

CISPPEME Treatment

This handout gives general information about this cancer treatment.

You will learn:

- who to contact for help
- what the treatment is
- how it is given
- what to expect while on treatment



This handout was created by Ontario Health (Cancer Care Ontario) together with patients and their caregivers who have also gone through cancer treatment. It is meant to help support you through your cancer treatment and answer some of your questions.

This information does not replace the advice of your health care team. Always talk to your health care team about your treatment.

Who do I contact if I have questions or need help?

My cancer health care provider is: _____

During the day I should contact: _____

Evenings, weekends and holidays: _____

What is this treatment?

CISPPEME is the code name of your lung or digestive tract cancer treatment regimen.

A regimen is a combination of medications to treat cancer.

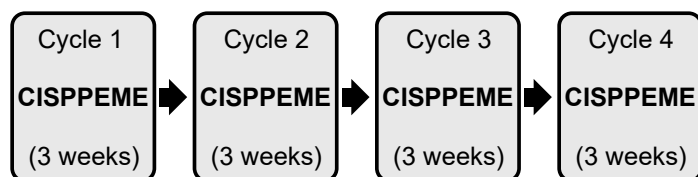
This regimen name is made up of one or more letters from the names of the 2 medications in your treatment.

Here are the names of the medications in this regimen:

CISP = CISPlatin
PEME = PEMEtrexed

For most people, treatment lasts **12 weeks**. The treatment is divided into **4 cycles**. Each cycle is **3 weeks** long.

Here is a picture of the schedule for CISPPEME treatment:



After 4 cycles, your health care team will talk to you about how your treatment is going and plan next steps. Some people may need to have more than 4 cycles to treat their cancer.

During each 3-week cycle, you will have CISPPEME treatment on day 1 at the hospital.

Each cycle looks like this:

Day 1 Treatment Day: Go to the hospital for CISPPEME Treatment.	2 No CISPPEME Treatment	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21



Remember To:

- ✓ Tell your health care team about all of the other medications you are taking.
- ✓ Keep taking other medications that have been prescribed for you, unless you have been told not to by your health care team.

How is this treatment given?

The medications in your treatment are given through an IV (injected into a vein) at the hospital.

You will have a blood test before each treatment cycle to make sure it is safe for you to get treatment.

What other medications are given with this treatment?

To Prevent Nausea and Vomiting

You will be given medications to help prevent nausea (feeling like throwing up) and vomiting (throwing up) before they start.

- These are called anti-nausea medications and include medications such as ondansetron (Zofran®), granisetron (Kytril®), aprepitant (Emend®), olanzapine (Zyprexa®) or others.

To Prevent Skin Rash

You will be given a medication to take starting the day before each CISPPEME treatment cycle to prevent skin rashes.

- The medication is a corticosteroid such as dexamethasone.

To Protect Healthy Cells and Lower Your Chance of Side Effects

- You will be given a prescription for folic acid tablets to take by mouth and vitamin B12 that will be given by a needle.
- You will start taking your folic acid and receive vitamin B12 at least 7 days before your first CISPPEME treatment.
- Keep taking them during treatment and for at least 21 days after your last CISPPEME treatment.
- Talk to your health care team about exactly how to take these medications.

DO this while on treatment

- ✓ DO tell your health care team about any other medical conditions that you have or had such as hearing problems, heart, liver or kidney problems, serious infections, low salt levels in the blood or any allergies.
- ✓ DO check with your health care team before getting any vaccinations, surgery, dental work or other medical procedures or if you have had previous radiation therapy.
- ✓ DO talk to your health care team about your risk of getting other cancers and heart problems after this treatment.
- ✓ DO drink plenty of fluids (unless told differently) to prevent kidney problems. Drink at least 6 to 8 cups (2 Litres) of water or other liquids per day on your treatment day and for 1-2 days afterwards, unless your healthcare team has told you to drink more or less.
- ✓ DO tell your health care team if you have any new pain, numbness or tingling of your hands or feet. This is especially important if you are having trouble doing tasks (like doing up buttons, writing, walking) or if you have severe pain or numbness.
- ✓ DO tell your health care team if you have any changes to your hearing such as not being able to hear as well as before, hearing new noise or ringing sounds in your ears.

