# Koselugo® (selumetinib)
## (Oral)

Document Number: IC-0530

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**Dates Reviewed: 05/2020, 11/2020, 11/2021, 11/2022**

## I. Length of Authorization [5,6,8]

Coverage is provided for 6 months and may be renewed (unless otherwise specified).

CNS Cancer:

- Coverage may be renewed up to a maximum of 26 cycles of treatment.

Histiocytic Neoplasms:

- Coverage may be renewed up to a maximum of 2 years of treatment.

## II. Dosing Limits

**A. Quantity Limit (max daily dose) [NDC Unit]:**

- Koselugo 10 mg capsules: 10 capsules per day
- Koselugo 25 mg capsules: 5 capsules per day

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

CNS Cancer & Histiocytic Neoplasms

- 125 mg daily

Neurofibromatosis Type-1 (NF1)

- 100 mg daily

## III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria [1]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals during treatment (e.g., every 3 months during the first year of treatment and every 6 months thereafter); **AND**

- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with strong or moderate CYP3A4 inducers (e.g., rifampin, efavirenz, carbamazepine, St. John's Wort, etc.)
  - Coadministration with strong or moderate CYP3A4 inhibitors (e.g., fluconazole, itraconazole, erythromycin, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented
  - Coadministration with vitamin E supplementation that exceeds the daily recommended dose or safe limits; **AND**
- Patient does not have severe hepatic impairment (i.e., Child-Pugh C); **AND**
- Patient will have a comprehensive ophthalmic exam prior to initiating therapy and at regular intervals during treatment, and for new or worsening visual changes; **AND**
- Serum creatinine phosphokinase (CPK) will be measured at baseline, periodically during treatment, and as clinically indicated; **AND**
- Treatment will not be used in combination with other MEK inhibitors (e.g., binimetinib, cobimetinib, trametinib, etc.); **AND**

**Neurofibromatosis Type-1 (NF1) † Φ** [1-4,7]

- Patient is at least 2 years of age; **AND**
- Patient has a diagnosis of neurofibromatosis type 1 (NF1) as confirmed by one of the following:
  - Patient has a positive genetic testing for NF1 as evidenced by heterozygous pathogenic variants in the *NF1*-gene
  - Patient meets at least one of the following diagnostic criteria for NF1:
    - Six or more café-au-lait macules (≥ 0.5 cm in pre-pubertal subjects or ≥ 1.5 cm in post-pubertal subjects)
    - Two or more neurofibromas or one plexiform neurofibroma
    - Freckling in the axillary or groin (inguinal) region
    - Optic pathway glioma
    - Two or more Lisch nodules or choroidal abnormalities
    - Distinctive bony lesion (dysplasia of the sphenoid bone, dysplasia or thinning of long bone cortex, anterolateral bowing of the tibia, or pseudarthrosis of a long bone)
    - First-degree relative with NF1; **AND**
- Patient has symptomatic plexiform neurofibromas (PN) (e.g., lesions causing significant morbidity defined by, but not limited to, head and neck lesions that could compromise the airway or great vessels, paraspinal lesions that can cause myelopathy brachial or lumbar plexus lesions that could cause nerve compression and loss of function, lesions that could result in major deformity [e.g., orbital lesions] or are significantly disfiguring, lesions of the extremity that cause limb hypertrophy or loss of function, and painful lesions); **AND**

- Patient has inoperable PN (i.e., PN cannot be completely removed without risk for substantial morbidity due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN)

**Central Nervous System (CNS) Cancers ‡** [5-6]

- Patient has pilocytic astrocytoma; **AND**
- Used as a single agent; **AND**
- Used for BRAF fusion or BRAF V600E activating mutation positive recurrent or progressive disease; **AND**
- Patient has had prior fractionated external beam radiation therapy (EBRT)

**Histiocytic Neoplasms ‡** [5]

- Used as a single agent; **AND**
- Patient has a MAP kinase pathway mutation, or no detectable mutation, or testing is not available; **AND**
- Patient has Langerhans Cell Histiocytosis (LCH); **AND**
  - Patient has multisystem disease with symptomatic or impending organ dysfunction; **OR**
  - Patient has single-system lung disease; **OR**
  - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate and >2 lesions; **OR**
  - Patient has CNS lesions; **OR**
  - Patient has relapsed or refractory disease

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s); Φ Orphan Drug

## IV. Renewal Criteria [1]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: cardiomyopathy, ocular toxicity (e.g., retinal vein occlusion, retinal pigment epithelial detachment, etc.), gastrointestinal toxicity (e.g., severe diarrhea, etc.), skin toxicity (e.g., severe skin rashes, etc.), increased creatine phosphokinase (e.g., rhabdomyolysis, etc.), bleeding, etc.; **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease of ≥ 10% from baseline and is not below the lower limit of normal (LLN); **AND**

