

HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use Oxaliplatin Injection safely and effectively. See full prescribing information for Oxaliplatin Injection.

Oxaliplatin Injection, solution for intravenous use

Initial U.S. Approval: 2002

WARNING: ANAPHYLACTIC REACTIONS See full prescribing information for complete boxed warning.

Anaphylactic reactions to Oxaliplatin Injection have been reported, and may occur within minutes of Oxaliplatin Injection administration. Epinephrine, corticosteroids, and antihistamines have been employed to alleviate symptoms. (5.1)

INDICATIONS AND USAGE

Oxaliplatin Injection is a platinum-based drug used in combination with infusional 5-fluorouracil (leucovorin), which is indicated for:
• adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor.
• treatment of advanced colorectal cancer. (1)

DOSE AND ADMINISTRATION

Administer Oxaliplatin Injection in combination with 5-fluorouracil/leucovorin every 2 weeks (2.1).
Day 1: Oxaliplatin Injection 85 mg/m² intravenous infusion in 250-500 mL 5% Dextrose Injection, USP and leucovorin 200 mg/m² intravenous infusion in 5% Dextrose Injection, USP both given over 120 minutes at the same time in separate bags using a Y-line, followed by 5-fluorouracil 400 mg/m² intravenous bolus given over 2 to 4 minutes, followed by 5-fluorouracil 600 mg/m² intravenous infusion in 500 mL 5% Dextrose Injection, USP (recommended) as a 22-hour continuous infusion.
Day 2: Leucovorin 200 mg/m² intravenous infusion over 120 minutes followed by 5-fluorouracil 400 mg/m² intravenous bolus given over 2 to 4 minutes followed by 5-fluorouracil 600 mg/m² intravenous infusion in 500 mL 5% Dextrose Injection, USP (recommended) as a 22-hour continuous infusion.
Reduce the dose of Oxaliplatin Injection to 75 mg/m² (adjuvant setting) or 65 mg/m² (advanced colorectal cancer) (2.2).

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if there are persistent grade 2 neurosensory events that do not resolve.
after recovery from grade 3/4 gastrointestinal toxicities (despite prophylactic treatment) or grade 4 neutropenia or grade 3/4 thrombocytopenia. Delay next dose until neutrophils $\geq 1.5 \times 10^9/L$ and platelets $\geq 75 \times 10^9/L$.

Discontinue Oxaliplatin Injection if there are persistent Grade 3 neurosensory events. (2.2)

Never reconstitute or prepare final dilution with a sodium chloride solution or other chloride-containing solutions. (2.3)

DOSE FORMS AND STRENGTHS

Single use vials of 50 mg or 100 mg oxaliplatin as a sterile, preservative-free aqueous solution at a concentration of 5 mg/mL. (3)

CONTRAINDICATIONS

Known allergy to Oxaliplatin Injection or other platinum compounds. (4.1)

WARNINGS AND PRECAUTIONS

Allergic Reactions: Monitor for development of rash, urticaria, erythema, pruritus, bronchospasm, and hypotension. (5.1)
Neurotoxicity: Reduce the dose or discontinue Oxaliplatin Injection if necessary. (5.2)
Pulmonary Toxicity: May need to discontinue Oxaliplatin Injection until interstitial lung disease or pulmonary fibrosis are excluded. (5.3)
Hepatotoxicity: Monitor liver function tests. (5.4)
Pregnancy: Fetal harm can occur when administered to a pregnant woman. Women should be apprised of the potential harm to the fetus. (5.5, 8.1)

ADVERSE REACTIONS

Most common adverse reactions (incidence $\geq 40\%$) were peripheral sensory neurotoxicity, neutropenia, thrombocytopenia, anemia, nausea, increase in transaminases and alkaline phosphatase, diarrhea, emesis, fatigue and stomatitis. Other adverse reactions, including serious adverse reactions, have been reported. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Hospira Inc. at 1-800-441-4100, or FDA at 1-800-FDA-1088. See www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling. Revised: 06/2009

Table 2 - Grading Scale for Paresthesia/Dysesthesias in Advanced Colorectal Cancer Patients

Table with 2 columns: Grade and Definition. Grade 1: Resolved and did not interfere with functioning. Grade 2: Interfered with function but not daily activities. Grade 3: Pain or functional impairment that interfered with daily activities. Grade 4: Persistent impairment that is disabling or life-threatening.

