each night, sleeping in a cool, dark and quiet room and avoiding screens or other blue lights before bedtime.
- Remain well hydrated throughout the day.
- Eat a well-balanced diet and engage in moderate exercise when you can, like walking, or exercises that include mindfulness practices such as yoga or tai chi.
- Consider restorative activities like reading, playing games or listening to music.
- Cognitive behavioural therapy where you work with a psychotherapist for a limited number of sessions has been shown to help you view challenging situations more clearly and respond to them in a more effective way.
- Keep a fatigue diary to identify patterns in your energy levels that can help you plan your day.
- Some stress reduction techniques can help too, including relaxed or deep breathing, meditation, spending time outside, scheduling social activities (within reason as you also need to plan daily time for rest), eating well, writing in a journal and learning a new hobby.

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[76] WHO (2019). Diarrhoea. Available at: https://www.who.int/health-topics/diarrhoea#tab=tab_1. Last accessed: December 2024.

[77] NHS Inform. Diarrhoea. Available at: https://www.nhsinform.scot/illnesses-and-conditions/stomach-liver-and-gastrointestinal-tract/diarrhoea/. Last accessed: December 2024.

[78] J&JWithMe. Chronic Lymphocytic Leukemia (CLL). Available at: https://www.janssenwithme.com/en/blood-cancer/chronic-lymphocytic-leukemia/living-with-cll. Last accessed: December 2024.

[79] Cancer Research UK – Managing and treating cancer fatigue. Available at: https://www.cancerresearchuk.org/about-cancer/coping/physically/fatigue/managing-treating-cancer-fatigue. Last accessed: December 2024.

## Neutropenia

Neutropenia means having low levels of neutrophils (a type of white blood cell) in your blood.[80] This increases your risk of infection.[78]

Neutropenic fever is the most common serious complication of cancer therapy and is defined as a single oral temperature greater than or equal to 38.3 degrees Celsius (101 degrees Fahrenheit) or a temperature greater than or equal to 38 degrees Celsius (100.4 degrees Fahrenheit) for at least an hour, with an absolute neutrophilic count (ANC) of less than 1500 cells/microliter.[81]

### What can you do?

- Neutropenia should be managed by your healthcare team. They should do regular blood tests to check your blood counts.[79]

## Headaches

Headaches are another commonly occurring side effect with some BTKis, usually in the early part of treatment.[60] They tend to be mild and of limited duration and typically occur 30 minutes after taking your tablet or capsule.[60] In most cases, these headaches subside after about four weeks and do not require medical intervention.[60]

### What can you do?[82]

- Stay hydrated by drinking lots of clear fluids (non-caffeinated, non-alcoholic and non-carbonated options are best).
- If recommended by your doctor or pharmacist, you may also take over-the-counter medicines, such as acetaminophen (paracetamol), which can be very helpful in relieving headaches.
- Tell your healthcare team if you are experiencing headaches that don't resolve. They can give you the appropriate painkillers to help.

## High blood pressure

People taking BTKis are at increased risk of high blood pressure, also known as hypertension.[83] Your treatment plan will therefore likely involve regularly monitoring of your blood pressure during health visits.

### What can you do?

- High blood pressure can be effectively managed by your doctor with antihypertensive agents.[80]
- During consultations with your primary care physician, it can sometimes be challenging for your healthcare team to obtain your blood pressure measurements e.g., if the consultation is done over a telephone. As such, you can take an active role in monitoring your blood pressure using an at-home blood pressure monitor that helps to track trends over time.
- For a more detailed guide on how to take a blood pressure reading, you can use the NHS 'check your blood pressure tool'.[84]

[80] Lymphoma Action. Neutropenia. Available at: https://lymphoma-action.org.uk/about-lymphoma-side-effects-treatment/neutropenia. Last accessed: December 2024.

[81] Punnapuzha S, Edemobi PK, Elmoheen A. Febrile Neutropenia. [Updated 2023 Mar 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541102/

[82] NHS. Headaches. Available at: https://www.nhs.uk/conditions/headaches/. Last accessed: December 2024.

[83] Quartermaine C, et al. (2023). Cardiovascular Toxicities of BTK Inhibitors in Chronic Lymphocytic Leukemia: JACC: CardioOncology State-of-the-Art Review. JACC: CardioOncology, 5(5), pp.570–590.

[84] NHS UK. Check your blood pressure reading. Available at: https://www.nhs.uk/health-assessment-tools/check-your-blood-pressure-reading. Last accessed: December 2024.

