Your treatment is called FOLFOX. It is commonly used to treat stomach and esophagus cancers and has also been used to treat other diseases. This treatment is made up of three drugs:

- 5-fluorouracil (flure-oh-YOOR-a-sill) or 5-FU
- leucovorin (loo-koe-VOR-in)
- oxaliplatin (ox-AL-i-PLA-tin) or Eloxatin® (eh-LOX-ah-tin)

5-FU and oxaliplatin are drugs that prevent cancer cells from dividing and growing, and can cause the cancer cells to shrink and die. Leucovorin helps increase the effectiveness of 5-FU. Your provider may substitute levoleucovorin (LEE-voe-loo-koe-VOR-in) for leucovorin in this treatment. Levoleucovorin also increases the effectiveness of 5-FU.

Before Starting Treatment, What Should I Tell My Healthcare Provider?

- Keep a list of all prescription or over-the-counter products you take, including vitamins, dietary supplements, herbal medicines and homeopathic remedies. Share this list with your health care provider at every visit. Also, always tell your provider before you start any new prescription or over-the-counter product.
- Use an effective birth control method during your treatment and for at least three months after the last dose. This treatment could harm an unborn baby. Tell your provider right away if you or your partner becomes pregnant.
- Do not breastfeed during treatment. It is not known if these drugs pass into breast milk.
- Some drugs can cause sterility. Talk with your provider about your options if you want to have children in the future.

You should not take this treatment if you:

- Have complete dihydropyrimidine dehydrogenase (DPD) deficiency.
- Are allergic to 5-FU, leucovorin, levoleucovorin, or any components of these drugs.
- Are allergic to capecitabine or any of its components because capecitabine is converted to 5-FU in the body.
- Are allergic to oxaliplatin or any of its components, or are allergic to other platinum drugs, such as cisplatin or carboplatin.
- Have an active infection.

What Do I Need to Know Before Starting FOLFOX?

- This treatment can increase your risk of anemia, bleeding and infection, including pneumonia (see “What Are the Possible Side Effects?”).
- 5-FU can cause a rash and a skin problem called hand-foot syndrome (see “What Are the Possible Side Effects?”).
- Tell your provider if you have heart disease. In rare cases, 5-FU can cause heart problems. Tell your provider right away if you have chest pain or pressure, flushing, shortness of breath, a cough, swelling of the hands or feet, or an irregular heartbeat.
- 5-FU can cause mouth sores (see “What Are the Possible Side Effects?”).
- 5-FU can cause diarrhea, which can be severe (see “What Are the Possible Side Effects?”).
- Tell your provider if you have dihydropyrimidine dehydrogenase (DPD) deficiency because you may have a higher risk of side effects from 5-FU. Your provider will watch you closely and decide if your dose needs to be changed or if your treatment needs to be stopped.
- In rare cases, 5-FU can cause central nervous system toxicities including, hyperammonemic encephalopathy. Tell your provider right away if you have any changes in your mental status, confusion, changes in your vision, trouble with balance or coordination.
- In rare cases, 5-FU and leucovorin can cause seizures and fainting when taken together. Tell your provider if you have a seizure disorder such as epilepsy or if you have ever had a seizure. You may have a higher risk for seizures if you have a history of seizures or if the cancer has spread to your brain.
• In rare cases, this treatment can cause a severe allergic reaction a few minutes after treatment. Tell your provider right away if you have a rash, itching, facial flushing, chest pain, trouble breathing, dizziness, fainting, or swelling of the lips, throat or tongue.

• Oxaliplatin can cause some of the nerve cells in your hands and feet to stop working properly. This condition is called neuropathy (see “What Are the Possible Side Effects?”). You may have a higher risk for severe neuropathy if you already had this condition before starting treatment. Tell your provider if you have numbness, tingling, pain, or a burning sensation in your hands or feet. Oxaliplatin can cause two types of neuropathy:

  - Acute or early-onset neuropathy. This type of neuropathy starts a few hours to two days after starting treatment and usually goes away within 14 days. Symptoms may include numbness, tingling, pain, or a burning sensation in the hands, feet, mouth or throat. Other less common symptoms include jaw spasm, a strange feeling on the tongue, eye pain, trouble speaking and chest pressure. It is common for acute neuropathy to come back after each dose of treatment. Cold temperatures and cold objects can cause symptoms or make symptoms worse. Avoid cold weather, cold foods and cold drinks during treatment and for five days after treatment.

