

**A**nother form of neuropathy that can happen while taking ELOXATIN® is long-term, persistent neuropathy. This form lasts longer than 2 weeks, unlike acute (short-term) neuropathy.

### Symptoms can feel much like the symptoms of acute neuropathy:

- Tingling sensations or numbness, usually in the feet or hands
- A feeling that it's hard to breathe or swallow

These symptoms can happen if you've never had acute neuropathy, and they may start even after you've had several treatments; they can last weeks or months before going away. Cold does not trigger this form of neuropathy.

### Chronic, long-term neuropathy may include:

- Constant pain, tingling, or numbness in your hands, feet, or around your mouth or throat
- Trouble with walking (stumbling, loss of balance)
- Trouble with activities of daily living such as writing or buttoning a shirt

Because the symptoms of persistent neuropathy do not lessen between treatments and can interfere with daily life, your doctor may choose to alter your treatment with ELOXATIN®.

### Your doctor may change your treatment in any or all of these ways during a cycle:

- Give ELOXATIN® for a longer treatment time
- A lower dose of ELOXATIN®
- Doses of calcium and magnesium given through your IV before and after ELOXATIN®



Usually the other part of your chemotherapy, called 5-FU/LV, will remain at the same dose, with the same infusion time as before. If your symptoms are very severe, your doctor may choose to give you another form of chemotherapy.

## Talk to your doctor and nurse

As with acute neuropathy, let your family, friends, and caregivers know that you may experience the above symptoms of persistent neuropathy. Always let your doctors and nurses know of any symptoms you may have during and between treatments so they can decide if and how to adjust your chemotherapy.

## Indications and Usage

Eloxatin® (oxaliplatin injection), used in combination with infusional 5-FU/LV, is indicated for

- Adjuvant treatment of stage III colon cancer patients who have undergone complete resection of the primary tumor. The indication is based on an improvement in disease-free survival, with no demonstrated benefit in overall survival after a median follow-up of 4 years
- Treatment of advanced carcinoma of the colon or rectum

## Clinical Safety Considerations

**ELOXATIN should be administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available.**

**Anaphylactic-like reactions to ELOXATIN have been reported and may occur within minutes of ELOXATIN administration. Epinephrine, corticosteroids, and antihistamines have been employed to alleviate symptoms, and discontinuation of ELOXATIN therapy may be required.**

- ELOXATIN should not be administered to patients with a history of known allergy to ELOXATIN or other platinum compounds. Hypersensitivity and anaphylactic/anaphylactoid reactions to ELOXATIN have been reported and were similar in nature and severity to those reported with other platinum compounds (ie, rash, urticaria, erythema, pruritus, and, rarely, bronchospasm and hypotension). These reactions occur within minutes of administration and should be managed with appropriate supportive therapy. Drug-related deaths from this reaction have been reported
- ELOXATIN may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised not to become pregnant while receiving ELOXATIN. It is not known whether ELOXATIN or its derivatives are excreted in human milk
- ELOXATIN has been associated with pulmonary fibrosis (<1% of study patients), which may be fatal. The combined incidence of cough and dyspnea was 7.4% (<1% grade 3, no grade 4) in the ELOXATIN plus 5-FU/LV arm compared to 4.5% (no grade 3, 0.1% grade 4) in the 5-FU/LV alone arm in the adjuvant colon cancer study. In this study, one patient died from eosinophilic pneumonia in the ELOXATIN combination arm. The combined incidence of cough, dyspnea, and hypoxia was 43% (7% grade 3 and 4) in the ELOXATIN plus 5-FU/LV arm compared to 32% (5% grade 3 and 4) in the irinotecan plus 5-FU/LV arm in patients with previously untreated colorectal cancer. In case of unexplained respiratory symptoms, ELOXATIN should be discontinued until pulmonary investigation excludes interstitial lung disease or pulmonary fibrosis
- ELOXATIN is associated with two types of primarily peripheral sensory neuropathy: an acute, reversible type of early onset and a persistent type (>14 days). In patients with advanced colorectal cancer, paresthesias occurred in 77% (all grades) and 18% (grade 3/4) of previously untreated patients. In previously treated patients, acute neuropathy occurred in 56% (all grades) and 2% (grade 3/4) of patients; persistent neuropathy occurred in 48% (all grades) and 6% (grade 3/4) of patients. In patients with stage II and III colon cancer, paresthesia was seen in 92% (all grades) and 13% (grade 3/4) of patients; 21% (all grades) and 0.5% (grade 3/4) of patients had residual paresthesia at 18-month follow-up
- Hepatotoxicity, as evidenced in the adjuvant study by increase in transaminases and alkaline phosphatase, was observed more commonly in the ELOXATIN combination arm. The incidence of increased bilirubin was similar on both arms. Changes noted on liver biopsies include: peliosis, nodular regenerative hyperplasia or sinusoidal alterations, perisinusoidal fibrosis, and veno-occlusive lesions. Hepatic vascular disorders should be considered and, if appropriate, investigated in case of abnormal liver function test results or portal hypertension not explained by liver metastases
- Monitoring of white blood cell count with differential, hemoglobin, platelet count, and blood chemistries (including ALT, AST, bilirubin, and creatinine) is recommended before each ELOXATIN cycle
- The safety and effectiveness of ELOXATIN plus 5-FU/LV in patients with renal impairment have not been evaluated. Since the primary route of platinum elimination is renal, this combination should be used with caution in patients with preexisting renal impairment. Clearance of these products may be decreased by coadministration of potentially nephrotoxic compounds, although this has not been specifically studied
- The incidence of diarrhea, dehydration, hypokalemia, leukopenia, fatigue, and syncope was higher in patients  $\geq 65$  years old
- Extravasation may result in local pain and inflammation that may be severe and lead to complications, including necrosis. Injection site reaction, including redness, swelling, and pain, has been reported
- There have been reports of prolonged prothrombin time and INR occasionally associated with hemorrhage in patients receiving ELOXATIN plus 5-FU/LV while on anticoagulants. Patients receiving ELOXATIN plus 5-FU/LV and requiring oral anticoagulants may require closer monitoring
- The most common adverse reactions in patients with stage II or III colon cancer receiving adjuvant therapy were peripheral sensory neuropathy, neutropenia, thrombocytopenia, anemia, nausea, increase in transaminases and alkaline phosphatase, diarrhea, emesis, fatigue, and stomatitis. The most common adverse reactions in patients with advanced colorectal cancer were peripheral sensory neuropathy, fatigue, neutropenia, nausea, emesis, and diarrhea



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**Eloxatin**®  
(OXALIPLATIN injection)