Approved Revision: Do Not Implement Until 6/2/21

Nelarabine (Arranon®)

NDC CODE(S) 00078-0683-XX ARRANON 5MG/ML Solution (NOVARTIS)

DESCRIPTION

Nelarabine is a nucleoside metabolic inhibitor whose complete activity of systemic toxicity and cytotoxicity is not fully understood. One pathway of its effectiveness is through demethylation and phosphorylation where it is subsequently converted into ara-GTP. Accumulation of ara-GTP in leukemic blasts allows for its incorporation into DNA which leads to the inhibition of DNA synthesis and cell death.

POLICY

- Nelarabine for the treatment of T-cell acute lymphoblastic leukemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Nelarabine for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma (Adult-Young Adult [AYA] and Adults)

- Patient is 18 years or older (unless otherwise specified); **AND**
  - Patient has not responded to or has relapsed following treatment with two or more chemotherapy regimens; **OR**
  - Used as consolidation therapy as a component of COG AALL0434 regimen (daunorubicin, vincristine, prednisone, and pegaspargase); **AND**
    - Patient is 15 years or older; **AND**
    - Patient is Philadelphia chromosome-negative; **OR**
  - Used for relapsed/refractory disease; **AND**
    - Patient is Philadelphia chromosome-negative; **AND**
      - Used as a single agent; **OR**
      - Used in combination with etoposide and cyclophosphamide; **OR**
    - Patient is Philadelphia chromosome-positive; **AND**
      - Patient is refractory to tyrosine kinase inhibitor therapy (e.g., imatinib, dasatinib, ponatinib, nilotinib, bosutinib, etc.); **AND**
        - Used as a single agent; **OR**
        - Used in combination with etoposide and cyclophosphamide

Pediatric Acute Lymphoblastic Leukemia

- Patient is 1 year or older; **AND**
  - Patient has not responded to or has relapsed following treatment with two or more chemotherapy regimens *(Note: includes T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma)*; **OR**
  - Used as consolidation therapy as a component of COG AALL0434 regimen (daunorubicin, vincristine, prednisone, and pegaspargase); **OR**
  - Used for relapsed or refractory disease in combination with etoposide and cyclophosphamide

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Initial Approval Criteria
- Disease stabilization or improvement as evidenced by a complete response [CR] (i.e., morphologic, cytogenetic or molecular complete response), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: any severe neurologic (central and/or peripheral) adverse reactions, hematologic adverse reactions (leukopenia/anemia/thrombocytopenia/neutropenia), tumor lysis syndrome, etc.

DOSAGE/ADMINISTRATION

INDICATION	DOSE
All indications	Adults 1500 mg/m2 IV on Days 1, 3, & 5 repeated every 21 days Pediatrics 650 mg/m2 IV daily for 5 consecutive days repeated every 21 days *Note: Continue treatment until evidence of disease progression or unacceptable toxicity.*

LENGTH OF AUTHORIZATION

Coverage is provided for six months and may be renewed.

DOSAGE LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

225 billable units per 21 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice

Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Arranon [package insert]. East Hanover, NJ; Novartis Pharmaceuticals; July 2019. Accessed November 2020.
2. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) Nelarabine. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2020.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Lymphoblastic Leukemia. Version 2.2020. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2020.
4. Winter SS, Dunsmore KP, Devidas M, et al. Improved Survival for Children and Young Adults With T-Lineage Acute Lymphoblastic Leukemia: Results From the Children's Oncology Group AALL0434 Methotrexate Randomization. J Clin Oncol. 2018 Oct 10;36(29):2926-2934. doi: 10.1200/JCO.2018.77.7250. Epub 2018 Aug 23.
5. Daniel J. DeAngelo, Daohai Yu, Jeffrey L. Johnson, 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 Jun 15; 109(12): 5136–5142.
6. Lexi-Comp Online. (2020). AHFS DI. Nelarabine. Retrieved January 14, 2021 from Lexi-Comp Online with AHFS.
7. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, November). Nelarabine. Retrieved January 14, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/2/2021

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