

## SIDE EFFECTS OF LYMPHOMA AND CLL TREATMENTS

A patient's guide to understanding lymphoma and chronic lymphocytic leukemia treatments, their short-term, long-term and late side effects, and management methods.



Lymphoma Canada is a registered charity and is Canada's only national organization focused entirely on lymphoma. Lymphoma Canada connects and empowers the lymphoma and CLL community. Together we are promoting early detection, finding new and better treatments, helping patients access those treatments, learning lymphoma's causes, and finding a cure.

#### **Our Mission:**

Empowering patients and the lymphoma community through education, support, advocacy and research.

#### **Our Vision:**

A life unlimited by lymphoma.

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**Warning:** The information in this document serves as a guide to facilitate appropriate discussions with your clinician. This should not be used in lieu of a conversation with your doctor or for any determinants of your healthcare including diagnosis, treatment, and management of side effects, symptoms or other health concerns. Your doctor has all information related to your specific treatment and health and is your most valuable and accurate source of information.

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### Overview

Lymphoma is the most common form of blood cancer and is the 5<sup>th</sup> most common cancer diagnosed in Canada. Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. With advances in research and new treatments for lymphoma and chronic lymphocytic leukemia (CLL) available to Canadians, there are a number of important considerations that may help decide between treatment options and how best to prepare and cope during and after a cancer treatment.

There are different factors that your clinician will consider when determining the best treatment option for you. This can include your lymphoma subtype, molecular characteristics of your lymphoma or CLL, whether you are receiving your first treatment or second-line therapy, third-line, etc., your health and fitness level, funding and accessibility of treatments, ease of use of therapy (i.e. oral, intravenous, infusion, etc.) and ultimately your preferences as a patient. It is therefore important that you as a patient, and your doctor, work together to find the best treatment for your lymphoma or CLL.

### There are different factors that your clinician will consider when determining the best treatment option for you:



Treatments for lymphoma or CLL can affect everyone differently, and sometimes it can be difficult to determine how a certain treatment will impact you, i.e. how well your lymphoma/CLL will respond to the treatment and the types of side effects you may experience. Therefore, it is important to speak with your doctor to understand the research and results behind a treatment. Further, it is important to understand the potential side effects of the treatment and establish appropriate expectations and management methods to recognize and cope with side effects if you begin to experience them.

This guidance document will provide you with an understanding of what side effects are, when they can occur and for how long, common side effects related to specific lymphoma/CLL therapies, management techniques, and suggestions for how to speak with your doctor about side effects and management.

Please take the time to speak with your doctor about all possible side effects (short-term, long-term, and late effects) related to your lymphoma or CLL treatment and how to appropriately recognize them, prepare for them and manage them.

If you are unfamiliar with a word or term, please refer to the glossary of medical terms at the end of this resource.

### What are Side Effects

A side effect is any effect that is secondary to the intended effect of a treatment. Side effects often occur due to the negative impact of the treatment on different cells throughout your body. The term "side effect" is commonly used to refer to the unwanted, harmful effects that result from treatment. However, it can also encompass therapeutic or beneficial effects. This guide will refer to the unwanted, harmful treatment-related side effects, and the term may be used interchangeably with "adverse effect" or "adverse event" or "toxicity".

Side effects can vary from person to person and even from one treatment cycle to the next. They can also differ in how long they last. Some reasons as to why treatment-related side effects may occur in one person and not another, or at different levels of severity or length of time, may include the overall health and fitness level of the patient, how much of the treatment the patient is receiving within a certain time period, and whether the treatment is localized (one area) or systemic (given to the whole body).

As side effects may differ from person-to-person, treatment-to-treatment and at different times throughout treatment, it is important to discuss with your doctor your potential risk for side effects. This may help you and your doctor decide on a treatment that aligns with your values and will also help you to set appropriate expectations during and after treatment. Further, knowing about the potential side effects of a treatment will help you recognize side effects and report them accurately.

#### It is important to understand that:

- Not all patients who received treatment for their lymphoma or CLL will experience side effects;
- Side effects are not always severe, they can be mild and short-term;
- Different therapies have different side effects, even if they may be in the same treatment category (i.e. chemotherapy);
- Doctors are familiar with side effects and may be able to treat them so that they are less severe and, sometimes, may be able to prevent them from happening altogether.

### Side effects can be categorized by how long you experience them as well as when you experience the side effect (i.e. during treatment or post-treatment):

- Short-term side effects are considered to be treatment side effects that develop during treatment and persist for a relatively short amount of time, often going away once treatment has ended.
- Long-term side effects are considered to be treatment side effects that persist for long periods of time, from weeks to months, beginning during or after treatment.
- Late side effects are considered to be treatment side effects that develop months or years after treatment has ended. As more people are now living longer following cancer treatment than ever before, more is becoming known about late treatment-related side effects and how to recognize and manage these.

### Treatment Options for Lymphoma and CLL Patients

Treatment for lymphoma and CLL is important depending on whether you have been diagnosed with an aggressive or indolent (slow-growing) subtype. You may require treatment right away or may instead enter into a "Watch and Wait" approach where you will be closely monitored for a length of time until you develop symptoms that may indicate the need to begin treatment. The watch and wait approach will let you avoid experiencing harmful treatment-related side effects when treatment may not provide you with improved disease responses. The goals of lymphoma or CLL treatments include bringing about and prolonging remission (cancer-free period), minimizing the number of lymph nodes/organs affected, preventing the development of symptoms and treating existing ones, improving the patient's quality of life, and potentially curing the patient. Therefore, your doctor will make the decision on when best to begin treatment to provide you with the best possible outcome.

A brief summary of treatment options for lymphoma and CLL patients has been provided below. **Please note that certain treatment options may only be approved for certain lymphoma subtypes and for certain lines of therapy.** Speak with your doctor about what treatment options you are eligible for, and which are accessible to you.

#### TREATMENT OPTIONS FOR LYMPHOMA AND CLL PATIENTS

#### **SURGERY**

Surgery may be an option for cancer that is localized (confined to one area) but is not a common treatment for lymphoma or CLL. During surgery, the cancerous area may be removed along with any surrounding tissue that might contain cancer cells. Surgery can be used to treat lymphomas that start in the spleen (splenectomy) or in certain organs outside of the lymph system.