DO NOT do this while on treatment



- ✗ DO NOT take any other medications, such as vitamins, over-the-counter (non-prescription) drugs, or natural health products without checking with your health care team.
- ✗ DO NOT start any complementary or alternative therapies, such as acupuncture or homeopathic medications, without checking with your health care team.
- ✗ DO NOT take anti-inflammatory medications (such as ibuprofen (Advil® or Motrin®), naproxen (Aleve®) or Aspirin® for 5 days before and 2 days after your CISPPEME treatment. They can make your side effects worse.
- ✗ DO NOT smoke or drink alcohol while on treatment without talking to your health care team first. Smoking and drinking can make side effects worse and make your treatment not work as well.

Will this treatment interact with other medications or natural health products?

Yes, the medications in this regimen can interact with other medications, vitamins, foods and natural health products. Interactions can make the treatment not work as well or cause severe side effects.

Tell your health care team about all of your:

- prescription and over-the-counter (non-prescription) medications
- natural health products such as vitamins, herbal teas, homeopathic medicines, and other supplements

Check with your health care team before starting or stopping any of them.

- If you take anti-inflammatory medications such as ibuprofen (Advil® or Motrin®) or naproxen (Aleve®) or Aspirin®, your health care team will ask you to stop taking them for at least 5 days before and 2 days after your CISPPEME treatment day.
- If you take seizure medications (such as phenytoin), your health care team may monitor your blood levels closely and may change your dose.



Talk to your health care team **BEFORE** taking or using these:

- Over-the-counter products such as dimenhydrinate (Gravol®)
- Natural health products such as St. John's Wort
- Supplements such as vitamin C
- Grapefruit juice
- Alcoholic drinks
- Tobacco
- All other drugs, such as marijuana or cannabis (medical or recreational)

What should I do if I feel unwell, have pain, a headache or a fever?

- ✓ **Always** check your temperature to see if you have a fever **before** taking any medications for fever or pain (such as acetaminophen (Tylenol®)).
 - Fever can be a sign of infection that may need treatment right away.
 - If you take these medications before you check for fever, they may lower your temperature and you may not know you have an infection.

How to check for fever:

Keep a digital (electronic) thermometer at home and take your temperature if you feel hot or unwell (for example, chills, headache, mild pain).

- You have a fever if your temperature taken **in your mouth (oral temperature)** is:
 - 38.3°C (100.9°F) or higher at any time
- OR
- 38.0°C (100.4°F) or higher for at least one hour.



If you do have a fever:

- ✓ **Try to contact your health care team. If you are not able to talk to them for advice, you MUST get emergency medical help right away.**
- ✓ Ask your health care team for the [Fever](#) pamphlet for more information.

If you do not have a fever but have mild symptoms such as headache or mild pain:

- ✓ Ask your health care team about the right medication for you. **Acetaminophen (Tylenol®)** is a safe choice for most people.



DO NOT take ibuprofen (Advil®, Motrin®), naproxen (Aleve®) or ASA (Aspirin®), as they may increase your chance of bleeding and can make side effects worse.



Talk to your health care team if you already take **low dose aspirin** for a medical condition (such as a heart problem). It may still be safe to take.

How will this treatment affect sex, pregnancy and breast feeding?

Talk to your health care team about:

- How this treatment may affect your sexual health
- How this treatment may affect your ability to have a baby, if this applies to you. CISPPEME treatment may affect your ability to make healthy sperm.

This treatment may harm an unborn baby. Tell your health care team if you or your partner are pregnant, become pregnant during treatment, or are breastfeeding.

- If there is **any** chance of pregnancy happening, you and your partner together must use **2 effective forms of birth control** at the same time while you are on treatment. Talk to your health care team about which birth control options are best for you, and how long you should use them after your last treatment dose.
- Do not donate sperm while on CISPPEME treatment. Talk to your health care team about how long to wait before you can donate sperm after your last treatment dose.
- Do not breastfeed while on this treatment. Talk to your health care team about how long to wait before you start breastfeeding after your last treatment dose, if this applies to you.