# Joint and muscle pain

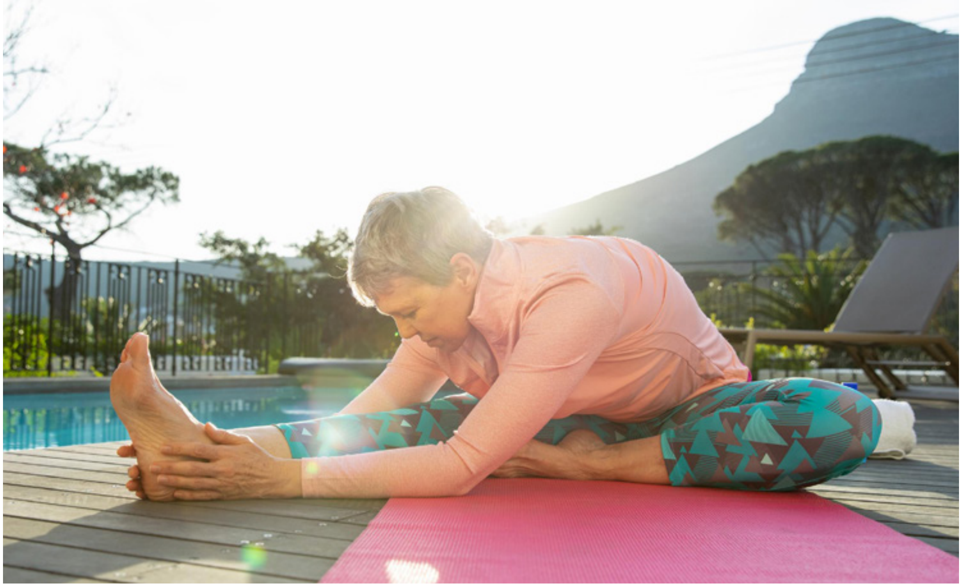
Joint pain (arthralgia), muscle pain (myalgia), severe cramps and muscle spasms are common in patients taking BTKis.[60]

In some cases, this can resolve by itself, but in others, arthralgia can be painful enough to impact function and mobility to the point where joint bandages need to be worn. Joint and muscle pain tend to occur in the first few months of treatment and can be more common in females than males.

## What can you do?

- Apply a hot compress (e.g., a heated wheat pack). This can help relieve muscle spasms/pain by bringing more blood to the area where it is applied. Be careful when using heat therapy; never applying heat to an infected, inflamed or irritated area of skin.
- Apply a cold compress (e.g., an ice pack). Cold compresses can help numb any pain in the joints and swelling by reducing inflammation in an infected area.[85]
- Warm (epsom salt) baths may help with relieving severe cramps, muscle spasms and/or myalgia.[86]
- Try light physical exercise and/or strengthening routines where manageable.[87]
- Take the time to stretch to relieve aches and relax.
- Some patients have said taking a magnesium supplement can help alleviate muscle pain and cramps but as with any dietary supplement, ensure you speak to your healthcare team before using one.
- Consider adding foods rich in magnesium to your diet to ensure you reach the recommended daily intake, including almonds, spinach, cashew nuts and peanuts.
- Similarly, potassium can help – bananas are a rich source, or it may be possible to supplement with potassium, but as with all supplements, always consult your doctor or pharmacist first.
- Unless recommended by your doctor and with close medical supervision, avoid anti-inflammatory agents with anti-platelet properties such as ibuprofen as they can further increase the bleeding risk associated with BTK inhibitors[88] (also see 'Combining other medicines and supplements with your BTKi treatment').
- If your joint and muscle pains persist in impacting your day-to-day wellbeing despite your management efforts, you should consult your treating physician for further guidance.

> “I have personally found the wearing of various elasticated support bandages which are tailored for the affected joint, i.e. elbow/knee/wrist, to be helpful. Usually, the pain and swelling are transient and will dissipate over three days. However, when severe, and strictly on medical advice, the pain may be able to be managed with an anti-inflammatory medicine, but it is important to discuss and take guidance from your healthcare team.”
>
> CLL patient, 52, Ireland



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[85] Johns Hopkins Medicine. Ice Packs vs. Warm Compresses For Pain Available at: https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/ice-packs-vs-warm-compresses-for-pain. Last accessed: December 2024.

[86] Shin HJ, et al. Magnesium and Pain. Nutrients. 2020 Jul 23;12(8):2184.

[87] Kuss B, et al. Practical management of chronic lymphocytic leukemia with acalabrutinib. Leuk Lymphoma. 2022 Dec;63(12):2785-2794.

[88] Nixon S, et al. How we manage patients with indolent B-cell malignancies on Bruton's Tyrosine Kinase Inhibitors: Practical Considerations for Nurses and Pharmacists. Current Oncology. 2023 Apr 18; 30(4): 4422-4245.