#### **CHEMOTHERAPY**

Chemotherapy is a systemic drug therapy, which means it affects the whole body. Chemotherapy targets and kills cells that grow and divide quickly, such as cancer cells. However, chemotherapy can target any cell in the body that grows and divides quickly, meaning that it can also harm healthy cells such as your hair, nails and the cells in your mouth and digestive tract. This is why chemotherapy can cause negative and impactful side effects, because it is damaging healthy cells. Chemotherapies can be used alone or in combination with other drugs.

#### RADIATION THERAPY

Radiation therapy is used when the lymphoma is localized to a specific area in the body, preventing it from spreading further. Radiation is often used in addition to surgery or chemotherapy and can be applied through external beam radiation or radioactive isotopes.

#### **TARGETED THERAPY**

Targeted therapy is a category of treatments that target the cancer's specific genetic or cellular markers or pathways that contribute to the growth of the cancer, essentially blocking these survival pathways to kill the cancer cells. This type of treatment limits the damage to healthy cells. Not all lymphomas and CLL have the same targets, therefore testing is needed to understand the characteristics of your lymphoma or CLL to determine the best treatment option for you. Targeted therapies can include:

- Monoclonal Antibody Therapy is designed to attack a specific target, known as an antigen, that is located on tumour cells as opposed to normal healthy cells. The attachment of a monoclonal antibody to its target antigen triggers the body's immune system to attack and kill the cancer cell. Not only does this make for a very effective cancer treatment, but it also greatly minimizes the side effects, as normal cells are minimally affected. There are a number of monoclonal antibodies used for lymphoma and CLL, some of which include:
  - Anti-CD20 Monoclonal Antibodies bind to a specific marker that is found on B-cells (a type of white blood cell), allowing them to be recognized by the immune system and destroyed. CD19 is another common pathway that is targeted by monoclonal antibodies.
  - Antibody Drug Conjugates are monoclonal antibodies that deliver a chemotherapy agent or toxin directly
    to the cancer cell without harming healthy cells. The drug is delivered specifically to the cancer cell that has
    the appropriate marker.
  - Bispecific T-cell Engager (BiTE) therapy is a type of antibody therapy with two arms. One arm attaches to a specific marker on the cancer cell while the other arm activates immune cells in the patient to kill the cancer cells.
- **Kinase Inhibitors** block a type of molecule called a kinase, which helps cells to grow and function, including cancer cells. By blocking (inhibiting) a kinase from working, this can essentially stop the cancer cell from growing. Some of the most common kinase inhibitors for lymphoma and CLL include:
  - Bruton Tyrosine Kinase (BTK) inhibitors work by blocking the enzyme BTK. BTK sends signals from the surface of the cell to the inside of the cell of B lymphocytes and CLL cells, helping the cell to grow and survive. BTK can also help the cancer cell survive. When BTK is blocked by these inhibitors, the cell can no longer survive and will be destroyed.
  - B-cell lymphoma 2 (BCL-2) inhibitors work by blocking BCL-2. BCL-2 is a regulator of cell death and can prevent the cell from being destroyed. It can also prevent cancer cells from being destroyed. When BCL-2 is blocked by these inhibitors, the cell will be destroyed.
  - PI3K pathway inhibitors work by blocking the phosphoinositide 3-kinase (PI3K) pathway which are a group of kinases that control critical survival pathways for the cell. By blocking the PI3K pathway, the cell will be destroyed.
- **Proteosome inhibitors** work by blocking the function of proteosomes within a cell. A proteosome helps the cell remove waste products. When proteosomes are blocked, the waste cannot be removed, and the cell will no longer function properly and will be destroyed.
- Immunomodulatory Drugs work by changing the way your immune system responds to lymphoma cells, helping it to work more effectively to destroy the cancer cells.

#### **BIOLOGIC THERAPY**

Biologic therapy (also called **immunotherapy**) uses the body's immune system to fight the cancer. It can also help to reduce some of the symptoms or side effects by helping to repair healthy cells damaged by the cancer. The healthy cells, when functioning properly, can then control the cancer or interfere with cancer cell growth. Biologic therapies may be used alone or in combination with chemotherapy and radiation treatment and can include:

- Radioimmunotherapy uses both radiation therapy and monoclonal antibody therapy to fight the lymphoma. A radioactive molecule (releases radiation overtime) is attached to a monoclonal antibody that recognizes a marker found only on cancer cells, allowing it to bind to the cancer cell and release radiation to attack the lymphoma and cancer cells that are nearby.
- Chimeric Antigen Receptor (CAR) T-Cell therapy is a type of systemic (full body) immunotherapy that changes a patient's own T-cells (type of white blood cell) to better detect and destroy the lymphoma. CAR-T therapy works by genetically engineering the T-cells taken from a blood sample of the patient and re-infusing these cells back into the patient after they have received low-dose (lymphodepleting) chemotherapy. This allows the CAR-T cells to grow and multiply and attack the lymphoma cells throughout the body.
- Immune Checkpoint Inhibitors are a type of therapy that turns off immune checkpoints. Immune checkpoints are an essential part of the immune system. They prevent an immune response from continuing, stopping it before it begins to destroy healthy cells. However, if an immune checkpoint is activated too early, it can also prevent the immune system from destroying the cancer cells. Immune checkpoint inhibitors block the immune checkpoints so that the immune system can kill the cancer cells.

#### **STEROIDS**

Steroids are substances that are naturally produced by the body but can also be artificially made and used as anti-inflammatory drugs. Steroids may be given alone for certain types of lymphomas but are more often given with chemotherapy to increase the effectiveness of the treatment. Steroids also reduce some of the possible side effects of chemotherapy.