  - Chronic neuropathy. This type of neuropathy can last for weeks or months. Symptoms of chronic neuropathy may include numbness, tingling, pain, or a burning sensation in the hands, feet, mouth or throat. Chronic neuropathy usually starts after several treatments with oxaliplatin. You can have chronic neuropathy even if you never have acute neuropathy.

A less common symptom of neuropathy is pharyngolaryngeal dysesthesia. This is a sensation of tightness or discomfort in the throat that can make it feel difficult to breathe or swallow. Although this symptom may be frightening, it is just a sensation and does not interfere with breathing. The sensation usually goes away on its own after a few minutes.

• Oxaliplatin can cause skin irritation if it accidentally leaks out of your vein during the infusion or if the same vein is used for every treatment. Tell your provider right away if you have redness, pain, burning or swelling where the medicine is injected.

• In rare cases, oxaliplatin can cause a brain condition called posterior reversible encephalopathy syndrome (PRES) Tell your provider right away if you have seizures, tiredness, confusion, vision changes or a headache that does not go away. If you have PRES, you will need to stop treatment.

• Tell your provider if you have kidney disease or kidney problems because you may have a higher risk of side effects from oxaliplatin. In rare cases, oxaliplatin can also cause kidney problems. If you have kidney problems, your treatment may need to be changed or stopped.

• Tell your provider if you have a history of liver disease or liver problems. You have a higher risk of side effects from oxaliplatin if your liver does not work well. In some cases, oxaliplatin can also cause liver problems. Tell your provider if your skin or eyes look yellow, your urine turns dark, you bleed or bruise more easily, or you have stomach pain.

• In rare cases, oxaliplatin can cause lung problems. Call your provider right away or seek emergency care if you have shortness of breath, difficulty breathing or a racing heart.

• In rare cases, oxaliplatin can cause changes in your heart rhythm. Tell your provider if you have long QT syndrome, chest pain, an abnormal heartbeat or shortness of breath. Your risk of having heart rhythm changes is higher if you do not have enough potassium or magnesium in your body.

• In rare cases, oxaliplatin can cause muscle damage called rhabdomyolysis. Tell your provider right away if you have muscle pain or swelling along with weakness, fever, or red-brown urine.

Your treatment can interfere with other substances, including:

• Celecoxib (Celebrex®)
• Drugs that harm the kidneys, such as amphotericin B and aminoglycosides (tobramycin, gentamicin and amikacin)
• Drugs used to treat heart rhythm abnormalities (anti-arrhythmics), such as quinidine, procainamide, amiodarone (Cordarone® or Nexterone®), sotalol (Betapace® or Sorine®) and ranolazine (Ranexa®)
• Glimepiride (Amaryl®), tolbutamide
• Phenytoin (Dilantin®) or fosphenytoin (Cerebyx®)
• Warfarin (Coumadin®)

Please note this list is a summary and does not contain all possible interactions. Tell your provider if you are taking any substances that can interact with your treatment.

How Will I Get the Treatment?

• Your provider will give you your treatment by injection into a vein. Your provider will determine your number of treatments.
• Your provider may give you medicines before your treatment for nausea and vomiting. Your provider may also give you medicines for the nausea and vomiting that can occur a few days after treatment.

• Do not share any medicine with others. Sharing medicine with anyone else could be harmful.