# Skin rashes and skin cancer risk

BTKi therapy may increase the likelihood of developing additional cancers, particularly skin cancer, so it is even more important to ensure that you check your skin regularly and follow sun protection guidance. If you are concerned about skin cancer, speak to your haematologist or doctor for further guidance.[89,90]

## What can you do?

- Cover up by wearing clothing made of cotton or natural fibres that have a close weave. This includes wearing long-sleeved tops and trousers, as well as wide-brimmed hats.[91]
- Use sunscreen with a high sun protection factor (SPF) of at least 30 and reapply enough of it (an average-sized adult needs at least 6-8 teaspoons of lotion) regularly.[87]
- Always wear sunglasses in bright sunlight.[87]
- Stay out of the sun in the hottest part of the day, this is usually between 11am-3pm.[87]
- Do not use a sunbed or sunlamp.[87]
- Check your skin regularly for any changes.[87]

Skin rashes associated with BTKis commonly fall into two categories: an early-onset palpable itchy rash with a variable appearance and severity or a mild non-itchy rash with red or purple bleed dots on the skin which typically appear later in the treatment cycle.[61]

Both tend to recover on their own without the need for specific treatment, decreasing over time.[61] However, if you notice the rash worsening or if it becomes particularly uncomfortable, it's important to consult your doctor. They can offer guidance on how to manage the symptoms or decide if any adjustments to your treatment are needed.

## What can you do?

- Try applying cold compresses to the affected areas.[92]
- Take a lukewarm bath with (colloidal) oatmeal.[93]
- Avoid water containing chlorine (e.g. swimming pools).[94]
- For itchy skin, gently apply unperfumed, moisturising cream.[88]
- If your rash persists, speak to your healthcare team who can prescribe medicine to stop itching and soothe your skin.
- In severe cases, a dermatology referral is recommended and the rash may be managed with topical corticosteroids and antihistamines.

# Mouth sores

Mouth sores and ulcers occur in some people receiving BTKi therapy and can be painful.[95]

## What can you do?[96]

- Keep your mouth and teeth clean.
- Consider using over-the-counter antimicrobial mouthwash or mouth rinse.
- Drink plenty of clear fluids.
- Chew sugar-free gum to keep the mouth moist.
- Inform your healthcare team who can help.

[89] IMBRUVICA Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/imbruvica-epar-product-information_en.pdf. Last accessed: December 2024.

[90] CALQUENCE Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/calquence-epar-product-information_en.pdf. Last accessed: December 2024.

[91] Macmillan Cancer Support. Preventing skin cancers. Available at: https://www.macmillan.org.uk/cancer-information-and-support/skin-cancer/preventing-further-skin-cancers. Last accessed: December 2024.

[92] NHS inform. Treatments for itchy skin. Available at: https://www.nhsinform.scot/illnesses-and-conditions/skin-hair-and nails/itchy-skin/treatments-for-itchy-skin/. Last accessed: December 2024.

[93] Health. How Can an Oatmeal Bath Help You? Available at: https://www.health.com/oatmeal-bath-8348505. Last accessed: December 2024.

[94] Cancer Research UK. Your skin, nails and cancer drugs. Available at: https://www.cancerresearchuk.org/about-cancertreatment/cancer-drugs/side-effects/skin-nails. Last accessed: December 2024.

[95] Zeynep Tuğba Güven. CLL-256 Monocytosis Developing in the Course of Chronic Lymphocytic Leukemia: Case Report. 2024;24;Sup 1: S349-S350

## Nail problems

Some patients experience nail thinning and fragility during treatment with a BTKi, typically with the formation of vertical ridges.[90]

### What can you do?

- Frequently use thick hand creams and nail oil.
- Apply (clear or coloured) nail polish to strengthen the nail.
- Wear wide-fitting shoes to avoid or reduce the likelihood of nail pain.
- Speak to your healthcare team who may recommend treating any textural changes in your hair or nails with a biotin supplement.
- Keep your nails short.

> “One of the side effects I experienced is that my fingernails have become less robust and sturdy - they are very brittle and razor-like and shatter and crack regularly. You can easily scratch yourself, which can cause bleeding, or damage your nails if you don’t protect your hands and nails. You could also be exposing yourself to an infection or anything else of that nature. So, the first step is to keep your fingernails short.”
>
> CLL patient, 61, UK

# Atrial fibrillation

Atrial fibrillation is an irregular and often very rapid heartbeat.[97] Symptoms might include heart palpitations (feelings of a fast, fluttering or pounding heartbeat), dizziness, light-headedness, chest pain, fatigue, shortness of breath, reduced ability to exercise and weakness.[98] If you experience these symptoms, you should mention them to your health team as they can recommend the most appropriate management strategy for you.