#### STEM CELL TRANSPLANTATION

Stem Cell Transplantation is a type of treatment that allows doctors to give patients high-dose chemotherapy, which is a stronger dose than regular chemotherapy. This stronger dose will effectively kill the cancer cells but severely damages the patient's bone marrow. Infusing previously collected blood stem cells following high-dose chemotherapy restores the damaged bone marrow. Transplants fall into three main donor categories; autologous (when a patient's own stem cells are removed and re-infused), allogeneic (when a donor's cells are infused into the patient) or syngeneic (when cells are donated by an identical twin). Stem cells are carefully frozen and stored while the patient receives chemotherapy and/or body radiation treatment to kill the harmful lymphoma cells. After therapy, frozen stem cells are thawed and infused into the patient to replenish the bone marrow. Depending on the type of stem cell transplant you receive, you may experience different side effects.

#### **CLINICAL TRIALS**

Clinical trials may be a possibility for eligible patients. There are a number of clinical trials for lymphoma and CLL patients that test a new treatment, the combination of existing treatments and/or treatments for new indications or lines of therapy (i.e. firstline, second-line, etc.). These trials look at the effectiveness (how well the therapy works) and safety (side effect profile) of the therapy as a first-line treatment (the first treatment you receive) or treatment in the relapsed/refractory setting. Speak with your doctor to see if you are eligible to receive treatment through a clinical trial and if this is the best option for you.

# How to Speak with your Doctor about Side Effects

Effective communication with your doctors and nurses is important. It ensures that you are able to make informed decisions and feel confident about the care that you are receiving throughout your lymphoma or CLL journey. By asking the proper questions and expressing your feelings or concerns, you and your healthcare team can work together to choose the optimal treatment plan for you.

An important tool that will help you in successfully communicating with your healthcare team is keeping a journal of your medical history and experience. This will help you to stay organized and be prepared for an active discussion with your healthcare team during your appointments. It can be challenging to remember a symptom or side effect you may have experienced weeks or even months ago that you wanted to discuss with your doctor. In a journal, you can record the **details of your symptoms and side effects** (i.e., date and time you experienced the side effect, length you experienced side effect for, how frequently you experienced it, how severe it was, etc.), the **treatments that you receive(d)** and the dates you receive(d) them, your **upcoming appointments** (may be useful to keep a calendar), and **any questions you have** to ask your doctor and the answers to those questions. By keeping these records, you will remember important information about your lymphoma or CLL journey and will be able to have informed discussions with your healthcare team.

It may be helpful to come to each appointment with a list of questions related to your treatment, its side effects or your overall wellbeing. Make sure questions are specific and brief, and prioritize them in order of importance to you. In the following pages of this guide, you can use these questions as a guide for what to ask your healthcare team about your treatment and its side effects prior to starting treatment, during treatment, and following treatment.

**You are your most important advocate.** Your healthcare team is there to help you. Let them. If you are dealing with troubling side effects, it is better to seek advice rather than wait to see if they resolve or become worse. Don't wait for your next scheduled appointment to contact your medical team about an important issue.

### QUESTIONS PRIOR TO STARTING TREATMENT

1. What are my treatment choices?

Which do you recommend for me and why?

What disease or health risks do I have that may make me more at risk to develop side effects or

not experience a positive response

4. What will my treatment course look like

treatment? How serious are they?

7. Can the side effects from the preferred treatment option be managed?

8. How will treatment affect my life? My work?

9. After treatment is complete, will I be cured or

10. What resources or support systems will I need to have in place before starting treatment to help me manage and cope with treatment?

11. Who do I communicate with if I experience any challenges during treatment or in the intervals between treatment cycles (if applicable)?
How do I get in contact with this person?

How long will they last?

My family?

in remission?

5. What are the possible risks or side effects of

6. Have you dealt with these side effects before?

to treatment?

What are the expected benefits of each type of treatment by themselves or in combination?

(i.e. how often will I need treatment and for how long, what monitoring tests will I need, etc.?)

2. Do I need more than one type of treatment?

**NOTES** 

### QUESTIONS DURING TREATMENT

### 1. How do I monitor for certain side effects or symptoms? 2. What symptoms or side effects should I report right away? How do I report them properly? 3. Are there any minor, short-lived side effects that I do not need to report immediately? 4. Are the side effects I am experiencing common? 5. How can my side effects be managed? 6. What should I do to try and stay healthy and strong during my treatment? 7. Are there any lifestyle changes I can make to minimize side effects or the risk of getting other side effects? 8. Are there any foods I should or should not eat? 9. My side effects are burdensome. Am I able to switch treatment options to one that does not cause as many side effects, or do I need to stop treatment altogether? 10. Where can I go for more information about my treatment and side effects?

**NOTES** 

### QUESTIONS POST-TREATMENT

**NOTES** 

- 1. What is my current disease and health status following treatment?
- 2. What will my monitoring schedule look like over the next 5-10+ years?
- 3. Should I expect to develop late side effects after treatment is complete? How long after treatment could these late side effects occur?
- 4. If side effects/symptoms occur months to years after treatment during my remission, does this mean my lymphoma or CLL has returned?

  What symptoms should I look out for that may indicate a recurrence?
- 5. How can my late side effects be managed? How do I report late side effects, especially years after I have completed treatment?
- 6. How long will it take for me to feel more like myself again?
- 7. What should I do to try and stay healthy and strong after my treatment?
- **8.** What life changes should I plan for in regards to my work, family, etc.? What support networks should I have in place to help me manage with and cope during my post-treatment journey?
- **9.** Who will oversee my care now that my treatment is complete?
- 10. Who should I contact if I have questions now or later in the future?

### Potential Side Effects of Lymphoma and CLL Treatments

Information about side effects related to lymphoma or CLL treatments are determined through clinical trial research and are published in product monographs (a scientific document on a drug product). Side effects can be listed or categorized based on how likely they are to occur (uncommon, common, very common). The list of side effects presented to you may not be fully inclusive, and you may experience a side effect that is not listed in a product monograph. Alternatively, you may not experience any side effects even if they are listed as very common. The product monograph provides you with a summary of side effects as they have been experienced by patients within clinical trial testing. Side effects may be reported as:

- Very Common (1 out of every 10 people taking that medicine will experience that side effect)
- Common (between one in 10 and one in 100 people are affected)
- Uncommon (between one in 100 and one in 1,000 people are affected)
- Rare (between one in 1,000 and one in 10,000 people are affected)
- Very Rare (fewer than one in 10,000 people are affected)

It is important to speak with your doctor to understand the possible side effects of a treatment, which are the most common, whether your doctor has experience treating these side effects and how to monitor and report any side effects you experience.