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FULL PRESCRIBING INFORMATION

WARNING: ANAPHYLACTIC REACTIONS

Anaphylactic reactions to Oxaliplatin Injection have been reported, and may occur within minutes of Oxaliplatin Injection administration. Epinephrine, corticosteroids, and antihistamines have been employed to alleviate symptoms of anaphylaxis. (See Warnings and Precautions (5.1))

1 INDICATIONS AND USAGE

Oxaliplatin Injection, used in combination with infusional 5-fluorouracil/leucovorin, is indicated for:

• adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor.
• treatment of advanced colorectal cancer.

2 DOSAGE AND ADMINISTRATION

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

2.1 Dosage

Administer Oxaliplatin Injection in combination with 5-fluorouracil/leucovorin every 2 weeks. For advanced disease, treatment is recommended until disease progression or unacceptable toxicity. For adjuvant use, treatment is recommended for a total of 6 months (12 cycles):

Day 1: Oxaliplatin Injection 85 mg/m² intravenous infusion in 250-500 mL 5% Dextrose Injection, USP and leucovorin 200 mg/m² intravenous infusion in 5% Dextrose Injection, USP both given over 120 minutes at the same time in separate bags using a Y-line, followed by 5-fluorouracil 400 mg/m² intravenous bolus given over 2 to 4 minutes, followed by 5-fluorouracil 600 mg/m² intravenous infusion in 500 mL 5% Dextrose Injection, USP (recommended) as a 22-hour continuous infusion.

Day 2: Leucovorin 200 mg/m² intravenous infusion over 120 minutes, followed by 5-fluorouracil 400 mg/m² intravenous bolus given over 2 to 4 minutes, followed by 5-fluorouracil 600 mg/m² intravenous infusion in 500 mL 5% Dextrose Injection, USP (recommended) as a 22-hour continuous infusion.

2.2 Dose Modification Recommendations

A dose reduction of Oxaliplatin Injection to 75 mg/m² and 5-FU by 20% (300 mg/m² bolus and 500 mg/m² 22-hour infusion) is recommended for patients after recovery from grade 3/4 gastrointestinal (despite prophylactic treatment) or grade 4 neutropenia or grade 3/4 thrombocytopenia. The next dose should be delayed until: neutrophils $\geq 1.5 \times 10^9/L$ and platelets $\geq 75 \times 10^9/L$.

2.3 Preparation of Infusion Solution

Do not freeze the concentrated solution.
A final dilution must never be performed with an aqueous solution of other chloride-containing solutions.
The solution must be further diluted in an infusion solution of 250-500 mL of 5% Dextrose Injection, USP.

After dilution with 250-500 mL of 5% Dextrose Injection, USP, the shelf life is 6 hours at room temperature (20-25°C (68-77°F)) or up to 24 hours under refrigeration (2-8°C (36-46°F)). After final dilution, protection from light is not required.

Oxaliplatin Injection is incompatible in solution with alkaline medications or media (such as basic solutions of 5-fluorouracil) and must not be mixed with those or administered simultaneously through the same infusion line. The infusion line should be flushed with 5% Dextrose Injection, USP prior to administration of any concomitant medication.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration and discarded if present.

Needles or intravenous administration sets containing aluminum parts that may come in contact with Oxaliplatin Injection should not be used for the preparation or mixing of the drug. Aluminum has been reported to cause degradation of platinum compounds.

3 DOSAGE FORMS AND STRENGTHS

Oxaliplatin Injection is supplied in single use vials containing 50 mg or 100 mg of oxaliplatin as a sterile, preservative-free aqueous solution at a concentration of 5 mg/mL.

4 CONTRAINDICATIONS

Oxaliplatin Injection should not be administered to patients with a history of known allergy to Oxaliplatin Injection or other platinum compounds. (See Warnings and Precautions (5.1)).