In rare cases, atrial fibrillation can lead to blood clots and may increase the risk of stroke, heart failure and other heart-related complications.[99]

Atrial fibrillation is one of the less common, but potentially more severe side effects of BTKi, with current data suggesting it affects less than 10% of patients.[100] Fewer than half of atrial fibrillation events are serious or life-threatening.[96] Some people with atrial fibrillation do not notice any symptoms. Instead, it is detected at health visits or by smartwatch and smartphone applications.[101]

## What can you do?

- If you experience any of the symptoms mentioned above, report it to your healthcare team.[102]
- If you have chest pain, seek immediate medical help.[98]
- Ask your doctor or nurse to teach you how to properly take your pulse at home, so you can self-monitor between appointments.
- Consider using a smartwatch to help monitor your heart rate and detect any irregularities. Smartwatches can provide valuable data that you can share with your healthcare provider during visits.[97]

While the above details some of the main side effects of a continuous BTKi treatment, it is not an exhaustive list, and others may occur. We therefore recommend talking to your healthcare team about your own treatment, what to look out for and how to manage any side effects that you experience.

In cases of persistent side effects, your healthcare team may suggest adjusting your BTKi dose, but never do so yourself without discussing it with your haematologist first. You can also find more information in the patient leaflet for the specific BTKi you have been prescribed.

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[96] NHS. Mouth ulcers. Available at: https://www.nhs.uk/conditions/mouth-ulcers/. Last accessed: December 2024.

[97] NHS. Overview: Atrial fibrillation. Available at: https://www.nhs.uk/conditions/atrial-fibrillation/. Last accessed: December 2024.

[98] Mayo Clinic. Atrial fibrillation: Overview. Available at: https://www.mayoclinic.org/diseases-conditions/atrial-fibrillation/symptoms-causes/syc-20350624. Last accessed: December 2024.

[99] NHS. Complications: Atrial fibrillation. Available at: https://www.nhs.uk/conditions/atrial-fibrillation/complications/. Last accessed: December 2024.

[100] Valla K, et al. Atrial Fibrillation: Considerations for the Use of BTK Inhibitors. Cancer Network Oncology. 2018 Nov; 32(11):574-575.

[101] Healthline. Do smartwatches accurately detect atrial fibrillation (AFib)? Available at: https://www.healthline.com/health-news/do-smartwatches-accurately-detect-atrial-fibrillation-afib. Last accessed: December 2024.

[102] MedicalNewstoday. Vital signs: What they are, ranges, and more. Available at: https://www.medicalnewstoday.com/articles/258118. Last accessed: December 2024.

# Your psychological and emotional wellbeing

As with any cancer, it is common to experience anxiety and depression throughout your BTKi treatment and recovery.[103] This can range from fear of doctor visits, tests and treatments to the stress of having to take precautionary steps to avoid infection or remembering to take your medication correctly every day. Many patients understandably worry about their CLL getting worse or coming back too.[99]

These side effects on your wellbeing can add to the already heavy emotional and psychological burden of living with CLL.[104] Symptoms include uncontrollable worry, trouble focusing your thoughts, muscle tension, trembling, restlessness and a dry mouth.[99]

Whatever symptoms you experience, the most important thing is not to ignore or dismiss how you are feeling and to try to find a way to deal with your anxiety that works for you.[105]

## What can you do?

- Try talking to a friend or relative about what is worrying you.
- Ask your healthcare team questions to help better understand your diagnosis, treatment and side effects.
- Use relaxation exercises such as deep breathing or guided meditation before or during a stressful situation.
- Find a regular activity you enjoy that can help take your mind off your diagnosis.
- Join local support groups and cancer support centres.
- If your psychological and emotional wellbeing is constantly affecting your day-to-day life, talk to your healthcare team about getting help from a psychologist, psychotherapist or counsellor.
- A doctor may also prescribe anti-anxiety tablets as part of your treatment if you are having very severe anxiety problems, such as panic attacks. It is important to consider whether this medication may be contraindicated to your BTKi and make a decision in consultation with your doctor.
- It is also important to discuss whether any other factors may be contributing to psychological and emotional symptoms – for example, your environment, hormones, menopause, sleep disturbances or apnoea - as treating some of these factors can also be helpful in improving mental health.

In the **Appendix**, you will find a selection of journal pages where you can keep note of any side effects that you experience. You can then discuss them during appointments with your healthcare team.

> **“Psychological challenges could stem from a multitude of different factors. There is always a fear of relapse and that your treatment might stop working. You might feel less independent than before, relying on a treatment that keeps you alive but changes your lifestyle. You may not be able to do things you used to do, and you have to adjust. Moments of discomfort or pain can also trigger a mental balancing act, making it even harder.”**
>
> CLL patient, 61, UK

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[103] American Cancer Society. Anxiety. Available at: https://www.cancer.org/cancer/managing-cancer/side-effects/emotional-mood-changes/anxiety.html. Last accessed: December 2024.

[104] Leukemia and Lymphoma Society. Anxiety and Depression. Available at: https://www.lls.org/treatment/managing-side-effects/mental-health. Last accessed: January 2025.