#### SIDE EFFECTS OF LYMPHOMA/CLL TREATMENT CATEGORIES

There are numerous lymphoma and CLL treatments available in Canada, each with its own side effect profiles. Listed in the table below are the major treatment categories, with treatment examples, along with a summarized list of common side effects. This table does not contain a full list of all reported side effects within each treatment category. It is important to remember that you may not experience any side effects. However, it is helpful to understand that side effects may occur and to be able to recognize and report them properly.

Treatment Category	Example of Treatment	Side Effects					
Surgery/biopsy	Splenectomy, lymph node biopsy	<ul> <li>Pain or tenderness at incision/removal site</li> <li>Bleeding/bruising or swelling</li> <li>Infection</li> <li>Allergic reaction</li> </ul>					
Chemotherapy	ABVD, CHOP, FC	Most common:  Decreased blood cell counts: anemia, neutropenia, thrombocytopenia Infusion and hypersensitivity reactions, injection site reaction Nausea/vomiting Fatigue Less common to common: Arterial/venous thromboembolism Diarrhea/constipation Fever/chills Hair loss Secondary cancer Neuropathy					
Radiation Therapy	Electron Beam Therapy, Total Body Irradiation	Most common:  Hair loss Fatigue Skin discoloration, dryness, redness Less common to common: Skin itching, irritation Secondary cancer Loss of taste/appetite					
<b>Biologic Therapy:</b> Radioimmunotherapy	lbritumomab Tiuxetan, Tositumomab	Most common:  Decreased blood cell counts: anemia, neutropenia, thrombocytopenia Shortness of breath, cough Abdominal pain Nausea/vomiting Fever Less common to common: Digestive complications: constipation, indigestion Infection Skin or mucous membrane reactions (rash)					
<b>Biologic Therapy:</b> CAR-T Cell Therapy	Axicabtagene Ciloleucal, Tisagenlecleucel	Most common: Cytokine release syndrome Neurologic complications Decreased blood cell counts: anemia, thrombocytopenia Infection Less common to common: Shortness of breath, cough Capillary leak syndrome Blood pressure changes (hypotension, swelling) Acute kidney injury Hypoxia Skin reactions (rash, itching) Muscle weakness, spasms					

Treatment Category	Example of Treatment	Side Effects
Biologic Therapy: Immune Checkpoint Inhibitors	Pembrolizumab, Nivolumab	Most common:  Nausea Diarrhea Fatigue Rash/itching Loss of appetite Less common to common: Inflammation of the gastrointestinal tract Inflammation of the lungs, or infection Severe skin reactions (blistering, dry skin, ulcers) Inflammation of the thyroid, adrenal or pituitary glands (headache, sleepiness, weight changes, dizziness, fainting)
<b>Biologic Therapy:</b> Monoclonal Antibody Therapy (anti-CD20)	Rituximab, Obinutuzumab (also function as maintenance therapies)	Most common:  Nausea/vomiting  Headache Less common to common:  Heart conditions (severe chest pain, irregular or uneven heart rate)  Progressive multifocal leukoencephalopathy  Hepatitis B  Tumor lysis syndrome
Targeted Therapy: Antibody Drug Conjugate	Brentuximab Vedotin, Polatuzumab Vedotin	Most common:  Decreased blood cell counts: anemia, neutropenia, thrombocytopenia Infection (fever, chills, sore throat) Less common to common:  Lung infection (shortness of breath, trouble breathing) Gastrointestinal problems (pain, nausea) or bleeding Fatigue Decreased weight, appetite
Targeted Therapy: BTK inhibitors	lbrutinib, Acalabrutinib, Zanubrutinib	Most common:  Decreased blood cell counts: anemia, neutropenia, thrombocytopenia Infection (urinary, sinus, lung) Bruising, bleeding New cancers of skin or other types of cancer Gastrointestinal problems (nausea, diarrhea) Less common to common: Tumor lysis syndrome Lung infection (shortness of breath), pleural effusion Heart problems (irregular heart beat)
Targeted Therapy: BCL-2 inhibitors	Venetoclax	Most common:  Decreased blood cell counts: anemia, neutropenia, thrombocytopenia  Sepsis  Less common to common:  Infection (urinary, lung), chills/fever  Bleeding/bruising  Changes in blood pressure (swelling, dizziness, headache)  Tumor lysis syndrome
Targeted Therapy: PI3K Pathway Inhibitors	ldelalisib	Most common:  Low white blood cell counts  Infection (fever, chills, cough)  Diarrhea  Less common to common:  Infections (urinary, lung, skin)  Swelling (legs and arms)  Allergic reactions

Treatment Category	Example of Treatment	Side Effects					
Targeted Therapy: Proteasome Inhibitors	Bortezomib	Most common: Fatigue, Gastrointestinal problems (diarrhea, nausea, vomiting, constipation) Infection (fever, cough, chills) Weight loss, anorexia Less common to common: Low platelet counts (bleeding, bruising) Neuropathy Changes in blood pressure (headaches)					
Targeted Therapy: Immunomodulatory drugs	Lenalidomide	Most common:  Decreased blood cell counts: anemia, neutropenia, thrombocytopenia Infections (chest or other areas)  Nausea Difficulty breathing Less common to common: Changes in blood pressure (swelling, headache, dizziness, dehydration), deep vein thrombosis Muscle weakness/joint pain Diarrhea					
Steroids	Dexamethasone, Prednisone	<ul> <li>Eye complications: Increased intraocular pressure; glaucoma; cataracts</li> <li>Neurologic complications: seizures, headache, impaired sensation, sensation of tingling, amnesia, dizziness; psychologic disorders</li> <li>Dermatologic complications</li> <li>Gastrointestinal challenges: nausea, vomiting, diarrhea or constipation, or more serious GI conditions</li> <li>Musculoskeletal challenges: muscle weakness, loss of muscle mass, osteoporosis</li> </ul>					
Stem Cell Transplant (SCT)	Autologous SCT	Side Effects related to High-Dose Chemotherapy (refer to chemotherapy section) Common Autologous-SCT side effects:  Infections  Mucositis – sores in mouth Fatigue  Nausea/vomiting  Decreased blood cell counts – anemia, thrombocytopenia  Diarrhea					
	Allogeneic SCT	Side Effects related to High-Dose Chemotherapy (refer to chemotherapy section) Common Allogeneic-SCT side effects:  Graft-versus-host disease Infections – Cytomegalovirus Mucositis – sores in mouth Fatigue Nausea/vomiting Decreased blood cell counts: anemia, thrombocytopenia Diarrhea					

This table includes the most frequently reported side effects for each treatment category based on summarized data from product monographs of lymphoma and CLL therapies approved in Canada. Data collected based on therapies available in 2021.