What are the side effects of this treatment?

The following table lists side effects that you may have when getting CISPPEME treatment. The table is set up to list the most common side effects first and the least common last. It is unlikely that you will have all of the side effects listed and you may have some that are not listed.

Read over the side effect table so that you know what to look for and when to get help. Refer to this table if you experience any side effects while on CISPPEME treatment.

Very Common Side Effects (50 or more out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Nausea and vomiting</p> <p>(May be severe)</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Nausea is feeling like you need to throw up. You may also feel light-headed. • You may feel nausea within hours to days after your treatment. <p>What to do?</p> <p>To help prevent nausea:</p> <ul style="list-style-type: none"> • It is easier to prevent nausea than to treat it once it happens. • If you were given anti-nausea medication(s), take them as prescribed, even if you do not feel like throwing up. • Drink clear liquids and have small meals. Get fresh air and rest. • Do not eat spicy, fried foods or foods with a strong smell. • Limit caffeine (like coffee, tea) and avoid alcohol. <p>If you have nausea or vomiting:</p> <ul style="list-style-type: none"> • Take your rescue (as-needed) anti-nausea medication(s) as prescribed. • Ask your health care team for the Nausea & Vomiting pamphlet for more information. • Talk to your health care team if: <ul style="list-style-type: none"> ◦ nausea lasts more than 48 hours ◦ vomiting lasts more than 24 hours or if it is severe 	<p>Talk to your healthcare team if nausea lasts more than 48 hours or vomiting lasts more than 24 hours or if it is severe</p>

Common Side Effects (25 to 49 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Neuropathy (Tingling, numb toes or fingers)</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Numbness or tingling of your fingers and toes may happen after starting your treatment. • It can also happen to other parts of your body. • Sometimes it can be painful and feel like a burning sensation, which may be severe. <p>What to do?</p> <ul style="list-style-type: none"> • Talk to your health care team if you have symptoms of neuropathy. • Numbness and tingling may slowly get better after your treatment ends. <p>In rare cases, it may continue long after treatment ends. If you continue to have bothersome symptoms, talk to your health care team for advice.</p>	<p>Talk to your health care team, especially if you have trouble doing tasks like doing up buttons, writing, moving, or if you have severe pain or numbness</p>
<p>Kidney problems</p> <p>(May be severe)</p> <p>Your health care team may check for proteins in your urine (pee) and your kidney function regularly with a blood test. You may have blood in your urine.</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Swelling in your hands, ankles, feet or other areas of your body. • Weight gain that is not normal for you. • Pain in your lower back. • Muscle twitches and cramps or itchiness that won't go away. • Nausea (feeling like you need to throw up) and vomiting. • Changes in urination (peeing) such as less urine than usual. <p>What to do?</p> <ul style="list-style-type: none"> • If you have any of these signs, talk to your health care team or go to your closest emergency department. 	<p>Get emergency medical help right away</p>

Common Side Effects (25 to 49 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>To prevent kidney infections:</p> <ul style="list-style-type: none"> • Drink at least 6 to 8 cups (2 litres) of water or other liquids per day unless your health care team has told you to drink more or less. • When you feel the need to pee, go as soon as possible. Do not wait or hold in the pee. 	
<p>Fatigue</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Feeling of tiredness or low energy that lasts a long time and does not go away with rest or sleep. <p>What to do?</p> <ul style="list-style-type: none"> • Be active. Aim to get 30 minutes of moderate exercise (you are able to talk comfortably while exercising) on most days. • Check with your health care team before starting any new exercise. • Pace yourself, do not rush. Put off less important activities. Rest when you need to. • Ask family or friends to help you with things like housework, shopping, and child or pet care. • Eat well and drink at least 6 to 8 glasses of water or other liquids every day (unless your health care team has told you to drink more or less). • Avoid driving or using machinery if you are feeling tired. <p>Ask your health care team for the Fatigue pamphlet for more information.</p>	<p>Talk to your health care team if it does not improve or if it is severe</p>

