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, 2/13/24, 2/18/25

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:

Dosing and frequency vary by protocol and/or treatment phase; refer to specific protocol.

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:

Neurotoxicity: **[US Boxed Warning]:** Severe neurotoxicities, including mental status changes, severe somnolence, seizures, and peripheral neuropathy (ranging from numbness and paresthesias to motor weakness and paralysis), have been reported. Adverse reactions associated with demyelination and ascending peripheral neuropathies similar in appearance to Guillain-Barré syndrome have also been reported. Neurologic toxicities may not fully return to baseline after treatment cessation.

Other: Bone marrow suppression; CNS depression; Tumor lysis syndrome; Renal and/or Hepatic impairment [NOTE: Detection of chronic or past HBV infection

requires a risk assessment to determine antiviral prophylaxis requirements, monitoring, and follow-up. Hepatitis B virus screening recommended

Contraindications

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

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.
13. 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.
14. Hwang JP, Feld JJ, Hammond SP, et al. Hepatitis B virus screening and management for patients with cancer prior to therapy: ASCO provisional clinical opinion update. J Clin Oncol.

2020;38(31):3698-3715.
15. *Winter SS, Dunsmore KP, Devidas M, et al. Safe integration of nelarabine into intensive chemotherapy in newly diagnosed T-cell acute lymphoblastic leukemia: Children's Oncology Group Study AALL0434. Pediatr Blood Cancer. 2015;62(7):1176-1183.*

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Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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			adverse reactions and Black Box Warnings sections. Removed the adverse effect section