5 WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

See boxed warning.
Grade 3/4 hypersensitivity, including anaphylactic/anaphylactoid reactions, to Oxaliplatin Injection has been observed in $\geq 2.3\%$ of colon cancer patients. These allergic reactions which can be fatal, can occur within minutes of administration and at any cycle, and were similar in nature and severity to those reported with other platinum-containing compounds, such as rashes, urticaria, erythema, pruritus, and, rarely, bronchospasm and hypotension. The symptoms associated with hypersensitivity reactions reported in the previously untreated patients were urticaria, pruritus, flushing of the face, diarrhea associated with oxaliplatin infusion, shortness of breath, bronchospasm, diaphoresis, chest pains, hypotension, disorientation and syncope. These reactions are usually managed with standard epinephrine, corticosteroid, antihistamine therapy, and may require discontinuation of therapy. Drug-related deaths associated with platinum compounds from anaphylaxis have been reported.

5.2 Neurotoxicity

Oxaliplatin Injection is associated with two types of neurotoxicity.
An acute, reversible, primarily peripheral, sensory neurotoxicity that is of early onset, occurring within hours or one to two days of dosing, that resolves within 14 days, and that frequently recurs with further dosing. The symptoms may be precipitated or exacerbated by exposure to cold temperature or cold objects and may usually present as transient paresthesia, dysesthesia and hypoesthesia in the hands, feet, perioral area, or throat. Jaw spasm, abnormal tongue sensation, dysarthria, eye pain, and a feeling of chest pressure have also been observed. The acute, reversible pattern of sensory neurotoxicity was observed in about 56% of study patients who received Oxaliplatin Injection with 5-fluorouracil/leucovorin. In any individual cycle acute neurotoxicity was observed in approximately 38% of patients. In adjuvant patients the median cycle of onset for grade 3 peripheral sensory neurotoxicity was 9 in the previously treated patients the median number of cycles administered on the Oxaliplatin Injection with 5-fluorouracil/leucovorin combination arm was 6.

An acute syndrome of pharyngolaryngeal dysphasia seen in 1 to 2 (grade 3/4) of patients previously untreated for advanced colorectal cancer, and the previously treated patients is characterized by subjective sensations of dysphagia or dyspnea, without any laryngospasm or bronchospasm (no stridor or wheezing). Ice (mucositis prophylaxis) should be avoided during the infusion of Oxaliplatin Injection because cold temperature can exacerbate acute neurological symptoms.

A persistent (≥ 14 days), primarily peripheral, sensory neurotoxicity that is usually characterized by paresthesias, dysesthesias, hypoesthesia, but may also include deficits in proprioception that can interfere with daily activities (e.g., writing, buttoning, swallowing, and difficulty walking from impaired proprioception). These forms of neurotoxicity occurred in 48% of the study patients receiving Oxaliplatin Injection with 5-fluorouracil/leucovorin. Persistent neurotoxicity can occur without any prior acute neurotoxicity event. The majority of the patients (80%) who developed grade 3 persistent neurotoxicity progressed from prior Grade 1 or 2 events. These symptoms may improve in some patients upon discontinuation of Oxaliplatin Injection.

In the adjuvant colon cancer trial, neurotoxicity was graded using a prestated module derived from the Neuro-Sensory section of the National Cancer Institute Common Toxicity Criteria (NCI CTC) scale, Version 1.1, as follows:

Grade 1: Mild paresthesias, loss of deep tendon reflexes.
Grade 2: Mild or moderate objective sensory loss, moderate paresthesias.
Grade 3: Severe objective sensory loss or paresthesias that interfere with function.
Grade 4: Not applicable.

Peripheral sensory neurotoxicity was reported in adjuvant patients treated with the Oxaliplatin Injection combination with a frequency of 92% (all grades) and 13% (grade 3). At the 28-day follow-up after the last treatment cycle, 60% of all patients had any grade (Grade 1-4), Grade 1-16% (Grade 2-3%), Grade 2-7% (Grade 3-1%) and 21% at 18 weeks of follow-up (Grade 1-17%, Grade 2-3%, Grade 3-1%).

In the advanced colorectal cancer studies, neurotoxicity was graded using a study-specific neurotoxicity scale, which was different from the NCI CTC scale. (Version 2.0) (See below).