Common Side Effects (25 to 49 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Too much or too little salt in your body</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Muscle spasms, cramping, weakness, twitching, or convulsions. • Irregular heartbeat, confusion or blood pressure changes. <p>What to do?</p> <p>Get emergency medical help right away for severe symptoms.</p>	<p>Get emergency medical help right away for severe symptoms</p>
<p>Change in your hearing</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Not being able to hear as well as before. • New noise or ringing sounds in your ears. • Changes in hearing usually go away over time. In some rare cases they may be permanent. <p>What to do?</p> <ul style="list-style-type: none"> • Tell your health care team if you have any of these symptoms. Your health care team may need to change your medication. 	<p>Talk to your health care team as soon as possible</p>

Common Side Effects (25 to 49 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Low neutrophils (white blood cells) in the blood (neutropenia)</p> <p>(May be severe)</p> <p>When neutrophils are low, you are at risk of getting an infection more easily. Ask your health care team for the Neutropenia (Low white blood cell count) pamphlet for more information.</p> <p>What to look for?</p> <ul style="list-style-type: none"> • If you feel hot or unwell (for example if you have chills or a new cough), you must check your temperature to see if you have a fever. • Do not take medications that treat a fever before you take your temperature (for example, Tylenol® (acetaminophen)). • Do not eat or drink anything hot or cold right before taking your temperature. <p>You have a fever if your temperature taken in your mouth (oral temperature) is:</p> <ul style="list-style-type: none"> • 38.3°C (100.9°F) or higher at any time OR • 38.0°C (100.4°F) or higher for at least one hour. <p>What to do?</p> <p>If your health care team has told you that you have low neutrophils:</p> <ul style="list-style-type: none"> • Wash your hands often to prevent infection. • Check with your health care team before getting any vaccines, surgeries, medical procedures or visiting your dentist. • Keep a digital thermometer at home so you can easily check for a fever. <p>If you have a fever:</p> <p>If you have a fever, try to contact your health care team. If you are unable to talk to the team for advice, you must get emergency medical help right away.</p>	<p>If you have a fever, try to contact your health care team. If you are unable to talk to the team for advice, you MUST get emergency medical help right away.</p>

Common Side Effects (25 to 49 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Low platelets in the blood</p> <p>(May be severe)</p> <p>When your platelets are low, you are at risk for bleeding and bruising. Ask your health care team for the Low Platelet Count pamphlet for more information.</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Watch for signs of bleeding: <ul style="list-style-type: none"> ◦ bleeding from your gums ◦ unusual or heavy nosebleeds ◦ bruising easily or more than normal ◦ black coloured stools (poo) or blood in your stools (poo) ◦ coughing up red or brown coloured mucus ◦ dizziness, constant headache or changes in your vision ◦ heavy vaginal bleeding ◦ red or pink coloured urine (pee) <p>What to do?</p> <p>If your health care team has told you that you have low platelets:</p> <ul style="list-style-type: none"> • Tell your pharmacist that your platelet count may be low before taking any prescriptions or over-the-counter medication. • Check with your healthcare team before you go to the dentist. • Take care of your mouth and use a soft toothbrush. • Try to prevent cuts and bruises. • Ask your health care team what activities are safe for you. • Your treatment may have to be delayed if you have low platelets. Your health care team may recommend a blood transfusion. <p>If you have signs of bleeding:</p> <ul style="list-style-type: none"> • If you have a small bleed, clean the area with soap and water or a saline (saltwater) rinse. Apply pressure for at least 10 minutes. <p>If you have bleeding that does not stop or is severe (very heavy), you must get emergency medical help right away.</p>	<p>Talk to your health care team if you have any signs of bleeding. If you have bleeding that doesn't stop or is severe (very heavy), you MUST get emergency help right away.</p>