**When Should I Call My Healthcare Provider?**

Call your provider right away if you have any of the following symptoms:

- Problems urinating or blood in your urine
- Seizures, vision changes or headaches that don’t go away
- Pain in the arms or legs or sudden shortness of breath
- Paralysis or weakness on one side of the face or body
- Rash with itching, trouble breathing, or swelling of the lips, throat, or tongue
- Irregular or rapid heartbeat, chest pain or tightness, shortness of breath or a cough that does not go away
- Depression or suicidal thoughts

**What Are the Possible Side Effects?**

All drugs can cause side effects, but every person reacts differently to each drug. The following chart lists the possible side effects that can occur with your treatment, how to recognize and minimize symptoms, and possible treatments.

| Side Effect                          | How to Minimize Side Effect                                                                                                                                  | When to Call Provider                                                                                               |
|--------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Neuropathy or Nerve Problems**     | • Try to stay out of the cold, and do not have cold foods or drinks for five days after treatment<br>• Try to stay out of extreme heat.<br>• Wear mittens or gloves, and socks and scarves<br>• Use caution with sharp objects<br>• Beware of hot coffee mugs, pots and pans and dishwater. You may not feel the heat until you are burned<br>• If you feel unsteady, be careful on stairs and in the shower. Consider moving area rugs so you do not trip and put non-slip bathmats in your tub and shower | Feeling pain, tingling, or numbness in your hands, legs, or feet.<br>• Pain that interferes with walking or normal daily activities<br>• Your provider may lower your dose or delay further treatment.                                                   |
| **Nausea/Vomiting**                  | • Eat small, frequent meals and bland foods, such as bananas, rice, applesauce and toast<br>• Eat food cold or at room temperature<br>• Do not eat fried, spicy or fatty foods<br>• Drink plenty of liquids during the day | Vomiting that is severe or that lasts several hours<br>• Your provider will give you medicine to help reduce nausea and vomiting.                                                                 |
|                                     |                                                                                                           |                                                                                                                       |
| **Diarrhea**                         | • Eat small, frequent meals and bland foods, such as bananas, rice, applesauce and toast<br>• Do not have caffeine; alcohol; raw fruits and vegetables; raw eggs; undercooked meats; spicy, fatty and greasy foods; milk and dairy products; foods that cause gas, such as beans; high fiber and high-fat foods; foods left un-refrigerated for more than two hours (one hour for egg dishes and cream or mayonnaise-based foods); bulk laxatives; and stool softeners<br>• Drink eight to ten glasses of clear liquids every day | Diarrhea that causes an extra four bowel movements a day, or lasts more than one day, or diarrhea at night or with a fever, cramps or bloody<br>• Your provider may prescribe medicine to help treat diarrhea.                                                                 |
|                                     |                                                                                                           |                                                                                                                       |
| **Risk of Infection (Less Common)**  | • Wash your hands often<br>• Brush and floss your teeth daily<br>• Clean any cuts right away<br>• Stay away from crowds and people with colds or other illnesses<br>• Make sure to cook foods thoroughly | Shaking, chills, or a fever of 100.5F or higher<br>• Your provider may give you an antibiotic to treat or prevent infection, a medicine to increase your white blood cell count, or may lower your dose or delay further treatment. |
### Side Effect

<table>
<thead>
<tr>
<th>Mouth Sores and Pain (Less Common. Symptoms are generally mild to moderate but can be severe.)</th>
<th>Rash (Less Common. Symptoms are generally mild to moderate.)</th>
<th>Anorexia or Appetite Loss (Less Common. Symptoms are generally mild to moderate.)</th>
<th>Constipation (Less Common. Symptoms are generally mild to moderate.)</th>
<th>Alopecia or Hair Loss (Less Common)</th>
<th>Hand-Foot Syndrome (Less Common. Symptoms are generally mild to moderate.)</th>
</tr>
</thead>
</table>
| • Pain, swelling, or redness of the mouth, tongue, and throat  
• “Coated tongue”  
• Difficulty talking, swallowing or eating  
• Bleeding ulcers and infection | • Usually mild and short-lived  
• Generally, appears on the arms and trunk (sometimes on the face)  
• May be itchy  
• May look like a flat, discolored area on the skin or a small, raised bump | • Not having an appetite  
• Feeling too nauseated to eat  
• Metallic or medicinal taste  
• Change in taste causing dislike for certain foods | • No bowel movement for one to two days  
• Small, hard, dry stools  
• Bloating, gas, cramps and pain | • Hair coming out in your brush, in the shower or on your pillow after sleeping  
• Loss of body hair | • Swelling or redness in the hands and feet that can prevent normal activity  
• Cracked or peeling skin  
• Tingling, numbness, or pain in the hands or soles of the feet |

