VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Arranon (nelarabine)

Date Developed: 9/3/13 by Albert Reeves MD

Effective Date: 10/22/13

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20, 8/3/21, 2/1/22, 1/31/23

Pharmacologic Category: Antineoplastic Agent, Antimetabolite;

Authorization Criteria: Treatment of relapsed or refractory T-cell acute lymphoblastic leukemia/lymphoma in patients ≥1 year of age following at least 2 chemotherapy regimens

Dosage:

Adult

I.V.: 1500 mg/m^2/dose on days 1, 3, and 5; repeat every 21 days until transplant, disease progression, or unacceptable toxicity.

Children and Adolescents:

IV: 650 mg/m^2/dose (various regimens depending on clinical situation; consult product information)

- **NOTE:** Adequate I.V. hydration recommended to prevent tumor lysis syndrome; allopurinol may be used if hyperuricemia is anticipated.

Major adverse reactions and Black Box Warnings:

>10%:

Cardiovascular: Peripheral edema (15%), edema (11%)

Central nervous system: Fatigue (50%), fever (23%), somnolence (7% to 23%; grades 2-4: 1% to 6%), dizziness (21%; grade 2: 8% adults), headache (15% to 17%; grades 2-4: 4% to 8%), hypoesthesia (6% to 17%; grades 2/3: children 5%, adults 12%), pain (11%)

Dermatologic: Petechiae (12%)

Endocrine & metabolic: Hypokalemia (11%)

Gastrointestinal: Nausea (41%), diarrhea (22%), vomiting (10% to 22%), constipation (21%)

Hematologic: Anemia (95% to 99%; grade 4: 10% to 14%), neutropenia (81% to 94%; grade 4: children 62%, adults 49%), thrombocytopenia (86% to 88%; grade 4: 22% to 32%), leukopenia (38%; grade 4: 7%), neutropenic fever (12%; grade 4: 1%)

Hepatic: Transaminases increased (12%; grade 3: 4%)

Neuromuscular & skeletal: Peripheral neuropathy (12% to 21%; grades 2/3: 11% to 14%), weakness (6% to 17%; grade 4: 1%), paresthesia (4% to 15%; grades 2/3: 3% to 4%), myalgia (13%)

Respiratory: Cough (25%), dyspnea (7% to 20%)

1% to 10%:

Cardiovascular: Hypotension (8%), sinus tachycardia (8%), chest pain (5%)

Central nervous system: Ataxia (2% to 9%; grades 2/3: children 1%, adults 8%), confusion (8%), insomnia (7%), depressed level of consciousness (6%; grades 2-4: 2%), depression (6%), seizure (grade 3: 1% adults; grade 4: 6% children), motor dysfunction (4%; grades 2/3: 2%), amnesia (3%; grade 2: 1%), balance disorder (2%; grade 2: 1%), sensory loss (1% to 2%), aphasia (grade 3: 1%), attention disturbance (1%), cerebral hemorrhage (grade 4: 1%), coma (grade 4: 1%), encephalopathy (grade 4: 1%), hemiparesis (grade 3: 1%), hydrocephalus (1%), intracranial hemorrhage (grade 4: 1%), lethargy (1%), leukoencephalopathy (grade 4: 1%), loss of consciousness (grade 3: 1%), mental impairment (1%), nerve paralysis (1%), neuropathic pain (1%), nerve palsy (1%), paralysis (1%), sciatica (1%), sensory disturbance (1%), speech disorder (1%)

Endocrine & Metabolic: Hypocalcemia (8%), dehydration (7%), hyper-/hypoglycemia (6%), hypomagnesemia (6%)

Gastrointestinal: Abdominal pain (9%), anorexia (9%), stomatitis (8%), abdominal distension (6%), taste perversion (3%)

Hepatic: Albumin decreased (10%), bilirubin increased (10%; grade 3: 7%, grade 4: 2%), AST increased (6%)

Neuromuscular & skeletal: Arthralgia (9%), back pain (8%), muscle weakness (8%), rigors (8%), limb pain (7%), abnormal gait (6%), noncardiac chest pain (5%), tremor (4% to 5%; grade 2: 2% to 3%), dysarthria (1%), hyporeflexia (1%), hypertonia (1%), incoordination (1%)

Ocular: Blurred vision (4%), nystagmus (1%)

Renal: Creatinine increased (6%)

Respiratory: Pleural effusion (10%), epistaxis (8%), pneumonia (8%), sinusitis (7%), wheezing (5%), sinus headache (1%)

Miscellaneous: Infection (5% to 9%)

