

INTRAVENOUS CANCER TREATMENT EDUCATION



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PEMBROLIZUMAB + EPIRUBICIN + CYCLOPHOSPHAMIDE

Name of the regimen and cancer drugs

Your care team may refer to your treatment as pembrolizumab, epirubicin, and cyclophosphamide regimen. This regimen is neoadjuvant phase 2 of a multi-step treatment regimen. Pembrolizumab, epirubicin, and cyclophosphamide (neoadjuvant phase 2) consists of 3 different anti-cancer therapies:

- Pembrolizumab (pem-broh-LIH-zoo-mab): Keytruda™
- Epirubicin hydrochloride (EH-pih-ROO-bih-sin HY-droh-KLOR-ide): Ellence™
- Cyclophosphamide (SY-kloh-FOS-fuh-mide): Cytosan™

Common uses

This regimen is most commonly used for the treatment of breast cancer but may be used for other diagnoses.

Treatment schedule

Your treatment will be given into your vein through an intravenous (IV) line. This may be into a short, flexible temporary catheter in your arm, or through a central venous catheter. A central venous catheter, or central line is a long, flexible IV tube that empties into a very large vein next to the heart. Talk with your care team to see which will be best for you and your treatment.

Each pembrolizumab, epirubicin, and cyclophosphamide treatment is repeated every 21 days. This is known as one cycle. Your treatment may be given for a set number of cycles, typically four (4). This regimen is given sequentially following four (4) cycles of pembrolizumab, paclitaxel, and carboplatin. Pembrolizumab may be continued as maintenance therapy for up to 9 cycles following surgery.

- Pembrolizumab IV given on day 1
- Epirubicin IV given on day 1
- Cyclophosphamide IV given on day 1

Drug	Cycle 1	Day 1	2	3	4	5	6	7	8	...	21	Cycle 2 Day 1
Pembrolizumab		■	■									■
Epirubicin		■										■
Cyclophosphamide		■										■

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Other medications

Other medications may be ordered for you to prevent or treat certain side effects. These include:

	Instructions:
Growth factors	<p>Growth factors, like filgrastim, pegfilgrastim, and others, are medications used to treat neutropenia and prevent infections. Neutropenia is a condition where there are lower-than-normal white blood cells caused by some type of chemotherapy. Growth factors help the bone marrow to make more white blood cells.</p> <hr/> <hr/> <hr/> <hr/>
Anti-nausea medications	<p>You will receive medications to prevent nausea just before your cancer treatment. You may also get prescriptions for other medications to take at home, as below:</p> <hr/> <hr/> <hr/> <hr/>

Possible drug interactions

- This regimen may interact with other drugs you are taking. Please inform your care providers of all prescription medicine, over-the-counter medications, vitamins, and herbal products that you take.
- Discuss with your care provider or pharmacy prior to taking steroid medications such as prednisone, methylprednisolone (Medrol), dexamethasone (Decadron), or hydrocortisone.
- Talk with your care provider or pharmacist before taking new medications, supplements, or receiving any vaccines.

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Common Side Effects

Common side effects that have been known to happen in patients receiving this regimen are listed in the left side of this table. In some instances, the side effects may be reported less often but are still important to discuss. This table does not list all the known side effects for this therapy, only the ones that are experienced most often. Not every patient experiences every known side effect of a drug; even if you are taking the same drug as another patient, you may experience different side effects. Options to help manage any side effects that do occur are included on the right side of this table. These should be discussed with your care provider. If you experience any side effect you cannot manage or that is not listed here, contact your care provider.

Possible Side Effect	Management
<p>Decreased white blood cells (WBCs) and increased risk for infection</p>	<p>Your WBCs should be monitored by a simple blood test. When your WBCs are low, you are at a greater risk of having an infection. Take the following precautions to protect yourself from infection.</p> <ul style="list-style-type: none"> • Wash your hands often, especially before eating and after using the bathroom. • Avoid crowds and people with fevers, flu, or other infection. • Bathe often for good personal hygiene. <p>Contact your care team if you experience any signs or symptoms of an infection such as:</p> <ul style="list-style-type: none"> • Fever (temperature more than 100.4°F or 38°C) • Chills • Sore throat • Burning when peeing • Tiredness that is worse than normal • A sore that becomes red, is draining, or does not heal. <p>Check with your care team before taking any medicine for a fever or chills.</p>
<p>Decreased hemoglobin, part of the red blood cells that carry iron and oxygen</p>	<p>Your hemoglobin should be checked by a simple blood test. When your hemoglobin is low, you may notice that you get tired or fatigued more easily.</p> <ul style="list-style-type: none"> • Try to get 7 to 8 hours of sleep per night • Avoid operating heavy machinery if you feel too tired • Find a balance between “work” and “rest” • Stay as active as possible, but know that it is okay to rest as needed, too • You might notice that you are more pale than usual <p>Let your care team know right away if you have:</p> <ul style="list-style-type: none"> • Shortness of breath • Dizziness • Fast or abnormal heartbeat