### How to Minimize Side Effect

| Brush teeth two to four times a day using a soft-bristle brush and fluoride toothpaste  
If you wear dentures, make sure they fit well and do not wear them overnight. Remove and brush them as well  
Ask your provider to suggest a mouthwash that does not contain alcohol  
Consider rinsing your mouth every 3 hours with a solution of 1/4 tsp. baking soda and 1/8 tsp. salt mixed in 1 cup of warm water  
Sip water during the day or use sugar-free candy or gum to keep your mouth wet  
Use lip balm to keep your lips moist  
Eat food cold or at room temperature  
Eat soft or pureed food  
Do not eat food that is acidic, spicy, salty, dry or rough, such as toast  
Do not smoke or use other tobacco products  
Suck on ice chips for 10 to 15 minutes before and after 5-FU injections | Do not stay in the heat for long periods of time  
Use creams or moisturizers often. Try wearing cotton gloves  
Do not use perfume, cologne or aftershave; these products can irritate the skin  
Drink plenty of fluids to help loosen your bowels  
Try eating six to eight small meals or snacks each day instead of three larger meals  
Vary your diet and try new foods and recipes  
Take a walk before meals, when possible. This may make you feel hungrier  
Eat with friends or family. When eating alone, listen to the radio or watch TV  
Cook dinners ahead of time and freeze them in small portions to minimize cooking smells  
Let others help with meals Tell them foods you don’t like  
Add mild spices to change flavor  
Have meals delivered to you through a program such as Meals on Wheels | Drink plenty of fluids to help loosen your bowels  
Try to eat foods that are high in fiber, such as bran, vegetables, whole wheat breads and fruit  
Have prunes or prune juice, which act like laxatives | You may not be able to prevent alopecia, but here are tips to help with hair loss:  
Use a soft hairbrush. Do not use brush rollers, color treat your hair or get a permanent | Wear gloves to wash dishes  
Do not use harsh household cleaners  
Do not stay in the heat for long periods of time  
Use creams or moisturizers often. Try wearing cotton gloves  
Do not use perfume, cologne or aftershave. These products can irritate the skin |

### When to Call Provider

| New sores, or patches in mouth, swollen tongue, or bleeding gums  
Your provider may give you medicine to help treat pain, or to treat fungal or viral infections. | Symptoms are bothersome or severe  
Your provider may prescribe creams (mild steroids, antihistamines or antibiotics) to treat the rash. | Loss of appetite or weight loss  
Your provider may suggest a stool softener. | Constipation that lasts more than two or three days or constipation with stomach pain  
Your provider may suggest a stool softener. | Severe pain, blisters, or swelling in the hands or feet that keeps you from doing normal activities  
Your provider may prescribe a cream to help with skin reactions or lower your dose or delay treatment. |
including “black box” warnings and precautions, is information regarding available treatments and known side effects changes