There are certain side effects that can result in a combination of different symptoms in the body. It is important to recognize all of the symptoms you are experiencing and to report these to your doctor immediately.

### Managing Side Effects

Lymphoma and CLL treatments may cause different side effects based on the treatment itself and the health and fitness of the patient receiving treatment. Each patient will have a different treatment experience, and it is important to communicate any side effects or symptoms that you experience with your doctor immediately.

Your doctor may use prophylaxis (preventative) treatments to limit the risk of developing certain side effects, for example the use of antiemetics (drugs that prevent vomiting), antinauseants (drugs that prevent nausea), antihistamines (drugs that prevent allergic reactions) or anticoagulants (drugs that lower the risk of blood clots). Additional preventative methods may be used to reduce your risk of a side effect, for example lowering your chance of infection by washing your hands or wearing a mask, or reducing your risk of blood clots (deep vein thrombosis) by using compression stockings or exercise. For late effects, screening methods may be used such as imaging or blood tests to detect a late side effect early, i.e. screening methods for secondary cancers.

Management of side effects may also be different depending on when the patient experiences the side effect. For example, side effects that a patient experiences during therapy may be managed by specific treatments, or if the side effects are frequent and severe, your doctor may reduce the dose or delay your treatment until the side effect resolves. For long-term side effects that are ongoing, lifestyle changes or continuous management may be needed to cope with the side effect. Preventative measures are often used to limit the impact of late side effects (i.e. screening tests), however treatment-related side effects can still occur many weeks, months or even years after the completion of treatment. Therefore, it is important that you continue to monitor and recognize symptoms and side effects during and following treatment.

It is important to have a strong support system as you receive treatment and even into follow-up and survivorship. Having a close family or friend that you see frequently may be able to help you recognize possible symptoms or side effects you are experiencing that you may not have noticed or may have thought it was caused by something else. They may also help you manage or cope with your side effects if you are unable to do so by yourself.

Your doctor may use different methods in order to limit the impact of the side effect or even fully resolve it. Possible recommendations that may come from your doctor have been included in the table below. If you are experiencing a side effect, communicate this immediately with your healthcare team, and discuss the different management options with your doctor before beginning any yourself.

DO NOT USE MANAGEMENT METHODS WITHOUT CONSULTING YOUR HEALTHCARE TEAM AND RECEIVING APPROVAL. This list is not inclusive of the different management methods your doctor may prescribe.

IF AT ANY TIME YOU ARE EXPERIENCING SEVERE SYMPTOMS OR SIDE EFFECTS, SEEK URGENT MEDICAL ATTENTION.

Side Effect	Management Methods
Mouth Sores and Sore Throat	<ul> <li>Stay hydrated and keep the tissues in your mouth and throat as moist as possible: clean teeth gently after each meal with a soft toothbrush, use lip moisturizer, avoid mouthwashes that contain alcohol; rinse mouth frequently with a salt and water combination;</li> <li>Eat softer, more digestible foods (less pain on swallowing and easier to digest): avoid citrus fruits, citrus juices and spicy foods.</li> </ul>
Diarrhea	<ul> <li>Diarrhea can cause dehydration. Therefore, to counter its effects, drink plenty of water and electrolytes; avoid milk products as they may worsen diarrhea;</li> <li>Take the medications your doctor recommends for controlling diarrhea.</li> </ul>
Constipation	<ul> <li>Set up a daily bowel care plan (keep track of bowel movements): over-the-counter products such as stool softeners or fiber supplements; eating more fiber-rich foods and increased fluids; avoiding foods that are more likely to cause gas or constipation. *Changes to diet or taking any laxatives or medication should involve a consultation with your healthcare team first;</li> <li>Eat at the same times each day, and try to move your bowels at the same time every day; go to the bathroom as soon there is an urge;</li> <li>Exercise to stimulate digestion and bowel movements.</li> </ul>
Nausea/Vomiting	<ul> <li>Adjust diet: consume mostly liquids for the first one to two days after your treatment (returning to solid foods once the feeling has subsided); avoid foods that are too hot, sweet or spicy; eat smaller meals more frequently;</li> <li>Get plenty of fresh air and try to avoid strong or unpleasant odours;</li> <li>If you do experience vomiting, be sure to stay hydrated with water and electrolytes;</li> <li>Take antiemetic/antinauseant medication before your treatment (if prescribed by your doctor).</li> </ul>
Change in Taste	<ul> <li>Keep your mouth fresh and clean; rinse mouth with a baking soda and water solution before you eat to taste foods better;</li> <li>Serve foods cold or at room temperature, this may help reduce tastes and smells to tolerate it better;</li> <li>Balance foods properly, i.e. if eating salty, try something sweet to balance the flavour.</li> </ul>
Loss of Appetite	<ul> <li>Avoid strong odours;</li> <li>Eat smaller, more frequent meals throughout the day;</li> <li>Certain foods may be more appealing than others, avoid unappealing food for a period of time and then gradually re-introduce;</li> <li>Continue to stay hydrated by consuming fluids (even if unappetizing) and eat healthy foods to stay strong.</li> </ul>
Hair Loss	<ul> <li>Pat your head dry rather than rubbing it vigorously with a towel;</li> <li>Avoid hair care: dryers, curling or straightening irons, dying hair;</li> <li>Wear a hat when exposed to the sun as areas of hair loss are very susceptible to sun damage.</li> </ul>
Fatigue	<ul> <li>Keep a diary to help you keep track of the times of day when you feel most tired, and adjust lifestyle or daily activities accordingly;</li> <li>Ask friends and family for help with daily tasks if needed;</li> <li>Exercise when you have the energy to do so and as long as your doctor approves; do not exercise late in the evening;</li> <li>Get the rest and sleep you need (i.e. take time off work). Try not to rest more than necessary, however, as this can sometimes make you feel even more tired;</li> <li>Avoid caffeine or other stimulants.</li> </ul>
Decreased Blood Cell Production	<ul> <li>Medication may be prescribed to normalize blood cell counts;</li> <li>Your doctor may pause your therapy or reduce the dose until your blood cell counts resolve.</li> <li>The treatment may be stopped if your blood cell counts cannot be resolved while on therapy.</li> </ul>
Skin Reactions	<ul> <li>Protect skin areas from further damage such as from the sun (limit exposure and wear sunscreen);</li> <li>Your doctor may prescribe an alcohol-free, fragrance-free lotion or cream to apply to the affected area;</li> <li>Your treatment may be paused or stopped if the skin reaction is severe at the time of treatment or shortly after treatment. You may be allergic to the treatment. Your doctor may prescribe medications (antihistamines) before treatment. If the allergic reaction continues, your doctor may alter your treatment course.</li> </ul>

