PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 03/26/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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 history 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 5.2024 – March 18, 2025) 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 3.2024 – January 7, 2025) recommend Koselugo as a single agent for the first-line or subsequent treatment of mitogen-activated protein kinase pathway mutation, no other detectable/actionable 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.

- **Koselugo™ (selumetinib capsules – AstraZeneca)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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, iv, or v):
      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 BOTH of the following (a and b):
         a) Patient has single system bone disease; AND
         b) Patient has not responded to treatment with a bisphosphonate; OR
         Note: Examples of bisphosphonates include pamidronate and zoledronic acid.
      iv. Patient has central nervous system disease; OR
      v. Patient has relapsed or refractory disease; AND
   B) The medication is used as a single agent.

CONDITIONS NOT COVERED

- **Koselugo™ (selumetinib capsules – AstraZeneca)**

is(are) considered experimental, investigational or unproven for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Koselugo™ capsules [prescribing information]. Wilmington, DE: AstraZeneca; January 2024.
2. Fangusaro J, Onar-Thomas A, Poussaint TY, et al. Selumetinib in children with *BRAF*-aberrant or neurofibromatosis type 1-associated recurrent, refractory or progressive low-grade glioma: a multi-center Phase II trial. *Lancet Oncol*. 2019;20:1011-1022.
3. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 17, 2025. Search term: selumetinib.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 4 .2024 – January 21, 2005). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on: March 17, 2025.
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.
7. Plotkin SR, Wick A. Neurofibromatosis and Schwannomatosis. *Semin Neurol*. 2018;38:73-85.
8. Hirbe AC, Gutmann DH. Neurofibromatosis type 1: A multidisciplinary approach to care. *Lancet Neurol*. 2014:13:834-843.
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 3.2024 – January 7, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on: March 17, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Circumscribed Glioma:** Pilocytic Astrocytoma condition of approval was revised to Circumscribed Glioma. Patient is > 21 years of age and was started on Koselugo prior to becoming 21 years of age was added as new option for approval. Patient has neurofibromatosis type 1 mutated glioma added as new optional for approval. **Langerhans Cell Histiocytosis:** Added new condition of approval.	04/12/2023
Annual Revision	No criteria changes.	04/10/2024
Annual Revision	**Langerhans Cell Histiocytosis:** Removed requirement that the patient has more than 2 bone lesions. Added option for approval that the patient has relapsed or refractory disease.	03/26/2025