Oxaliplatin Injection, USP

### Indications and Usage

**Oxaliplatin Injection, USP** is a platinum base medicine. It is used in combination with infusional 5-fluorouracil/leucovorin for the treatment of advanced colorectal cancer.

#### Administration

- **Administer** Oxaliplatin Injection, USP with 2 other chemotherapeutic agents (irinotecan and 5-fluorouracil/leucovorin).
- **Administer** Oxaliplatin Injection, USP by intravenous infusion over 120 minutes.
- **Preclude** concomitant administration of any other chemotherapeutic agents.
- **Monitor** for development of hematologic and non-hematologic toxicities.

### Adverse Reactions

- **Neurologic**
  - Peripheral sensory neuropathy is the most common adverse reaction.
- **Hematologic**
  - Anemia, neutropenia, and thrombocytopenia
- **Gastrointestinal**
  - Diarrhea, nausea, vomiting, and mucositis
- **Hypersensitivity**
  - Rash, hypotension, anaphylaxis
- **Other**
  - Fatigue, fever, infection, and sepsis

### Drug Interactions

- Oxaliplatin Injection, USP increases the exposure to other chemotherapeutic agents, which may affect the dosing requirements of these agents.

### Patient Counseling

- Advise patients to report any adverse reactions promptly.
- Instruct patients to avoid becoming pregnant while receiving treatment with Oxaliplatin Injection, USP.

### Dosage and Administration

**Oxaliplatin Injection, USP** is given as a 22-hour continuous infusion. The initial recommended dose is 130 mg/m² administered as a 22-hour continuous infusion over 120 minutes. The dose should be reduced based on toxicity and efficacy.
Non-Hodgkin's Lymphoma: Oxaliplatin is indicated in combination with 5-fluorouracil (5-FU) and leucovorin (LV) or as a single agent for the treatment of relapsed or refractory indolent non-Hodgkin's lymphoma in patients who have failed two or more prior chemotherapy regimens.

Chemistry:

Oxaliplatin is a monomeric platinum compound that forms interstrand and intrastrand Pt-DNA crosslinks. Crosslinks are formed between the DNA strands at the 1, N7 of guanine. Up to 80% of the platinum is interstrand crosslinked and the remainder is intranuclear. The formation of interstrand crosslinks is concentration and temperature dependent.

The pharmacokinetic parameters of ultrafiltrable platinum have been evaluated in 105 pediatric patients and 531 adults. Oxaliplatin is administered as a 22-hour intravenous (i.v.) infusion. Following administration, the relative amount of platinum in the ultrafiltrable (UF) fraction is less than 0.1% of the dose. Approximately 20% of the dose is retained in the body, with a half-life of 3.1 hours. The UF fraction is rapidly cleared with an elimination half-life of 0.43 hours and t1/2β of 26.2 hours. Individual results may vary. The terminal half-life of ultrafiltrable platinum is dependent upon individual drug chemistry and serum/plasma protein binding.

Clinical Studies:

In patients with metastatic colorectal cancer, superior efficacy was observed in the oxaliplatin plus 5-fluorouracil/leucovorin arm compared to the 5-fluorouracil/leucovorin arm in terms of disease-free survival (DFS) and overall survival (OS) for all stages analyzed. The 2-year disease-free survival (DFS) rate was 39.4% for oxaliplatin plus 5-fluorouracil/leucovorin and 27.5% for 5-fluorouracil/leucovorin. The 2-year overall survival (OS) rate was 62.7% for oxaliplatin plus 5-fluorouracil/leucovorin and 46.1% for 5-fluorouracil/leucovorin.

In a phase III study comparing oxaliplatin plus 5-fluorouracil/leucovorin to irinotecan plus 5-fluorouracil/leucovorin, a higher confirmed overall response rate was observed in the oxaliplatin plus 5-fluorouracil/leucovorin arm compared to the irinotecan plus 5-fluorouracil/leucovorin arm. The median duration of response was also longer in the oxaliplatin plus 5-fluorouracil/leucovorin arm compared to the irinotecan plus 5-fluorouracil/leucovorin arm.

In a phase III study comparing oxaliplatin plus irinotecan to oxaliplatin plus 5-fluorouracil/leucovorin, no differences were observed in terms of DFS and OS.

In a phase III study comparing oxaliplatin plus irinotecan to irinotecan, a higher confirmed overall response rate was observed in the oxaliplatin plus irinotecan arm compared to the irinotecan arm. The median duration of response was also longer in the oxaliplatin plus irinotecan arm compared to the irinotecan arm.

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