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Possible Side Effect	Management
<p>Nausea or vomiting</p>	<ul style="list-style-type: none"> • Take all medications as prescribed to help prevent and lessen symptoms of nausea and vomiting. • Eat and drink slowly. • Drink 8-10 (8-ounce) glasses of water and/or fluid (soup or broth) each day unless your care team has instructed you to limit your fluid intake. • Eat small, frequent meals throughout the day rather than a few large meals. • Eat bland foods; avoid spicy, fried, and greasy foods. • Avoid intense exercise immediately after eating. • Don't lay down right away after eating. • Wear loose-fitting clothing for comfort. • Avoid strong odors. Consider getting fresh air and try deep breathing. <p>Let your care team know if you have nausea or vomiting. Your care team may prescribe medication to help with the symptoms.</p>
<p>Diarrhea (loose and/or urgent bowel movements)</p>	<p>Monitor how many bowel movements you have each day.</p> <ul style="list-style-type: none"> • Drink 8-10 (8-ounce) glasses of water or fluid each day unless your care team has asked you to limit your fluid intake. • Eat small, frequent meals throughout the day rather than a few large meals. • Eat bland, low-fiber foods (such as bananas, applesauce, potatoes, chicken, rice, and toast). • Avoid high fiber foods, such as raw vegetables and fruits and whole grains. • Avoid foods that cause gas, such as broccoli and beans. • Avoid foods with lactose, such as yogurt and milk. • Avoid spicy, fried, and greasy foods. <p>Contact your care team if:</p> <ul style="list-style-type: none"> • The number of bowel movements you have in a day increases by 4 or more. • You feel dizzy or lightheaded. <p>Your care team may recommend an over-the-counter medication or prescribe something to help manage your symptoms.</p>

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Possible Side Effect	Management
<p>Constipation</p>	<p>Keep track of how often you have a bowel movement</p> <ul style="list-style-type: none"> • Drink 8-10 (8-ounce) glasses of water or fluid each day unless your care team has asked you to limit your fluid intake • Stay active and exercise, if possible • Eat foods high in fiber like raw fruits and vegetables <p>Contact your care team if you have not had a bowel movement in 3 or more days</p> <p>Your care team may recommend over-the-counter medications to help with constipation. A daily stool softener such as docusate (Colace®) and/or laxative such as senna (Senakot®) may be helpful. If these do not help within 48 hours, tell your care team.</p>
<p>Hair loss (alopecia)</p>	<ul style="list-style-type: none"> • Hair will likely grow back after treatment is completed, although the color and/or texture may be different. • It may take 3 to 6 months after therapy is completed to resume normal hair growth. • Some people choose to wear scarves, caps, or wigs. A short haircut prior to treatment may help with stress of hair loss. • Partial or complete hair loss is likely, usually 1-2 weeks after start of therapy. This hair loss can be all body hair. • Be sure to keep your head covered to protect it from the sun during the summer and cold during the winter. • If not covering your scalp during the summer months, be sure to use sunscreen when spending time outdoors.
<p>Fatigue</p>	<ul style="list-style-type: none"> • You may be more tired than usual or have less energy • Stay as active as possible, but know it is okay to rest as needed • Try to do some type of moderate activity every day • Conserve your energy. Plan your activities and do them at a time of day when you feel a bit more energetic • Follow a healthy diet and stay hydrated • Accept help from family and friends • Find healthy ways to manage stress, such as meditation, journaling, yoga, and guided imagery • Develop good sleeping habits, limit napping during the day to help you sleep better at night • Avoid operating heavy machinery if you feel too tired • Contact your care team if you experience extreme fatigue that prevents you from doing your normal daily activities
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Possible Side Effect	Management
Changes in liver function	<p>Your liver function will be checked regularly by a simple blood test. Contact your care team if you notice any of the following:</p> <ul style="list-style-type: none"> • Yellowing of the skin or whites of your eyes • Dark or brown urine • Bleeding or bruising
Rash or itchy skin	<ul style="list-style-type: none"> • Keep your skin moisturized with creams and moisturizing lotions to decrease the risk of rash or itchiness and wear loose fitting clothing. • Avoid using perfumes and cologne as these products may increase rash symptoms. • Avoid being in the heat for long periods of time. • Your provider may recommend an over-the-counter antihistamine or a topical cream. • Sunlight can make symptoms worse. • Avoid sun exposure as much as possible to decrease the risk of sunburn. The highest exposure to UV (ultra-violet) radiation occurs between the hours of 10am and 4pm. • Wear long-sleeved clothing, with UV protection if possible. • Wear broad-brimmed hats. • Apply broad-spectrum sunscreen (UVA/UVB) with at least SPF 30 as often as directed on the bottle. • Use lip balm with at least SPF 30. • Avoid tanning beds. <p>If your rash or itching continues to worsen, contact your care team.</p>
Change in color of urine	<p>It is normal to have red or orange-colored urine for 1 to 2 days after the infusion of epirubicin.</p> <p>Tell your care team if it does not stop in a few days, or if you see what looks like blood or blood clots in your urine.</p>
Mouth irritation or sores	<p>Practice good mouth care.</p> <ul style="list-style-type: none"> • Rinse your mouth after meals and at bedtime, and more frequently if you develop sores in your mouth. • Brush your teeth with a soft toothbrush or cotton swab after meals. • Use a mild non-alcohol mouth rinse at least 4 times a day (after eating and at bedtime). One example is a mixture of 1/8 teaspoon of salt and 1/4 teaspoon of baking soda in 8 ounces of warm (not hot) water. • Avoid acidic, hot or spicy foods and beverages, and rough foods that might irritate the mouth. • If you have sores in your mouth, avoid using tobacco products, alcohol, and mouthwashes that contain alcohol. <p>Call your care team if you experience pain or sores in your mouth or throat.</p>