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling. Revised: 06/2009

Table 1 - NCI CTC Grading for Neurotoxicity in Adjuvant Patients

Table with 5 columns: Grade, No change or none, Mild paresthesias, loss of deep tendon reflexes, Mild or moderate objective sensory loss, moderate paresthesias, Severe objective sensory loss or paresthesias that interfere with function, Not applicable.

Peripheral sensory neurotoxicity was reported in adjuvant patients treated with the Oxaliplatin Injection combination with a frequency of 92% (all grades) and 13% (grade 3). At the 28-day follow-up after the last treatment cycle, 60% of all patients had any grade (Grade 1-4), Grade 1-16% (Grade 2-3%), Grade 2-7% (Grade 3-1%) and 21% at 18 weeks of follow-up (Grade 1-17%, Grade 2-3%, Grade 3-1%).

In the advanced colorectal cancer studies, neurotoxicity was graded using a study-specific neurotoxicity scale, which was different from the NCI CTC scale. (Version 2.0) (See below).

Table 2 - Grading Scale for Paresthesia/Dysesthesias in Advanced Colorectal Cancer Patients

Table with 2 columns: Grade and Definition. Grade 1: Resolved and did not interfere with functioning. Grade 2: Interfered with function but not daily activities. Grade 3: Pain or functional impairment that interfered with daily activities. Grade 4: Persistent impairment that is disabling or life-threatening.

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The following table provides adverse reactions reported in the adjuvant therapy colon cancer clinical trial (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and infusional 5-fluorouracil/leucovorin arm for events with overall incidences $\geq 5\%$ and for NCI grade 3/4 events with incidences $\geq 1\%$.

Table 3 - Adverse Reactions Reported in Patients with Colon Cancer receiving Adjuvant Treatment ($\geq 5\%$ of all patients and with $\geq 1\%$ NCI Grade 3/4 events)

Table with 5 columns: Adverse Reaction (WHO/PrE), All Grades (%), Grade 3/4 (%), All Grades (%), Grade 3/4 (%). Rows include Allergic Reaction, Fatigue, Abdominal Pain, Skin Disorder, Injection Site Reaction, Nausea, Diarrhea, Vomiting, Stomatitis, Anorexia, Fever, Infection, Overall Peripheral Sensory Neurotoxicity, Rhinitis, Epistaxis, Weight Increase, Conjunctivitis, Headache, Dyspnea, Pain, Lacrimation Abnormal, Alopecia, Constipation, Taste Perversion, Dyspepsia, Mouth Dryness, Sensory Disturbance.

Includes thrombosis related to the catheter.

The following table provides adverse reactions reported in the adjuvant therapy colon cancer clinical trial (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and infusional 5-fluorouracil/leucovorin arm for events with overall incidences $\geq 5\%$ but with incidences $< 1\%$ NCI grade 3/4 events.

Table 4 - Adverse Reactions Reported in Patients with Colon Cancer receiving Adjuvant Treatment ($\geq 5\%$ of all patients, but with $< 1\%$ NCI Grade 3/4 events)

Table with 3 columns: Adverse Reaction (WHO/PrE), All Grades (%), All Grades (%). Rows include Hematology/Infection, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*.

5.3 Pulmonary Toxicity

Oxaliplatin Injection has been associated with pulmonary fibrosis ($< 1\%$ of study patients), which may be fatal. The combined incidence of cough and dyspnea was 4% (any grade) and $< 1\%$ (grade 3) with no grade 4 events in the Oxaliplatin Injection plus infusional 5-fluorouracil/leucovorin arm compared to 4.5% (any grade) and no grade 3 or 4 and 0.1% (grade 4) events in the infusional 5-fluorouracil/leucovorin alone arm in adjuvant colon cancer patients. In this study, one patient died from eosinophilic pneumonia in the Oxaliplatin Injection combination arm. The combined incidence of cough and dyspnea was 4% (any grade) and $< 1\%$ (grade 3) with no grade 4 events in the irinotecan plus 5-fluorouracil/leucovorin arm of unknown frequency for patients with previously untreated colorectal cancer. In a case of unexplained respiratory symptoms such as non-productive cough, dyspnea, crackles, or radiological pulmonary infiltrates, Oxaliplatin Injection should be discontinued until further pulmonary investigation excludes interstitial lung disease or pulmonary fibrosis.