Less Common Side Effects (10 to 24 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Low appetite</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Loss of interest in food or not feeling hungry. • Weight loss. <p>What to do?</p> <ul style="list-style-type: none"> • Try to eat your favourite foods. • Eat small meals throughout the day. • You may need to take meal supplements to help keep your weight up. • Talk to your health care team if you have no appetite. <p>Ask your health care team for the Loss of Appetite pamphlet for more information.</p>	<p>Talk to your health care team if it does not improve or if it is severe</p>
<p>Mouth sores</p> <p>(May be severe)</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Round, painful, white or gray sores inside your mouth that can occur on the tongue, lips, gums, or inside your cheeks. • In more severe cases they may make it hard to swallow, eat or brush your teeth. • They may last for 3 days or longer. <p>What to do?</p> <p>To help prevent mouth sores:</p> <ul style="list-style-type: none"> • Take care of your mouth by gently brushing and flossing regularly. • Rinse your mouth often with a homemade mouthwash. • To make a homemade mouthwash, mix 1 teaspoonful of baking soda and 1 teaspoonful of salt in 4 cups (1L) of water. • Do not use store-bought mouthwashes, especially those with alcohol, because they may irritate your mouth. 	<p>Talk to your health care team as soon as you notice mouth or lip sores or if it hurts to eat, drink or swallow</p>

Less Common Side Effects (10 to 24 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>If you have mouth sores:</p> <ul style="list-style-type: none"> • Avoid hot, spicy, acidic, hard or crunchy foods. • Your doctor may prescribe a special mouthwash to relieve mouth sores and prevent infection. • Talk to your health care team as soon as you notice mouth or lip sores or if it hurts to eat, drink or swallow. <p>Ask your health care team for the Oral Care (Mouth Care) pamphlet for more information.</p>	
<p>Rash; dry, itchy skin</p> <p>(May be severe)</p> <p>What to look for?</p> <ul style="list-style-type: none"> • You may have cracked, rough, flaking or peeling areas of the skin. • Your skin may look red and feel warm, like a sunburn. • Your skin may itch, burn, sting or feel very tender when touched. • The rash may be seen in areas where you have had radiation before. <p>What to do?</p> <p>To prevent and treat dry skin:</p> <ul style="list-style-type: none"> • Use fragrance-free skin moisturizer. • Protect your skin from the sun and the cold. • Use sunscreen with UVA and UVB protection and a SPF of at least 30. • Avoid perfumed products and lotions that contain alcohol. • Drink 6 to 8 cups of non-alcoholic, non-caffeinated liquids each day, unless your health care team has told you to drink more or less. <p>Rash may be severe in some rare cases and cause your skin to blister or peel. If this happens, get emergency medical help right away.</p>	<p>Talk to your health care team if it does not improve or if it is severe</p>

Less Common Side Effects (10 to 24 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Diarrhea</p> <p>(May be severe)</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Loose, watery, unformed stool (poo) that may happen days to weeks after you get your treatment. <p>What to do?</p> <p>If you have diarrhea:</p> <ul style="list-style-type: none"> • Take anti-diarrhea medication if your health care team prescribed it or told you to take it. • Do not eat foods or drinks with artificial sweetener (like chewing gum or 'diet' drinks), coffee and alcohol. • Eat many small meals and snacks instead of 2 or 3 large meals. • Drink at least 6 to 8 cups of liquids each day, unless your health care team has told you to drink more or less. • Talk to your health care team if you can't drink 6 to 8 cups of liquids each day when you have diarrhea. You may need to drink special liquids with salt and sugar, called Oral Rehydration Therapy. • Talk to your health care team if your diarrhea does not improve after 24 hours of taking diarrhea medication or if you have diarrhea more than 7 times in one day. <p>Ask your health care team for the Diarrhea pamphlet for more information.</p>	<p>Talk to your health care team if no improvement after 24 hours of taking diarrhea medication or if severe (more than 7 times in one day)</p>

Less Common Side Effects (10 to 24 out of 100 people)	
Side effects and what to do	When to contact health care team
<p>Liver problems</p> <p>(May be severe)</p> <p>Your health care team may check your liver function with a blood test. Liver changes do not usually cause any symptoms.</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Rarely, you may develop yellowish skin or eyes, unusually dark pee or pain on the right side of your belly. This may be severe. <p>What to do?</p> <p>If you have any symptoms of liver problems, get emergency medical help right away.</p>	<p>Get emergency medical help right away</p>

Below are more side effects that are possible with your treatment. It is not known how common they are.