[105] Cancer Research UK. How to cope with fear, anxiety and panic. Available at: https://www.cancerresearchuk.org/about-cancer/coping/mental-health-cancer/how-cancer-make-you-feel/fear-anxiety-panic/how-cope-fear-anxiety-panic. Last accessed: December 2024

# Living well during BTKi treatment for CLL

## When to talk to your healthcare team

Every visit or consultation is an opportunity to talk to your healthcare team about any questions or concerns you have. You may also be able to contact a nurse/specialist nurse outside of these visits.

Think about how much you want to know about your cancer. Some people want to learn only the basics and leave the details to their healthcare team, while others want to understand all the facts and information themselves.

This is a personal decision. However, learning more about your cancer can help you feel more confident and empowered to be part of the decision-making process about your care. Having more open and informed dialogue with your doctor can also help them better meet your needs, monitor your condition, manage your medication and deliver more personalised care.

And, of course, always alert your healthcare team if you begin experiencing new side effects or if you notice any worsening of your symptoms or condition.

## How to talk to your healthcare team

A little planning can go a long way in preparing for your consultation. Your doctors and nurses are busy (understandably), and it can help to have done some pre-reading in advance.

The guidelines below can also be useful in getting the most out of every conversation:

- Try to note down and prioritise your questions in advance, making sure you have that list to hand during your consultation. You can use the journal section in the **Appendix** for this.
- Take a list of current medications and any relevant notes from your previous appointment.
- Bring a partner/care partner with you to the appointment. They can take notes, provide an additional perspective and help you concentrate fully on the conversation. This can be especially helpful if you are hard of hearing or have memory issues.
- Sometimes your clinical nurse specialist (CNS) or nurse will be present at these consultations – ask them to write down important information for you.
- Share how you've felt throughout the entire period since your last appointment, not just how you currently feel, to provide a more comprehensive view of your health. To help you do this, keep a record of your symptoms or any side-effects you have been experiencing between visits to ensure you report important details, even if they occurred weeks ago.
- Consider recording your appointment, so you can refer back to the discussions. This can be done using an app on your phone. But remember to ask for your healthcare team's consent first.
- Reiterate details, like the pronunciation of drug names or side-effects that are mentioned – this will help ensure you are able to capture these key points accurately.
- Remember that no question is a 'silly' question.
- Ask for signposting or information guides where further information would be useful to you.
- Ask for the details of a local patient advocacy group.
- Flag any side effects that you may be experiencing (for more detailed information, see 'Possible BTKi side effects').

## Did you know?

**Patients who feel informed about their disease can experience better outcomes and care experiences.[106]**

**Remember, if you experience chest pain, shortness of breath, ankle swelling, heart palpitations and major bleeding/bruising that will not stop, contact your healthcare team immediately; do not wait for your next appointment.**

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[106] Krist AH, et al. Engaging Patients in Decision-Making and Behavior Change to Promote Prevention. Stud Health Technol Inform. 2017;240:284-302.

## Top tip

**Here are some questions you could consider asking during your treatment consultations, along with which member of your healthcare team is best placed to answer:**

### For your haematologist:

- Can you provide more detail on how this medication works against my condition?
- What side effects may I experience? Will these side effects go away? When?
- What are the risks of long-term effects from my treatment?
- Will I feel sick when I take this medication?
- Are there recent advances in treatment that might be relevant to my case?
- How often should I have follow-up visits and tests while on this treatment?
- What are the signs that my condition might be worsening, despite treatment?
- What tests will I need? How many times will I need them?

### For your GP or primary care physician:

- How might this treatment interact with my other medications?
- Are there any symptoms or side effects that I should report to you immediately?
- What should I do if I miss a dose of medication?
- Are there any patient groups or support programmes that can help me stick with my treatment schedule?
- How might this treatment affect my overall health and/or any other conditions I have?
- Who should I contact after hours if I have an urgent concern?

## How to talk to friends and family members about your diagnosis and treatment

Talking about your diagnosis is a personal decision and there is no right and wrong approach; it is up to you. However, the following tips may help guide you in deciding how and when to speak to those close to you.

**Do it your way** – do not feel you have to communicate with everyone face to face. Perhaps a phone call, email or letter would make the experience more comfortable for you. Likewise, could another friend or family member share the load of informing people?[107]

**Take it slow** – during the first conversation, start gradually, presenting your news in small chunks and focusing on the things most important to you. This can make it easier for you both to digest what you are saying. Check what the other person already knows too as it might avoid you having to repeat yourself.[103]

**Be honest** – you might be tempted to 'put on a brave face' or even keep your diagnosis secret from loved ones. If possible, try to be open with them. Your friends and family will want to support you. Knowing about your fears, concerns and treatment prognosis will help them do so.[103]

**Do not feel you have to keep talking** – when you have said what you want to say, your friend or family member may not know how to respond. That doesn't mean you have to keep talking. Just have a hug, hold hands or spend some quiet time in each other's company.[103]

## How to get the most out of life with CLL

Living with CLL and undergoing a continuous BTKi treatment can be challenging – both physically and emotionally. However, there are some steps you can take to enjoy life as much as possible at the same time.

