Olaratumab: Drug information

(For additional information see "Olaratumab: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Lartruvo

Pharmacologic Category

Antineoplastic Agent, Monoclonal Antibody; Antineoplastic Agent, PDGFR-alpha Blocker

Dosing: Adult

Soft tissue sarcoma: IV: 15 mg/kg on days 1 and 8 every 3 weeks (in combination with doxorubicin) for 8 cycles; after 8 cycles are completed, continue olaratumab (as a single agent) until disease progression or unacceptable toxicity (Tap 2016).

Premedications: On day 1 of cycle 1, premedicate with diphenhydramine (25 to 50 mg IV) and dexamethasone (10 to 20 mg IV) prior to olaratumab.

Note: Dexrazoxane was allowed on day 1 of cycles 5 to 8 to reduce the potential for doxorubicin-related cardiotoxicity (Tap 2016).

Dosing: Renal Impairment

CrCl 30 to 89 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling; however, mild to moderate impairment has no clinically relevant impact on olaratumab pharmacokinetics.

CrCl <30 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment

Mild (total bilirubin within normal limits and AST greater than the upper limit of normal [ULN] or total bilirubin >1 up to 1.5 times ULN and any AST) to moderate (total bilirubin >1.5 up to 3 times ULN and any AST) impairment: There are no dosage adjustments provided in the manufacturer's labeling; however, mild to moderate impairment has no clinically relevant impact on olaratumab pharmacokinetics.

Severe impairment (total bilirubin >3 times ULN and any AST): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Adjustment for Toxicity

Hematologic toxicity: Neutropenic fever/infection or grade 4 neutropenia lasting longer than 1 week:

Withhold olaratumab until the absolute neutrophil count (ANC) is ≥1,000/mm^3 and then resume with the dose permanently reduced to 12 mg/kg.

Infusion reaction:

Grade 1 or 2: Interrupt infusion; after resolution resume with the rate reduced by 50%.

Grade 3 or 4: Discontinue permanently.

Note: Doxorubicin may also require dosage modification.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous [preservative free]:

Lartruvo: 190 mg/19 mL (19 mL); 500 mg/50 mL (50 mL)

Generic Equivalent Available (US) No

Administration

Infuse over 60 minutes. Do not infuse as an IV push or bolus. Flush the IV line with normal saline at the end of infusion. Do not coadminister electrolytes or other medications through the same IV line.

If refrigerated, allow infusion solution to reach room temperature prior to administration. Infusion must be completed within 28 hours of dilution (when stored appropriately; see Storage/Stability).

Hazardous Drugs Handling Considerations

Hazardous agent (meets NIOSH 2016 criteria). This medication is not on the NIOSH (2016) list; however, it meets the criteria for a hazardous drug. Drugs are classified as hazardous based on their properties; the properties of a hazardous drug include one or more of the following characteristics: carcinogenic, teratogenic (or other developmental toxicity), reproductive toxicity, organotoxic at low doses, genotoxic, and/or new agents with structural or toxicity profiles similar to existing hazardous agents.

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and CSTDs are required during administration (NIOSH 2016).

Use **Soft tissue sarcoma:** Treatment (in combination with doxorubicin) of adults with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.

Medication Safety Issues

Sound-alike/look-alike issues:

Olaratumab may be confused with obinutuzumab, ofatumumab, olaparib, omalizumab

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

>10%:

Central nervous system: Fatigue (69%), neuropathy (22%), headache (20%), anxiety (11%)

Dermatologic: Alopecia (52%)

Endocrine & metabolic: Hyperglycemia (52%), hypokalemia (21%), hypophosphatemia (21%), hypomagnesemia (16%)

Gastrointestinal: Nausea (73%), mucositis (53%), vomiting (45%), diarrhea (34%), decreased appetite (31%), abdominal pain (23%)

Hematologic & oncologic: Lymphocytopenia (77%, grades 3/4: 44%), neutropenia (65%, grades 3/4: 48%), thrombocytopenia (63%, grades 3/4: 6%), prolonged partial thromboplastin time (33%, grades 3/4: 5%)

Hepatic: Increased serum alkaline phosphatase (16%)

Neuromuscular & skeletal: Musculoskeletal pain (64%)

Ophthalmic: Xerophthalmia (11%)

Miscellaneous: Infusion related reaction (13% to 14%)

1% to 10%: Immunologic: Development of IgG antibodies (4%; all patients had neutralizing antibodies; however, therapeutic effects of antibodies could not be assessed)

Contraindications

There are no contraindications listed in the manufacturer's labeling.

Warnings/Precautions

Concerns related to adverse effects:

• GI toxicity: Nausea, vomiting, diarrhea, mucositis, and abdominal pain have been reported, with a higher incidence in patients treated with olaratumab and doxorubicin, compared to doxorubicin alone.

• Hematologic toxicity: A higher incidence of grade 3 and 4 lymphopenia and neutropenia have been reported in patients treated with olaratumab and doxorubicin, compared to doxorubicin alone. Thrombocytopenia (all grades) also had a higher incidence in the combination arm.

• Infusion reaction: Olaratumab is associated with infusion reactions; most infusion reactions occurred with the first or second cycle. Grade 3 or higher reactions have occurred, including a fatal

case. Symptoms of infusion reactions have included flushing, dyspnea, bronchospasm, and/or fever/chills; severe cases included hypotension, anaphylactic shock, or cardiac arrest. Premedication with diphenhydramine and dexamethasone is recommended. Monitor for signs/symptoms of infusion reactions during and after infusion (resuscitation equipment should be readily available). May require treatment interruption (followed by rate reduction) or permanent discontinuation.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Pregnancy Implications

Based on its mechanism of action, olaratumab would be expected to cause fetal harm if administered to a pregnant woman. Animal reproduction studies have not been conducted. Adequate contraception during therapy and for 3 months following the last dose is recommended in women of reproductive potential.

Breast-Feeding Considerations

It is not known if olaratumab is excreted in breast milk. Due to the potential for serious adverse reactions in a nursing infant, breast-feeding is not recommended by the manufacturer during therapy and for 3 months following the last dose.

Monitoring Parameters

CBC with differential. Monitor for signs/symptoms of infusion reactions.

Mechanism of Action

Olaratumab is a human (recombinant) IgG1 antibody which expressly binds to platelet-derived growth receptor alpha (PDGFR-α) to prevent binding of PDGF-AA, PDGF-BB, and PDGF-CC and block receptor activation and disrupt PDGF receptor signaling. The PDGF-alpha receptor has a role in cell differentiation, growth, and angiogenesis and has demonstrated antitumor activity in sarcomas (Tap 2016).

Pharmacodynamics/Kinetics

Distribution: V_{ss}: 7.7 L

Half-life, elimination: ~11 days (range: 6 to 24 days)

Pricing: US

Solution (Lartruvo Intravenous)

190MG/19ML (19 mL): $1076.16

500 mg/50 mL (50 mL): $2832.00

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Lartruvo (AT, CZ, DE, DK, EE, FR, HR, LT, LV, NO, PT, SK)

REFERENCES

1. *Lartruvo (olaratumab) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; October 2016.*
2. *Tap WD, Jones RL, Van Tine BA, et al. Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial. Lancet. 2016;388(10043):488-497. [PubMed 27291997]*
3. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed December 27, 2016.*

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