5.4 Hepatotoxicity

Hepatotoxicity as evidenced in the adjuvant study, by increase in transaminases (57% vs. 5.4%) and alkaline phosphatase (42% vs. 20%) was observed more commonly in the Oxaliplatin Injection combination arm than in the control 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, should be investigated in case of abnormal liver function test results or portal hypertension, which cannot be explained by liver metastases. (See Clinical Trials Experience (6.1)).

5.5 Use in Pregnancy

Pregnancy Category D
Oxaliplatin Injection may cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of Oxaliplatin Injection in pregnant women. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with Oxaliplatin Injection. (See Use in Specific Populations (8.1)).

5.6 Recommended Laboratory Tests

Standard monitoring of the white blood cell count with differential, hemoglobin, platelet count, and blood chemistries (including ALT, AST, bilirubin and creatinine) is recommended before each Oxaliplatin Injection cycle. (See Dosage and Administration (2)).

There have been reports while on study and from post-marketing surveillance of prolonged prothrombin time and INR occasionally associated with hemorrhage in patients who received Oxaliplatin Injection plus 5-fluorouracil/leucovorin while on anticoagulants. Patients receiving Oxaliplatin Injection plus 5-fluorouracil/leucovorin and requiring oral anticoagulants may require closer monitoring.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Serious adverse reactions including anaphylaxis and allergic reactions, neurotoxicity, pulmonary toxicities and hepatotoxicities can occur. (See Warnings and Precautions (5.1)).

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

There have been reports while on study and from post-marketing surveillance of prolonged prothrombin time and INR occasionally associated with hemorrhage in patients who received Oxaliplatin Injection plus 5-fluorouracil/leucovorin while on anticoagulants. Patients receiving Oxaliplatin Injection plus 5-fluorouracil/leucovorin and requiring oral anticoagulants may require closer monitoring.

6.2 ADVERSE REACTIONS

Two hundred and fifty-nine patients were treated in the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination arm of the randomized trial in patients previously untreated for advanced colorectal cancer. (See Clinical Studies (14)). The adverse reaction profile in this study was similar to that seen in other studies and the adverse reactions in this trial are shown in the tables below.

Both 5-fluorouracil and Oxaliplatin Injection are associated with gastrointestinal and hematologic adverse reactions. When Oxaliplatin Injection is administered in combination with 5-fluorouracil, the incidence of these events is increased.

The incidence of death within 30 days of treatment in the previously treated study, regardless of causality, was 5% with the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination, 5% with irinotecan plus 5-fluorouracil/leucovorin, and 3% with Oxaliplatin Injection plus irinotecan. Deaths within 60 days from initiation of therapy were 2.3% with the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination, 5.1% with irinotecan plus 5-fluorouracil/leucovorin, and 3.1% with Oxaliplatin Injection plus irinotecan. The following table provides adverse reactions reported in the previously untreated for advanced colorectal cancer study (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination arm for events with overall incidences $\geq 5\%$ and for grade 3/4 events with incidences $\geq 1\%$.

Table 5 - Adverse Reactions Reported in Patients Previously Untreated for Advanced Colorectal Cancer Clinical Trial ($\geq 5\%$ of all patients and with $\geq 1\%$ NCI Grade 3/4 events)

Table with 5 columns: Adverse Reaction (WHO/PrE), All Grades (%), All Grades (%), All Grades (%), All Grades (%). Rows include Allergic Reaction, Hypersensitivity, Thrombosis, Hypotension, Fatigue, Abdominal Pain, Myalgia, Pain, Vision abnormal, Neuralgia, Skin reaction - hand/foot, Injection site reaction, Nausea, Diarrhea, Vomiting, Stomatitis, Anorexia, Mouth Dryness, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*.

Includes thrombosis related to the catheter.

The following table provides adverse reactions reported in the previously untreated for advanced colorectal cancer study (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination arm for events with overall incidences $\geq 5\%$ but with incidences $< 1\%$ NCI grade 3/4 events.