### Review your priorities

Think about the relationships, places and activities that give you the most pleasure or meaning and, wherever possible, prioritise spending time on them. Check your calendar regularly and cancel anything you feel may overload you or that you simply do not want to do.

You could also consider keeping a fatigue diary to help plan your activities according to patterns in your energy levels. And try to block out regular time just for you, whether that's to rest, exercise or enjoy a hobby.

### Exercise when you can

Living a healthy, active lifestyle can help you improve your energy levels, manage the stresses of treatment and maintain a sense of independence and achievement in life.[108,109]

In fact, physical exercise in people with cancer has been shown to reduce fatigue, improve fitness and strength, reduce depression and anxiety, improve sleep and boost mood. Aerobic exercise, such as cycling or walking, can also help reduce your risk of obesity, high blood pressure or heart disease.[104] Meanwhile, resistance training has been found to offer a range of health benefits, including increased bone density, reduced pain and higher self-esteem.[105]

Always talk to your healthcare team before starting any new physical activity routine.

> **“Physical exercise is probably the one thing that helps me more than anything else. It's important to stay active but also know your limits. Some exercises you can do, some you can't, and it's different for everyone. Moderation and not overdoing it are key. It's about being aware of your own vulnerabilities.”**
>
> CLL patient, 61, UK

### Eat well

While there is not currently a specific recommended diet for CLL, there are certain foods and drinks that can help improve your immune function, maintain a healthy weight and boost your overall wellbeing, all of which may alleviate some of the symptoms associated with the disease and its treatment.[110]

Unprocessed foods are best, especially those that are high in fibre and nutrients, including fruits, vegetables and whole grains.[111] Lean proteins like beans, lentils, skinless white-meat poultry and fish and foods containing healthy fats, such as oily fish, olive oil, avocado, nuts and seeds, can also be good for your physical, psychological and emotional wellbeing.[108] Drink plenty of fluids too – at least 1,200 ml per day, which is just under two pints, or around six and eight large glasses or mugs, but preferably more. Filtered water is great but any sugar-free liquids, such as tea, coffee or herbal teas like mint, peppermint or ginger are fine too.[108]

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[107] Macmillan Cancer Support. Talking about cancer booklet. Available at: https://www.macmillan.org.uk/cancer-information-and-support/stories-and-media/booklets/talking-about-cancer. Last accessed: December 2024.

[108] Mayo Clinic Staff (2018). 10 great reasons to love aerobic exercise. Mayo Clinic. Available at: https://www.mayoclinic.org/healthy-lifestyle/fitness/in-depth/aerobic-exercise/art-20045541. Last accessed: December 2024.

[109] Westcott, W.L. (2012). Resistance training is medicine: Effects of strength training on health. Current Sports Medicine Reports. 11(4), pp.209–216.

Where possible, try to avoid processed and spicy foods as well as those that are high in sugar.[108] Similarly, it is a good idea not to eat excess red meat, unpasteurised dairy, blue cheese or raw/undercooked foods and try to avoid drinking lots of sugary drinks and alcohol. When buying cooked foods, ensure it is piping hot before you eat it to limit your risk of foodborne illnesses. Always store food at the correct temperature too, thoroughly wash your hands before cooking and do not eat anything more than 24 hours after defrosting.

Sometimes, people with CLL struggle to keep their weight steady, so if you do find yourself losing too much weight, talk to your healthcare team about ways to increase your calorie intake even when your appetite is low. Likewise, we know that food and drink can be a great source of pleasure in life, so do not feel you have to avoid everything you enjoy. The occasional treat can be a great way to boost your mood and emotional wellbeing.

## Tips for eating well[102]

**Below are eight general tips for a healthy, nutritious diet. You can find more information about each tip here. These tips are designed for everyone, not just people living with CLL, so always consult your healthcare team before making any changes to your diet or exercise routine.**

1. Just over a third of what you eat should be higher fibre, starchy carbohydrates, such as wholewheat pasta, brown rice or potatoes with their skins on
2. Eat at least five portions of a variety of fruit and vegetables every day
3. Eat at least two portions of fish a week, including at least one portion of oily fish, like salmon, sardines or mackerel
4. Cut down on saturated fat and sugars, which tend to be found in foods like fatty meats, biscuits, cakes and butter
5. Limit how much salt you eat; ideally no more than six grams a day for adults
6. Try to exercise regularly throughout the week to help manage your weight (your healthcare team can help recommend a suitable amount for you)[113]
7. Stay hydrated by drinking six to eight glasses of non-alcoholic fluids every day
8. Do not skip breakfast; have a wholegrain, lower sugar cereal with semi-skimmed milk and fruit instead

### Look after your psychological and emotional wellbeing

As well as following some of the advice in the 'Psychological and Emotional Wellbeing' section, an important thing is to remember you are not alone in these feelings. Maintaining a strong support system made up of friends, family, colleagues and your healthcare team can really help you manage those feelings. You may also wish to contact CLL patient advocacy groups (PAGs) or online support communities, some recommendations for which you can find in 'Other Sources of Support', which you can find in 'Other Sources of Information' and 'Support' on the next page.