Side effects and what to do	When to contact health care team
<p>Hair thinning or loss (mild)</p> <p>What to look for?</p> <ul style="list-style-type: none"> • Your hair may become thin or fall out during or after treatment. • In most cases, your hair will grow back after treatment. The texture or colour may change. • In very rare cases, hair loss may be permanent. <p>What to do?</p> <ul style="list-style-type: none"> • Use a gentle soft brush. • Do not use hair sprays, bleaches, dyes and perms. 	<p>Talk to your health care team if this bothers you</p>
<p>Mild joint, muscle pain or cramps</p> <p>What to look for?</p> <ul style="list-style-type: none"> • New pain in your muscles or joints, muscle cramps, or feeling achy. <p>What to do?</p> <ul style="list-style-type: none"> • Take pain medication (acetaminophen or opioids such as codeine, morphine, hydromorphone, oxycodone) as prescribed. • Read the above section: "What should I do if I feel unwell, have pain, a headache or a fever?" before taking acetaminophen (Tylenol®), ibuprofen (Advil®, Motrin®), naproxen (Aleve®) or Aspirin. These medications may hide an infection that needs treatment or they may increase your risk of bleeding. • Rest often and try light exercise (such as walking) as it may help. <p>Ask your health care team for the Pain pamphlet for more information.</p>	<p>Talk to your health care team if it does not improve or if it is severe</p>

Side effects and what to do	When to contact health care team
<p>Hiccups</p> <p>What to look for?</p> <ul style="list-style-type: none"> You may feel a slight tightening sensation in your chest, abdomen or throat and make a “hic” sound <p>What to do?</p> <p>To help prevent hiccups:</p> <ul style="list-style-type: none"> Drink clear fluids and avoid large meals. 	<p>Talk to your health care team if it does not improve or if it is severe</p>
<p>Taste changes</p> <p>What to look for?</p> <ul style="list-style-type: none"> Food and drinks may taste different than usual. <p>What to do?</p> <ul style="list-style-type: none"> Eat foods that are easy to chew, such as scrambled eggs, pasta, soups, cooked vegetables. Taste foods at different temperatures, since the flavour may change. Try different forms of foods, like fresh, frozen or canned. Experiment with non-spicy foods, spices and seasonings. 	<p>Talk to your health care team if it does not improve or if it is severe</p>

Other rare, but serious side effects are possible with this treatment.

If you have **any** of the following, talk to your cancer health care team or get emergency medical help right away:

- Seizures, confusion, trouble speaking, difficulty moving your arms or legs, balancing yourself or weakness on one side of your body
- Chest pain, irregular heartbeat or fainting (passing out)
- Pain, swelling or hardening of a vein in your arm or leg
- New coughing, or coughing up blood
- New shortness of breath or other breathing problems
- Unusual weight gain
- Sudden, severe pain in your belly
- Personality changes, memory problems
- Any changes to your vision
- Signs of allergic reaction: fever, rash, swollen face, lip or tongue, chest or throat tightness. It may happen during or shortly after the treatment is given to you.

- Red or purple patches on the skin, rash/patches that do not turn white when pressed
- Red, itchy, bruised, and/or swollen skin where the injection was given
- Red-brown coloured pee, severe tiredness or weakness, bruising easily
- Coldness in your fingers or toes and/or white patches on them (especially when in cold temperatures)

For more information on how to manage your symptoms ask your health care provider, or visit: <https://www.cancercareontario.ca/symptoms>.

Notes

November 2023 Updated "How will this treatment affect sex, pregnancy and breast feeding" section

For more links on how to manage your symptoms go to www.cancercareontario.ca/symptoms.

The information set out in the medication information sheets, regimen information sheets, and symptom management information (for patients) contained in the Drug Formulary (the "Formulary") is intended to be used by health professionals and patients for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or side effects of a certain drug, nor should it be used to indicate that use of a particular drug is safe, appropriate or effective for a given condition.

A patient should always consult a healthcare provider if he/she has any questions regarding the information set out in the Formulary. The information in the Formulary is not intended to act as or replace medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.