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>How to Minimize Side Effect</th>
<th>When to Call Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anemia (Rare)</strong></td>
<td>• Fatigue or weakness</td>
<td>• Feel so tired that you cannot perform normal functions</td>
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<tr>
<td></td>
<td>• Dizziness</td>
<td>• Dizziness or feeling lightheaded</td>
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<tr>
<td></td>
<td>• Pale skin</td>
<td>• Your provider may give you a medicine to increase your red blood cell count, lower</td>
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<td></td>
<td>• Feeling out of breath</td>
<td>your dose, or delay further treatment.</td>
</tr>
<tr>
<td></td>
<td>• Feeling cold</td>
<td>• Your provider may lower your dose or delay further treatment.</td>
</tr>
<tr>
<td><strong>Risk of Bleeding (Rare)</strong></td>
<td>• Unusual bleeding or easy bruising</td>
<td>• Unusual bleeding, easy bruising, or tiny red spots on your skin</td>
</tr>
<tr>
<td></td>
<td>• Black or tar-like stools</td>
<td>• Your provider may lower your dose or delay further treatment.</td>
</tr>
<tr>
<td></td>
<td>• Blood in your urine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Small red spots on your skin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bleeding gums or nosebleeds</td>
<td></td>
</tr>
<tr>
<td><strong>Nail Changes</strong></td>
<td>• Darkening of the nails that usually grows out with the nail</td>
<td>• Symptoms are bothersome or severe</td>
</tr>
<tr>
<td></td>
<td>• Vertical or horizontal bands on the nails</td>
<td>• Your provider may give you an antibiotic if you have an infection in the nail bed.</td>
</tr>
<tr>
<td><strong>Fluid Retention</strong></td>
<td>• Swelling around the eyes, lower legs, ankles, feet or stomach</td>
<td>• Severe fluid retention that causes sudden weight gain or swelling in the stomach,</td>
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<tr>
<td></td>
<td>• Slight weight gain</td>
<td>hands, or feet</td>
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<tr>
<td></td>
<td>• Hands feel tight when making a fist</td>
<td>• Your provider may give you a diuretic (water pill) to reduce the amount of fluid in</td>
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<td></td>
<td></td>
<td>your body.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Your provider may lower your dose or delay further treatment.</td>
</tr>
</tbody>
</table>

The following side effects can occur with the individual drugs in this treatment but were not reported in the clinical trials.

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>How to Minimize Side Effect</th>
<th>When to Call Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nail Changes</strong></td>
<td>• Trim nails often and keep them clean</td>
<td>• Your provider may lower your dose or delay further treatment.</td>
</tr>
<tr>
<td></td>
<td>• Wear gloves for cleaning and gardening to minimize damage and prevent infection</td>
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<tr>
<td></td>
<td>• Do not wear nail polish or false fingernails until the nails have grown out and returned to normal</td>
<td></td>
</tr>
<tr>
<td><strong>Fluid Retention</strong></td>
<td>• Check your weight often</td>
<td>• Severe fluid retention that causes sudden weight gain or swelling in the stomach,</td>
</tr>
<tr>
<td></td>
<td>• Try not to eat salty foods</td>
<td>hands, or feet</td>
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<tr>
<td></td>
<td>• If your feet are swollen, put them up or go for a walk</td>
<td>• Your provider may give you a diuretic (water pill) to reduce the amount of fluid in</td>
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<td>• Your provider may lower your dose or delay further treatment.</td>
</tr>
</tbody>
</table>

*Side effects listed as “Common” usually occur in more than 25 percent of patients. Those listed as “Less common” usually occur in about 5 to 25 percent of patients. Side effects that are “Rare” usually occur in fewer than 5 percent of patients. Other side effects may vary in how often they occur.

**Notes**

This information was compiled from manufacturers’ information and online reference sources. Additional product information, including “black box” warnings and precautions, is available from the manufacturer and other sources. Every effort was made to ensure that the information is accurate and complete at the time of publication, but the information is not all-inclusive, may be out of date, and may contain inaccuracies or typographical errors. Information regarding available treatments and known side effects changes frequently, and McKesson Specialty Health undertakes no responsibility to update this document. This information is provided “AS IS”, “WITH ALL FAULTS” and “AS AVAILABLE”. ALL WARRANTIES, EXPRESS AND IMPLIED, ARE DISCLAIMED (INCLUDING, BUT NOT LIMITED TO, AND IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). Each patient’s situation is unique and the information presented may not apply to your situation. Patients should consult with an appropriate clinician for specific evaluation, advice, diagnosis, and treatment tailored to their situation. Use of this information shall not be construed to create a practitioner-patient relationship or similar relationship with any McKesson entity.

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References:

FOLFOX (Gastric and Esophageal)