### Be prepared when you travel

If you are thinking of travelling or going on holiday, talk to your healthcare team about your plans. They can let you know of any special precautions you may need to take, such as protecting yourself against diarrhoea, and provide advice on coping with hot climates. Always be sun smart to mitigate the risk of secondary skin cancer. They can also give you information on where to find local sources of help for any unexpected medical emergencies.

If you are taking BTKis, the good news is that this medication does not need to be refrigerated, making it safe and easy to take with you. However, do make sure you bring enough to cover your full trip, including some spares stored in a different bag or pocket in case any of your luggage gets lost in transit or you experience any travel delays. It is a good idea to pack (at least some of) your medication in your hand luggage for peace of mind. Carry (and regularly use) hand sanitiser and wear a mask on public transport, including the plane, to protect against infection.

Try to keep to your regular routine if possible, including taking your medication at the same time of day as you would do, despite being on holiday – this may mean keeping water (or food) by your bedside to take your medication first thing in the morning depending on your specific protocol.

[110] Leukemia & Lymphoma Society. Healthy Eating. Available at: https://www.lls.org/managing-your-cancer/food-and-nutrition. Last accessed: December 2024.

[111] Health. A Guide to an Unprocessed Foods Diet, Available at: https://www.health.com/nutrition/eat-clean-give-up-processed-foods#. Last accessed: December 2024.

[112] NHS Live Well. 8 tips for healthy eating. Available at: https://www.nhs.uk/live-well/eat-well/how-to-eat-a-balanced-diet/eight-tips-for-healthy-eating/. Last accessed: December 2024.

[113] NHS (2022). Physical activity guidelines for adults aged 19 to 64. [online] nhs.uk. Available at: https://www.nhs.uk/live-well/exercise/physical-activity-guidelines-for-adults-aged-19-to-64/. Last accessed: December 2024.

Check your travel insurance to ensure you are covered should you need urgent treatment abroad, for your CLL or otherwise. You may wish to consult your local CLL patient support group to see what recommendations they may have regarding insurance and the healthcare system in the country you are residing or the country you are travelling to.

## Other sources of information and support

Your healthcare team should always be your first point of contact for questions and guidance about your treatment. However, alongside this guide, there are several other places where you can find valuable information and support.

Remember, though, that when researching specific medications, side effects or CLL guidance, it is crucial to seek reliable sources. Always double check your findings with your healthcare team before taking any action.

- CLLAN resource hub – a global directory of patient services and resources allowing you to search by country to find organisations providing CLL support.
- The European Medicines Agency website – features a 'Find Medicine' directory that lets you retrieve information on a specific medicine.

# How to support someone undergoing BTKi therapy

## Tips for talking to and caring for CLL patients

The burden of living with chronic lymphocytic leukaemia (CLL) and undergoing continuous BTKi therapy does not just affect patients themselves. It can also have an impact on those close to them.

As a friend, family or carer, it is natural that you may want to support and look after your loved one. Here are some helpful ways to do so.

### Start the conversation

Offering to help can have a profound effect on the health and wellbeing of someone living with cancer. Get started by asking 'How'. The person you care for may need something different than what you thought.

### Help meet their healthcare/medical needs

Partner with the person you care for on managing their healthcare needs, including:

- Helping them keep track of their medical appointments and daily medication schedule
- Working with them to plan and prioritise their questions before consultations
- Driving them to and from appointments, as well as being there to take notes or offer moral support
- Collect prescriptions for them, including planning ahead to ensure they always have enough to stick to their treatment schedule
- Monitor for side effects and help them to immediately alert their healthcare team if you notice any
- Support them in managing side effects when they occur (for details, 'see Possible BTKi side effects')

### Provide emotional support

CLL diagnosis and treatment can negatively impact a patient's emotional and psychological wellbeing. This can happen at any time, with symptoms often evolving and changing over time too. Sharing this burden with a supportive care partner can be invaluable. So, you can help by:

- Encouraging them to talk about how they are feeling, including any worries about the physical and emotional effects of their cancer or their treatment
- Being a good listener if and when they do want to talk
- Being a calming and positive presence
- Working with their healthcare team to arrange more formal support, such as a counsellor or psychologist, if required

### Helping keep daily life on track

From time to time, the person you are caring for may feel too tired or weak to manage everyday things. Helping with household tasks, such as cooking, cleaning and shopping, can make a huge difference. It may be necessary to give physical support too, such as helping someone in and out of bed, or helping with personal care, like bathing and going to the toilet.