Table 6 - Adverse Reactions Reported in Patients Previously Untreated for Advanced Colorectal Cancer Clinical Trial ($\geq 5\%$ of all patients but with $< 1\%$ NCI Grade 3/4 events)

Table with 4 columns: Adverse Reaction (WHO/PrE), All Grades (%), All Grades (%), All Grades (%). Rows include Allergic/Immunology, Cardiovascular, Constitutional Symptoms/Pain/Ocular/Visual, Dermatology/Skin, Hematology/Infection, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*.

Includes thrombosis related to the catheter.

The following table provides adverse reactions reported in the previously untreated for advanced colorectal cancer study (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination arm for events with overall incidences $\geq 5\%$ but with incidences $< 1\%$ NCI grade 3/4 events.

Table 7 - Adverse Reactions Reported in Previously Treated Colorectal Cancer Clinical Trial ($\geq 5\%$ of all patients and with $\geq 1\%$ NCI Grade 3/4 events)

Table with 5 columns: Adverse Reaction (WHO/PrE), All Grades (%), All Grades (%), All Grades (%), All Grades (%). Rows include Allergic/Immunology, Cardiovascular, Constitutional Symptoms/Pain/Ocular/Visual, Dermatology/Skin, Hematology/Infection, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*.

Includes thrombosis related to the catheter.

The following table provides adverse reactions reported in the previously treated study, regardless of causality, was 5% with the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination, 5% with irinotecan plus 5-fluorouracil/leucovorin, and 3% with Oxaliplatin Injection plus irinotecan. Deaths within 60 days from initiation of therapy were 2.3% with the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination, 5.1% with irinotecan plus 5-fluorouracil/leucovorin, and 3.1% with Oxaliplatin Injection plus irinotecan. The following table provides adverse reactions reported in the previously untreated for advanced colorectal cancer study (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination arm for events with overall incidences $\geq 5\%$ and for grade 3/4 events with incidences $\geq 1\%$.

Table 8 - Adverse Reactions Reported in Previously Treated Colorectal Cancer Clinical Trial ($\geq 5\%$ of all patients but with $< 1\%$ NCI Grade 3/4 events)

Table with 5 columns: Adverse Reaction (WHO/PrE), All Grades (%), All Grades (%), All Grades (%), All Grades (%). Rows include Allergic/Immunology, Cardiovascular, Constitutional Symptoms/Pain/Ocular/Visual, Dermatology/Skin, Hematology/Infection, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*.

Includes thrombosis related to the catheter.

The following table provides adverse reactions reported in the previously treated study, regardless of causality, was 5% with the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination, 5% with irinotecan plus 5-fluorouracil/leucovorin, and 3% with Oxaliplatin Injection plus irinotecan. Deaths within 60 days from initiation of therapy were 2.3% with the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination, 5.1% with irinotecan plus 5-fluorouracil/leucovorin, and 3.1% with Oxaliplatin Injection plus irinotecan. The following table provides adverse reactions reported in the previously untreated for advanced colorectal cancer study (See Clinical Studies (14)) by body system and decreasing order of frequency in the Oxaliplatin Injection and 5-fluorouracil/leucovorin combination arm for events with overall incidences $\geq 5\%$ and for grade 3/4 events with incidences $\geq 1\%$.

Table 9 - Adverse Reactions Reported in Patients Previously Untreated for Advanced Colorectal Cancer Clinical Trial ($\geq 5\%$ of all patients and with $\geq 1\%$ NCI Grade 3/4 events)

Table with 5 columns: Adverse Reaction (WHO/PrE), All Grades (%), All Grades (%), All Grades (%), All Grades (%). Rows include Allergic/Immunology, Cardiovascular, Constitutional Symptoms/Pain/Ocular/Visual, Dermatology/Skin, Hematology/Infection, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*, Infection normal ANC**, Infection low ANC**, Fever, Hypertension, Hypokalemia, Dehydration, Hypoalbuminemia, Hyponatremia, Urinary frequency, Hepatic/Metabolic/Laboratory/Renal, Hyperkalemia, Hypocalcemia, Anorexia, Dry Skin, Constipation, Diarrhea-obstomy, Gastrointestinal NOS*.