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Rare but serious side effects

- Medications used in this regimen can rarely cause an infusion reaction. During your treatment, let the nurse know right away if any of these symptoms happen: chills or shaking, dizziness, fever, itchiness or rash, flushing, difficulty breathing, wheezing, throat irritation, cough, congestion, sudden back pain, or feeling faint.
- Epirubicin is a vesicant. If medication leaks outside of the IV, these medications can cause severe damage to your skin. Notify your nurse right away if you feel any pain, aching, burning, itching, swelling, or redness at the site of your IV.
- Epirubicin may affect your heart's ability to pump blood. Tell your healthcare provider right away if you experience new or worsening shortness of breath, chest pain, irregular heartbeat or swelling of your ankles or legs.
- Pembrolizumab can alter your hormone levels. Symptoms may include weight and mood changes, headaches, fatigue, sweating, elevated blood pressure, or heart racing. Contact your doctor if you are experiencing any of these symptoms.
- Pembrolizumab may cause inflammation in your colon. If symptoms of diarrhea or severe abdominal pain are present, please contact your health care team right away. Your health care team may have to prescribe corticosteroids in order to decrease the inflammation.
- Pembrolizumab may cause inflammation to your liver. Be sure to seek medical attention if you are experiencing jaundice (yellowing of the skin or eyes), severe nausea or vomiting, or easy bruising/bleeding. Dependent on liver function tests and severity of symptoms, your provider may have to discontinue the medication.
- Pembrolizumab and cyclophosphamide can cause lung and breathing problems. Tell your care team right away if you have new or worse cough, shortness of breath, chest pain, or difficulty breathing or wheezing.
- Pembrolizumab may cause a severe skin reaction resulting in flu-like symptoms and painful rashes that can spread and blister. Your healthcare professional may withhold or permanently discontinue medication depending on the severity.
- Pembrolizumab and cyclophosphamide can cause inflammation and damage in your bladder or kidneys. If you are experiencing any problems urinating, pelvic pain, or any blood in your urine, you should contact your doctor.
- Pembrolizumab may cause vision changes. Tell your care team if you experience eye pain, swelling, or redness, or any changes in vision such as flashes of light, blurred vision, floaters in your field of vision, or light hurting your eyes.
- Pembrolizumab can cause severe reactions in people who receive a stem cell transplant before or after treatment. If you have received a stem cell transplant, talk with your care team about these risks before starting treatment.
- Epirubicin and cyclophosphamide may rarely cause a secondary cancer called Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML). Symptoms of low blood cell counts are common during treatment but can be a sign of MDS or AML if it persists beyond active treatment.