Side Effect	Management Methods
Peripheral Neuropathy	<ul> <li>Medication may be prescribed by your doctor to help ease symptoms;</li> <li>Other treatments that may help to ease nerve pain include electrical nerve stimulation, occupational therapy, physical therapy, relaxation therapy, guided imagery, distraction, acupuncture, biofeedback. Speak with your doctor about these options;</li> <li>Avoid things that seem to make it worse, such as hot or cold temperatures, or snug clothes or shoes;</li> <li>Don't drink alcohol as it could cause nerve damage on its own and might make it worse;</li> <li>Talk to your doctor about whether it is safe for you to exercise;</li> <li>If the neuropathy is in a certain area of your body, try to limit your use of that area. For example if in your feet, sit down as much as possible, even while brushing your teeth or cooking.</li> </ul>
Chemo Brain (Cognitive problems)	<ul> <li>Exercise can improve your thinking and ability to focus. Speak with your doctor about an appropriate exercise plan;</li> <li>Meditation can help improve brain function by increasing your focus and awareness;</li> <li>Use a detailed daily planner, notebooks, reminder notes, or your smart phone to track your tasks as well as any memory problems you may have;</li> <li>Do the most demanding tasks at the time of the day when you feel your energy and focus levels are the highest;</li> <li>Exercise your brain. Take a class, do word puzzles, or learn a new language;</li> <li>Get enough rest and sleep;</li> <li>Eat healthily and avoid alcohol;</li> <li>Set up and follow routines. Try to keep the same daily schedule;</li> <li>Pick a certain place for commonly lost objects (like keys) and put them there each time. Try not to multi-task and focus on one thing at a time.</li> </ul>
Fertility/Sexual Health	<ul> <li>Don't assume your doctor or nurse will ask you about fertility and if it is important to you. You might need to start the conversation. Discussions are best performed prior to starting treatment.</li> <li>Collecting and freezing sperm, eggs, or embryos before treatment;</li> <li>Protecting a patient's reproductive organs during treatment (i.e. during radiation);</li> <li>Ask a member of your health care team to check your medications for possible side effects that could affect your fertility;</li> <li>Speak with your doctor about medical treatment if you are experiencing pain or fatigue as it relates to your sexual health;</li> <li>Ask for a referral to a sexual health therapist who specializes in treating cancer survivors.</li> </ul>
Fever	<ul> <li>If you start feeling warm or cold (chills), check your temperature every two to three hours and record temperature readings. If available, call your cancer care team if you have a fever. If your cancer care team is unavailable, neutropenic fever (fever accompanied by low white blood cell count) is considered a medical emergency; go to the emergency department to receive the care you need.</li> <li>Drink plenty of liquids (such as water, fruit juices, ice pops, and soups);</li> <li>Get enough rest;</li> <li>Use a cold compress on your forehead if you feel hot;</li> <li>Do not take medication to reduce your fever without asking your doctor.</li> </ul>
Hot Flashes/Sweating	<ul> <li>Your doctor may prescribe medications such as low doses of certain antidepressants and high blood pressure medications that may help control hot flashes. Hormone therapy or other vitamins, minerals, and other supplements may help with sweating and hot flashes;</li> <li>If recommended by your cancer team, you can get over-the-counter medications, such as fever reducers or mild pain relievers;</li> <li>Certain treatments such as massage, acupuncture, yoga, and cognitive behavioral interventions may help;</li> <li>Make lifestyle changes, such as increasing your physical activity, managing your weight, and avoiding alcohol and tobacco.</li> </ul>
Infusion and Immune Reactions	<ul> <li>You may be prescribed medications by your doctor to stop the reaction and help manage your symptoms;</li> <li>Your doctor may consider altering your treatment such as changing your treatment dose, holding your treatment until the symptoms resolve, or even permanently stopping the drug if your symptoms are severe.</li> </ul>