<1% (Limited to important or life-threatening): Craniospinal demyelination, neuropathy (peripheral) (similar to Guillain-Barré syndrome), opportunistic infection, pneumothorax, progressive multifocal leukoencephalopathy (PML), respiratory arrest, rhabdomyolysis, tumor lysis syndrome

Contraindications

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

Adverse Effects:

Bone marrow suppression; CNS depression; Detection of chronic or past HBV infection requires a risk assessment to determine antiviral prophylaxis requirement; Tumor lysis syndrome Neurotoxicity: **[U.S. Boxed Warning]: Severe neurotoxicity, including mental status changes, severe somnolence, seizure, and peripheral neuropathy (ranging from numbness to motor weakness or paralysis), has been reported. Observe closely for signs and symptoms of neurotoxicity; discontinue if ≥ grade 2. Adverse effects associated with demyelination or similar to Guillain-Barré syndrome (ascending peripheral neuropathies) have also been reported. Neurologic toxicities may not fully return to baseline after treatment cessation.** Neurologic toxicity is dose-limiting. Risk of neurotoxicity may increase in patients with concurrent or previous intrathecal chemotherapy or history of craniospinal irradiation.

References:

1. Berg SL, Blaney SM, Devidas M, et al, "Phase II Study of Nelarabine (Compound 506U78) in Children and Young Adults With Refractory T-Cell Malignancies: A Report from the Children's Oncology Group," *J Clin Oncol*, 2005, 23(15):3376-82. [PubMed 15908649]
2. Commander LA, Seif AE, Insogna IG, et al, "Salvage Therapy With Nelarabine, Etoposide, and Cyclophosphamide in Relapsed/Refractory Paediatric T-Cell Lymphoblastic Leukemia and Lymphoma," *Br J Haematol*, 2010, 150(3):345-51. PMID: 20528871 [PubMed 20528871]
3. DeAngelo DJ, Yu D, Johnson JL, et al, "Nelarabine Induces Complete Remissions in Adults With Relapsed or Refractory T-Lineage Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma: Cancer and Leukemia Group B Study 19801," *Blood*, 2007, 109(12):5136-42. [PubMed 17344466]
4. Gandhi V, Plunkett W, Rodriguez CO Jr, et al, "Compound GW506U78 in Refractory Hematologic Malignancies: Relationship Between Cellular Pharmacokinetics and Clinical Response," *J Clin Oncol*, 1998, 16(11):3607-15. [PubMed 9817282]
5. Gandhi V, Plunkett W, Weller S, et al, "Evaluation of the Combination of Nelarabine and Fludarabine in Leukemias: Clinical Response, Pharmacokinetics, and Pharmacodynamics in

Leukemia Cells," *J Clin Oncol*, 2001, 19(8):2142-52. [PubMed 11304766]
6. Gandhi V, Tam C, O'Brien S, et al, "Phase I Trial on Nelarabine in Indolent Leukemias," *J Clin Oncol*, 2008, 26(7):1098-105. [PubMed 18309944]
7. Gökbuget N, Basara N, Baurmann H, et al, "High Single-Drug Activity of Nelarabine in Relapsed T-Lymphoblastic Leukemia/Lymphoma Offers Curative Option With Subsequent Stem Cell Transplantation," *Blood*, 2011, 118(13):3504-11. [PubMed 21715318]
8. Griggs JJ, Mangu PB, Anderson H, et al, "Appropriate Chemotherapy Dosing For Obese Adult Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline," *J Clin Oncol*, 2012, 30(13):1553-61. [PubMed 22473167]
9. Kisor DF, "Nelarabine: A Nucleoside Analog With Efficacy in T-Cell and Other Leukemias," *Ann Pharmacother*, 2005, 39(6):1056-63. [PubMed 15870141]
10. Kisor DF, Plunkett W, Kurtzberg J, et al, "Pharmacokinetics of Nelarabine and 9-beta-D-Arabinofuranosyl Guanine in Pediatric and Adult Patients During a Phase I Study of Nelarabine for the Treatment of Refractory Hematologic Malignancies," *J Clin Oncol*, 2000, 18(5):995-1003. [PubMed 10694549]
11. Kurtzberg J, Ernst TJ, Keating MJ, et al, "Phase I Study of 506U78 Administered on a Consecutive 5-Day Schedule in Children and Adults With Refractory Hematologic Malignancies," *J Clin Oncol*, 2005, 23(15):3396-403. [PubMed 15908652]
12. National Institute for Occupational Safety and Health (NIOSH), "NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2012." Available at http://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf. Accessed January 21, 2013.

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