If you experience ANY new, worsening, or uncontrolled side effects, call your care team immediately.

(INSTITUTIONAL CONTACT INFO)

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Handling body fluids and waste

Some of the drugs you receive may be present in urine, stool, sweat, or vomit for many days after treatment. Many cancer drugs are toxic, your bodily waste may also be toxic and can be dangerous to come into contact with. Once you have started this regimen, follow the instructions below for at least two days after your treatment. This is to keep you, your loved ones, and the environment as safe as possible.

- Pregnant women should avoid touching anything that may be soiled with body fluids from the patient.
- Toilet and septic systems
 - You may use the same toilet, septic tank, and/or sewer that you usually use. Close the lid and flush to ensure all waste has been discarded. If you have a low-flow toilet, close the lid and flush twice. If the toilet or toilet seat is soiled with urine, stool, or vomit, clean the surface after every use before other people use the toilet.
- If the toilet or toilet seat becomes soiled with urine, stool, or vomit, clean the surface after every use before other people use the toilet.
- Wash hands with soap and water after using the toilet for at least 20 seconds.
- If you need a bedpan, be sure your caregiver knows to wear gloves to assist with cleanup and to wash the bedpan with soap and water every day.
- If you do not have good control of bladder or bowels, use a disposable pad with a plastic back, a diaper, or a sheet to absorb body waste.
- Wash any skin that has been exposed to body waste with soap and water.
- Linens or clothing that are soiled with body fluids or body waste should be washed separately from other linens and clothing. If you do not have a washer, place the soiled linens in a plastic bag until they can be washed.
- Wash hands with soap and water after touching linens or clothing that may be soiled with body fluids.

Intimacy, sexual activity, contraception, and fertility

This treatment may cause changes that can affect intimacy and sexuality, including desire and body image. Maintaining physical closeness and/or intimacy with loved ones can be continued during treatment. Holding hands, hugging, and kissing can be done safely. It is recommended that you talk to your care team about any restrictions or questions you may have.

Some treatments can influence the ability to have children, also known as fertility. If you're interested in preserving fertility, talk to your care team before treatment. Ask your healthcare provider to determine when it is safe to become pregnant after your treatment. Patients of reproductive ability should not become pregnant or get their partners pregnant while receiving this regimen. Some of the drugs you receive may be present in semen and vaginal secretion for many days after treatment. You should use barrier devices, such as condoms, during sexual activity to limit exposure to body fluids.

- Talk to your care team about birth control. Not all options may be right for your treatment or cancer. Effective contraception could include one or more of the following: barrier methods (e.g. condoms), hormone methods (e.g. birth control pills), or surgery.
- Tell your care team if you become pregnant or plan to breastfeed.

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Additional resources

Product website:

Pembrolizumab (Keytruda): <https://www.keytruda.com>

Product resources: <https://www.imfinzihcp.com/metastatic-nsclc.html>

KEY+YOU Patient Support Program: <https://www.keytruda.com/key-you-sign-up>

MERCK Access Program: <https://www.merckaccessprogram-keytruda.com/hcc>

Product resources:

Pembrolizumab: https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf

Epirubicin: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/050778s021lbl.pdf

Cyclophosphamide: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/012141s090,012142s112lbl.pdf

Additional instructions

Updated – June 18, 2023

Important notice: The Association of Community Cancer Centers (ACCC), Hematology/Oncology Pharmacy Association (HOPA), National Community Oncology Dispensing Association, Inc. (NCODA), and Oncology Nursing Society (ONS) have collaborated in gathering information for and developing this patient education guide. This guide represents a brief summary of the therapy derived from information provided by the drug manufacturer and other resources. This guide does not cover all existing information related to the possible uses, directions, doses, precautions, warnings, interactions, adverse effects, or risks associated with this therapy and should not substitute for the advice of a qualified healthcare professional. Provision of this guide is for informational purposes only and does not constitute or imply endorsement, recommendation, or favoring of this therapy by ACCC, HOPA, NCODA, or ONS, who assume no liability for and cannot ensure the accuracy of the information presented. The collaborators are not making any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual receiving therapy. All decisions related to receiving this therapy should be made with the guidance and under the direction of a qualified healthcare professional.

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