Side Effect	Management Methods
Lymphedema (swelling)	<ul> <li>Avoid over-using the affected area;</li> <li>Practice good skin care. When you have lymphedema, your risk of infection is higher. Keep your skin clean and dry and use moisturizers regularly to keep your skin from cracking. Protect your skin from the sun;</li> <li>If your limb starts to ache, lie down and raise it above the level of your heart to help drain some of the swelling;</li> <li>Regular exercise is a key part of lymphedema management. Talk with your doctor or therapist to learn what type of exercise program is right for you;</li> <li>Manual lymphatic drainage (MLD) is a type of massage that can help move the extra fluid to other parts of the body and decrease swelling;</li> <li>Complete decongestive therapy can involve different treatments (skin care, massage, compression bandaging, exercises, and elevating the affected part of the body) to lower fluid volume;</li> <li>Intermittent pneumatic compression is a type of compression that uses a device that fills with air and then deflates off and on (like a blood pressure cuff) to move the extra fluid out of the affected area;</li> <li>You may be fitted for compression garments to the affected area;</li> <li>Surgery may be used as a last resort if the lymphedema can't be controlled by other measures. Surgery can have its own complications.</li> </ul>
Shortness of Breath	<ul> <li>Monitor your breathing. If available, call your cancer care team if you suddenly experience shortness of breath without cause (i.e. exercise or physical activity). If your cancer care team is unavailable, shortness of breath (especially if accompanied by other concerning symptoms), may be considered a medical emergency. Go to the emergency department to receive the care you need.</li> <li>To help with the flow of breathing, sit up or raise your upper body to a 45° angle by raising the bed or using pillows;</li> <li>Your doctor may prescribe medications or treatments to help you with your breathing (i.e. oxygen, medicine for relief of wheezing, inhalers, or nebulizers);</li> <li>Perform pursed-lip breathing: Inhale deeply through your nose and exhale through pursed lips for twice as long as it took to inhale;</li> <li>Try muscle relaxation to reduce anxiety, as anxiety can make breathing problems worse.</li> </ul>
Sleep Problems	<ul> <li>Sleep as much as your body tells you to, but when you're awake, try to limit your nap time and try to exercise at least once a day. Talk to your health care team about an exercise plan;</li> <li>Avoid alcohol and caffeine and try warm, caffeine-free drinks before sleep. Limit the amount of liquid you consume before bed to prevent having to use the washroom frequently;</li> <li>Talk to your doctor about a referral to a sleep specialist, if needed;</li> <li>Try using different cognitive behavioral interventions that can help you relax physically and mentally (breathing exercises, meditation, mindfulness, music, hypnosis, or guided imagery);</li> <li>If you are diagnosed with restless legs syndrome (RLS), it might be managed with different treatment or therapy options (dietary supplements, exercises, medicine);</li> <li>If sleep apnea is diagnosed, a continuous positive airway pressure device (CPAP) mask may be prescribed;</li> <li>Review your list of medicines with your health care team as different medications, sleeping pills, or pain relievers can affect sleep. Take your medications at the same time every day.</li> </ul>
Change in Weight	<ul> <li>Weight Loss</li> <li>Quick weight loss can be a sign of dehydration, which can be serious. Weight loss of more than three pounds in a week should be reported to your doctor. Be sure to drink enough water and other liquids with nutrients and calories;</li> <li>Choose foods and snacks that are high in calories, nutrients and protein to increase weight;</li> <li>Ask your doctor for a referral to a dietitian or nutritionist to help you with your meal plans.</li> <li>Weight Gain</li> <li>Some may notice a weight gain if they have lymphedema, or, sometimes certain anti-cancer drugs cause your body to hold on to extra fluid. If this is the case, your doctor may recommend that you speak with a registered dietitian or nutritionist;</li> <li>Choose healthier, lower calorie foods (read food labels) and become more aware of portion sizes;</li> <li>Limit your salt intake to lower the amount of fluid you retain;</li> <li>Your doctor may recommend exercise programs or may refer you to a physical therapist.</li> </ul>

These are just some possible management techniques that your doctor may recommend. If you experience any symptoms or side effects during treatment or following treatment (even years following your cancer treatment into remission), contact your doctor immediately to report these issues and receive the care and support that you need.

### Track Your Side Effects

This side effect log can be used to track your symptoms or side effects that occur during treatment and following treatment. These should be reported to your doctor. Make sure you record your treating doctor's appropriate contact information.

#### **DOCTOR CONTACT INFORMATION AND TREATMENT HISTORY**

Name	
Phone number/email	
Hospital where you received treatment	
Type of treatment you received	
Date you started treatment	
Date you finished treatment	

#### SYMPTOM AND SIDE EFFECT TRACKER

Date	Symptom/ Side Effect	Severity			Severity Comments this to	Report your tor?	Recommended Treatment/ Care	Date Side Effect Stopped
		MILD	MODERATE	SEVERE	YES	NO		

### Glossary of Terms

#### **ACUTE KIDNEY INJURY (AKI)**

Acute kidney injury and electrolyte (essential minerals) disturbances can occur in patients receiving certain cancer treatments that are removed from the body through the kidney, causing damage to the kidney cells. This can lead to different problems including low urine output, swelling in the arms and legs, fatigue, shortness of breath, nausea, chest pain, and/or confusion.

#### **ALOPECIA (HAIR LOSS)**

Hair loss can occur with certain cancer treatments. These cancer treatments destroy all rapidly dividing cells which includes cancer cells, but unfortunately also includes healthy cells like hair cells.

#### **ANEMIA**

Anemia is a condition in which the number of red blood cells is below normal. This condition can cause different symptoms such as fatigue, shortness of breath, dizziness, headaches, a fast heartbeat, and/or cause your skin to turn pale.

#### ARTERIAL/VENOUS THROMBOEMBOLISM

Patients treated with certain therapies are at a higher risk of thromboembolism which is an obstruction of a blood vessel by a blood clot that has become dislodged from another area of circulation. A venous thromboembolism (VTE) can include deep vein thrombosis (blood clot forms in a deep vein, such as the lower leg) or pulmonary embolism (blood clot that traveled to the lung), while an arterial thromboembolism can include a heart attack and stroke; each has their own set of symptoms.

#### **CAPILLARY LEAK SYNDROME**

Capillary leak syndrome is a condition in which fluid leaks out of small blood vessels (capillaries) and flows into surrounding tissues, resulting in dangerously low blood pressure. This can also cause swelling of the arms and legs, sudden weight gain, and thickening of the blood.

#### **CATARACTS**

Cataracts are the clouding of the lens of your eye, which is normally clear. Most cataracts develop slowly over time, causing symptoms such as blurry vision.

#### CHEMO-BRAIN (ALSO REFERRED TO AS BRAIN FOG OR COGNITIVE IMPAIRMENT)

Chemo-brain is a problem with thinking and memory that can happen during or after cancer treatment. It is not known exactly what causes chemo-brain but is thought to be a side effect of cancer drugs that enter into the bloodstream and travel to the brain. Some symptoms can include difficulty with thinking, concentrating, or remembering things.

#### **CONSTIPATION**

Constipation is when you have infrequent bowel movements and stool that may be hard, dry, and difficult to pass. You may also experience stomach cramps, bloating, and nausea when you are constipated.

