PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Koselugo Prior Authorization Policy
- Koselugo™ (selumetinib capsules – AstraZeneca)

REVIEW DATE: 04/10/2024

OVERVIEW

Koselugo, a kinase inhibitor, is indicated for the treatment of **neurofibromatosis type 1** (NF1) in patients ≥ 2 years of age with who have symptomatic, inoperable plexiform neurofibromas.[1]

Koselugo is a mitogen-activated protein kinase kinases 1 and 2 (MEK1/2) inhibitor.[1]

Disease Overview

Neurofibromatoses are a group of tumor suppressor syndromes that predisposes patients to an increased risk of nervous system tumors including neurofibromas, malignant peripheral nerve sheath tumors, and gliomas.[5,6] NF1 is the most common of the neurofibromatoses, occurring in approximately one in 2,500 to 3,000 individuals worldwide.[7,8] NF1 is an autosomal dominant disorder, with 50% of children of affected parents inheriting the mutated NF1 tumor-suppressor gene.[5,7] However, up to 50% of the cases occur spontaneously in patients without a family of NF1.[5-9]

Plexiform neurofibromas are benign nerve sheath tumors that can occur anywhere in the body,[8] affect up to 50% of patients with NF1,[5] and are often present at birth.[7,8] These tumors tend to grow the fastest in the first decade of life,[7,8] and can continue to grow into adolescence and early adulthood.[7] Plexiform neurofibromas may be asymptomatic and only detected with MRI,[5,8] or may cause significant pain,[5,7] disfigurement,[5] bone destruction,[7] and loss of nerve function.[5] Due to the risk of transformation to malignant peripheral nerve sheath tumors, patients with any change in the signs or symptoms of plexiform neurofibromas should be assessed for malignant transformation.[5,8]

Other Uses with Supportive Evidence

In a Phase II, open-label trial, the efficacy of Koselugo was assessed in patients 3 to 21 years of age with recurrent, refractory, or progressive pilocytic astrocytoma with either *KIAA1549-BRAF* fusion or *BRAF V600E* mutation.[2] Koselugo 25 mg/m^2/dose was administered twice daily for up 2 years if the patient did not have progressive disease or unacceptable adverse events. A total of 25 patients were enrolled with a median age of 9.2 years, and 52% were female. A partial response was achieved in 36% of patients, 36% of patients had stable disease, and 28% had disease progression. The 2 year progression-free survival was 70% and 44% of patients have not progressed after a median of 36.4 months of follow-up.

Guidelines

Koselugo is addressed in National Comprehensive Cancer Network (NCCN) guidelines:

- **Central nervous system cancers:** Clinical practice guidelines (version 1.2023 – March 24, 2023) recommend Koselugo for the treatment of recurrent or progressive circumscribed glioma with *BRAF* fusion or *BRAF V600E* activating mutation positive; or neurofibromatosis type 1 mutated glioma, as a single agent.[3,4]
- **Histiocytic Neoplasms:** Clinical practice guidelines (version 1.2024 – March 15, 2024) recommend Koselugo as a single agent for the first-line or subsequent treatment of mitogen-activated protein kinase pathway mutation, no detectable mutation, or testing not available for

multisystem Langerhans cell histocytosis (LCH), single-system lung LCH, multifocal (> 2 lesions) single system bone LCH not responsive to a bisphosphonate, and central nervous system LCH.[10]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Koselugo. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Koselugo is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Neurofibromatosis Type 1.** Approve for 1 year if the patient meets ALL of the following (A and B):
   - **A)** Patient meets ONE of the following (i or ii):
     - **i.** Patient is 2 to 18 years of age; OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient is ≥ 19 years of age; AND
       - **b)** Patient has been previously started on therapy with Koselugo prior to becoming 19 years of age; AND
   - **B)** Prior to starting Koselugo, the patient had symptomatic, inoperable plexiform neurofibromas, according to the prescriber.

Other Uses with Supportive Evidence

2. **Circumscribed Glioma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient meets ONE of the following (i or ii):
     - **i.** Patient is 3 to 21 years of age; OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient is > 21 years of age; AND
       - **b)** Patient has been previously started on therapy with Koselugo prior to becoming 21 years of age; AND
   - **B)** Patient has recurrent, refractory, or progressive disease; AND
   - **C)** Tumor meets ONE of the following (i, ii, or iii):
     - **i.** Tumor is *BRAF* fusion positive; OR
     - **ii.** Tumor is *BRAF V600E* activating mutation positive; OR
     - **iii.** Patient has neurofibromatosis type 1 mutated glioma; AND
   - **D)** The medication will be used as a single agent.

3. **Langerhans Cell Histiocytosis.** Approve for 1 year if the patient meets ALL of the following (A and B):
   - **A)** Patient meets ONE of the following (i, ii, iii, or iv):
     - **i.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has multisystem Langerhans cell histiocytosis; AND
       - **b)** Patient has symptomatic disease or impending organ dysfunction; OR
     - **ii.** Patient has single system lung Langerhans cell histiocytosis; OR

iii. Patient meets ALL of the following (a, b, and c):
- **a)** Patient has single system bone disease; AND
- **b)** Patient has not responded to treatment with a bisphosphonate; AND
  Note: Examples of bisphosphonates include pamidronate and zoledronic acid.
- **c)** Patient has more than 2 bone lesions; OR

iv. Patient has central nervous system disease; AND

B) The medication is used as a single agent.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Koselugo is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Koselugo™ capsules [prescribing information]. Wilmington, DE: AstraZeneca; January 2024.
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3. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 1, 2024. Search term: selumetinib.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on: April 1, 2024.
5. US National Institute of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2020 March 23]. Available at: https://clinicaltrials.gov/ct2/results?cond=&term=selumetinib&cntry=&state=&city=&dist=. Search term: selumetinib.
6. Ly KI, Blakeley JO. The diagnosis and management of neurofibromatosis type 1. *Med Clin N Am*. 2019;103:1035-1054.
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9. Cimino PJ, Gutmann DH. Neurofibromatosis type 1. *Handb Clin Neurol*. 2018;148:799-811.
10. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – March 15, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on: April 1, 2024.