### Take care of yourself

Taking care of someone else, especially a loved one, can be emotionally and physically draining. Make sure you get enough sleep, eat a well-balanced diet and find time to engage in physical activity. Additionally, it's important to protect both yourself and your loved one by taking preventive measures, such as staying up to date on vaccinations and wearing a mask around them if you are feeling unwell. By taking care of yourself, you can offer them your best possible support. For more guidance on how to support a loved one, view the 'Guidance for Carers' booklet on J&J With Me.

### Further support and information

As a care partner, it is important to know that you are not alone and that the feelings you have are shared by many others in a similar situation. Finding your own support network is just as important for you as it is for the person you are caring for.

Speak with your doctor or cancer care practitioners for advice on local support groups for care partners. These may include:

- Eurocarers is a European network providing support, advice and connections for all care partners, no matter the age or health needs of the person they are looking after.

# Glossary of helpful terms

Definitions of words you may read and/or hear during treatment for CLL

## A

**Allogeneic stem cell transplantation (ASCT)** – A procedure that takes stem cells from a healthy donor and transplants them to people with relapsed or refractory high-risk CLL.

**Anaemia** – A condition in which someone does not have enough healthy red blood cells or hemoglobin (proteins) to carry oxygen to the body's tissues.

**Atrial fibrillation** – An irregular and often very rapid heartbeat. A possible side effect of BTKi treatment.

**Arthralgia** – Joint pain. A possible side effect of BTKi treatment.

## B

**Binet system** – The most widely used method of classifying the stages of CLL in Europe.

**Bone Marrow** – The soft, spongy tissue found in the centre of most bones and containing many blood vessels.

**Bruton’s tyrosine kinase inhibitors (BTKis)** – Drugs that block proteins on the surface of CLL cells, called B-cell receptors, to control their growth. Also known as continuous BTKis due to the fact they must currently be taken on an ongoing basis.

## C

**Chronic lymphocytic leukaemia (CLL)** – A cancer that affects the blood and bone marrow and is characterised by the overproduction of abnormal white blood cells called lymphocytes.

**Cognitive behavioural therapy (CBT)** – A talking therapy that may help you manage your feelings by changing the way you think and behave. Can be used to reduce levels of fatigue.

## F

**Flow cytometry** – A test for CLL in which a machine is used to check if the lymphocytes in your blood sample contain abnormal B-cells markers

## I

**Immunocompromised** – Having a weakened immune system. People who are immunocompromised, such as those living with CLL, have a reduced ability to fight infections and other diseases.

## L

**Lymph node / Lymph gland** – Small vessels that help transport white blood cells around the body to help fight infections.

**Lymphocyte** – A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue.

**Lymphocytosis** – A condition in which patients have a higher than usual lymphocyte count. Is often harmless and short-lasting but can sometimes be due to something more serious, such as a blood cancer or chronic infection.

## M

**Monoclonal B-cell lymphocytosis** – A condition in which individuals have an increased number of B cells in their blood, giving them a higher risk of developing CLL.

**Myalgia** – Muscle pain. A possible side effect of BTKi treatment.

## N

**Neutropenia** – A condition in which someone has low levels of neutrophils (a type of white blood cell) in their blood, increasing their risk of infection. A possible side effect of BTKi treatment.

**Neutrophil** – A type of white blood cell that helps your immune system fight infections and heal injuries.

## P

**PAG** – Stands for Patient Advocacy Group. Organisations that provide information, resources and support for CLL patients and their carers.

## R

**Rai system** – The most widely used method of classifying the stages of CLL in the USA.

**Relapse** – Also called recurrence, this is when a patient’s cancer comes back after treatment, either in the same place it first started or somewhere else in their body.

## S

**Small lymphocytic lymphoma (SLL)** – The same disease as CLL but used when the cancer cells are located mainly in the lymph nodes.

## T

**Targeted therapies** –Treatments that target the specific genes and proteins on or within cells that are helping a cancer to grow and survive. Currently, the two main types are Bruton Tyrosine Kinase Inhibitors (BTKis) and B-cell lymphoma inhibitors (Bcl2s).

# Appendix

## Partners

This guide was developed by Johnson & Johnson in collaboration with various key partners.

### They are:

- Patient representatives from the CLL Advocates Network (CLLAN)
- Professor Patrick Thornton, Consultant Haematologist, Honorary Professor RCSI, and Clinical Director of Hermitage Medical Clinic and Beaumont Hospital Laboratory
- Geraldine Walpole, Advanced Nurse Practitioner in Haematology, Sligo University Hospital

# Journal notes

## Side effects I am experiencing

# Medications I am taking

# Questions for my doctor

# General notes

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