#### CYTOKINE RELEASE SYNDROME

Cytokine release syndrome is caused by a large, rapid release of cytokines (immune substances) into the blood from immune cells affected by the immunotherapy. High levels of cytokines can be harmful and cause inflammation throughout the body. Signs and symptoms of cytokine release syndrome include fever, nausea, headache, rash, rapid heartbeat, low blood pressure, and trouble breathing.

#### **CYTOMEGALOVIRUS (CMV)**

Cytomegalovirus is a type of virus that once infected with you will have for life. Most people will not know they have it. However, if your immune system is weakened, such as when receiving cancer treatment, the virus becomes active and symptoms can appear which may include fever, sore throat, fatigue and swollen glands. If left untreated, it can become severe and affect organ function.

#### **DIARRHEA**

Diarrhea means having bowel movements that are soft, loose, or watery more often than normal. This can cause you to become dehydrated or malnourished (loss of essential nutrients).

#### **GASTROINTESTINAL (GI) PERFORATION**

GI perforation can be caused by certain treatments that lead to severe bowel dilation (swelling) or weakening of the tissue that can cause it to tear or rip. This can cause symptoms including severe pain, nausea, vomiting, tenderness and infection. This can be serious and lead to further health complications.

#### **GLAUCOMA**

Glaucomas are a group of eye disorders that involve damage over time to the optic nerve (nerve fibers that carry visual messages to the brain from the eye). This damage is at least partly caused by increased pressure in the eye; this causes loss of vision.

#### **GRAFT-VERSUS-HOST DISEASE (GVHD)**

Graft-versus-host disease is a potentially serious complication following allogeneic stem cell transplantation. It occurs when the donor's cells (the graft) view the patient's healthy cells (the host) as foreign and attack and damage them. Symptoms can include skin irritation and redness, nausea/vomiting, jaundice (yellowing of the skin/eyes), shortness of breath or cough, weight loss, mucositis, and/or hair loss.

#### **HEPATITIS B**

Patients with past Hepatitis B Virus (HBV) infection receiving anticancer treatment may have a high risk of HBV reactivation. Symptoms can include yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting and abdominal pain.

#### **HYPOTENSION**

Hypotension is defined as lower than normal blood pressure readings and can cause symptoms such as fatigue, dizziness, nausea, rapid or irregular heart beat, fever, chills, or cause your skin to turn pale.

#### **HYPOXIA**

Hypoxia is when there is low oxygen in your tissues which can be caused by other side effects of cancer therapy such as lower lung capacity (i.e. tumor reduced the size of the lung), anemia (low number of red blood cells) and/or emotional distress (i.e. hyperventilation). Symptoms can include fatigue, confusion, changes in skin colour (blue tinge), rapid heartbeat or breathing, or wheezing.

#### INFUSION RELATED REACTION

Infusion related reactions are allergic reactions due to treatment. Symptoms can include itching, rash, wheezing and swelling. Your treatment may be slowed down or stopped until the symptoms go away.

#### INJECTION SITE REACTION

Injection site reactions are local skin reactions that can occur when the drug escapes the veins or catheter into the skin and can cause skin irritation symptoms such as tenderness, warmth, burning, redness or itchiness at the site of injection.

#### **MUCOSITIS**

Mucositis occurs when cancer treatments break down the rapidly dividing cells lining the gastrointestinal tract (which goes from the mouth to the anus). This leaves the tissue open to sores and infection. Symptoms can include swollen mouth/gums, sores or ulcers, pain, difficulty swallowing/talking, dryness, and changes to saliva.

#### **MUCOUS MEMBRANE REACTION**

Hypersensitivity reactions in and around the mouth may produce a wide range of signs and symptoms including redness or whiteness in and around the mouth, swelling of the lips, tongue and cheeks, and/or ulcers and blisters.

#### **NEUROPATHY**

Some chemotherapy drugs and other treatments for cancer can cause damage to peripheral nerves causing neuropathy, which is a set of symptoms caused by damage to nerves that control the sensations and movements of our arms, legs, hands, and feet. This may include numbness, tingling, pain, weakness, spasms or twitches.

#### **NEUTROPENIA**

Neutropenia is a condition in which there is a lower than normal number of neutrophils, a type of white blood cell that helps to fight infections. This condition can lead to more frequent or serious infections as well as a number of symptoms such as fever, sore throat, rash, diarrhea, and redness or swelling around a wound.

Febrile neutropenia is when you experience a fever alongside neutropenia and this is considered a medical emergency that requires immediate care.

#### **OSTEOPOROSIS**

Osteoporosis can develop when the body breaks down more bone tissue than it can replace, and the bones become weak and fragile. It can be caused by certain cancer treatments and may be a late treatment-related side effect.

#### PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Progressive multifocal leukoencephalopathy is caused by a virus that is normally unreactive in the body until the immune system becomes weakened, such as with cancer treatment. Symptoms can include limb weakness, visual loss, and/or cognitive or behaviour changes.

#### **SECONDARY CANCER**

A secondary cancer is a new cancer, which is different from the lymphoma or CLL you were initially treated for, and develops after treatment for lymphoma.

#### **SEPSIS**

Sepsis is the body's extreme response to an infection. When you experience an infection, your immune system responds by releasing cells and molecules to fight it. However, if this immune response gets out of control, it can cause extensive inflammation (sepsis). This can be life-threatening and cause organs to function poorly or abnormally. Sepsis can cause a rapid heart rate, fatigue, difficulty breathing among other symptoms, and requires medical treatment.

#### **THROMBOCYTOPENIA**

Thrombocytopenia is a condition where the number of platelets, cells that are involved in blood clotting, are below normal. This condition can cause symptoms such as increased bruising and excessive bleeding from cuts or nosebleeds.

#### **TUMOR LYSIS SYNDROME (TLS)**

Tumour lysis syndrome can result from cancer treatment, where the anticancer drug causes a quick death of a large number of cancer cells. This makes the cells break down and enter the bloodstream where they can change the blood's chemistry. This can result in serious complications such as kidney failure, irregular heartbeat, and stroke.



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