- LVEF was obtained within the previous 3 months for ≤ 1 year of treatment; **OR**
- LVEF was obtained within the previous 6 months for > 1 year of treatment

**CNS Cancer** [6]

- Patient has not exceeded a maximum of twenty-six (26) cycles of treatment

**Histiocytic Neoplasms** [5,8]

- Patient has not exceeded a maximum of two (2) years of treatment

## V. Dosage/Administration [1,6,8]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Neurofibromatosis Type-1</td><td>Administer 25 mg/m² orally twice daily until disease progression or unacceptable toxicity.
<table>
<tr><th>Body Surface Area*</th><th>Recommended Dosage</th></tr>
<tr><td>0.55 – 0.69 m²</td><td>20 mg in AM; 10 mg in PM</td></tr>
<tr><td>0.70 – 0.89 m²</td><td>20 mg twice daily</td></tr>
<tr><td>0.90 – 1.09 m²</td><td>25 mg twice daily</td></tr>
<tr><td>1.10 – 1.29 m²</td><td>30 mg twice daily</td></tr>
<tr><td>1.30 – 1.49 m²</td><td>35 mg twice daily</td></tr>
<tr><td>1.50 – 1.69 m²</td><td>40 mg twice daily</td></tr>
<tr><td>1.70 – 1.89 m²</td><td>45 mg twice daily</td></tr>
<tr><td>≥ 1.90 m²</td><td>50 mg twice daily</td></tr>
</table>
* The recommended dosage for patients with a BSA less than 0.55 m² has not been established.<br>Note: reduce the dose to 20 mg/m² orally twice daily for patients with moderate hepatic impairment (Child-Pugh B).</td></tr>
<tr><td>Histiocytic Neoplasms</td><td>Administer 25 mg/m² orally twice daily in a 28-day cycle for up to 2 years in the absence of disease progression or unacceptable toxicity</td></tr>
<tr><td>CNS Cancers</td><td>Administer 25 mg/m² orally twice daily in a 28-day cycle for up to 26 cycles</td></tr>
</table>

## VI. Billing Code/Availability Information

HCPCS Code(s):

- J8999 – Prescription drug oral, chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drugs or biologicals

NDC(s):

- Koselugo 10 mg capsules: 00310-0610-xx
- Koselugo 25 mg capsules: 00310-0625-xx

## VII. References


1. Koselugo [package insert]. Wilmington, DE; AstraZeneca Pharmaceuticals, LP; December 2021. Accessed October 2022.
2. Gross AM, Wolters PL, Dombi E, et al. Selumetinib in Children with Inoperable Plexiform Neurofibromas. N Engl J Med. 2020 Apr 9;382(15):1430-1442. doi: 10.1056/NEJMoa1912735. Epub 2020 Mar 18.
3. Dombi E, Baldwin A, Marcus LJ, et al. Activity of Selumetinib in Neurofibromatosis Type 1-Related Plexiform Neurofibromas. N Engl J Med. 2016 Dec 29;375(26):2550-2560. doi: 10.1056/NEJMoa1605943.
4. Friedman JM. Neurofibromatosis 1. GeneReviews. www.ncbi.nlm.nih.gov/books/NBK11109/ (Accessed September 2021).
5. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) selumetinib. National Comprehensive Cancer Network, 2022. 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 October 2022.
6. Fangusaro J, Onar-Thomas A, Poussaint TY, et al. Selumetinib in paediatric patients with BRAF-aberrant or neurofibromatosis type 1-associated recurrent, refractory, or progressive low-grade glioma: a multicentre, phase 2 trial. Lancet Oncol 2019;20:1011-1022.
7. Legius E, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. Genet Med. 2021 Aug;23(8):1506-1513. doi: 10.1038/s41436-021-01170-5.
8. Allen CE, Eckstein O, Williams PM, et al. Selumetinib in patients with tumors with MAPK pathway alterations: Results from Arm E of the NCI-COG pediatric MATCH trial. J Clin Oncol. 2021;39(suppl 15):10008. doi:10.1200/JCO.2021.39.15_suppl.10008


## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---|---|
| C71.0 | Malignant neoplasm of cerebrum, except lobes and ventricles |
| C71.1 | Malignant neoplasm of frontal lobe |
| C71.2 | Malignant neoplasm of temporal lobe |
| C71.3 | Malignant neoplasm of parietal lobe |
| C71.4 | Malignant neoplasm of occipital lobe |
| C71.5 | Malignant neoplasm of cerebral ventricle |
| C71.6 | Malignant neoplasm of cerebellum |
| C71.7 | Malignant neoplasm of brain stem |

| ICD-10 | ICD-10 Description |
|---|---|
| C71.8 | Malignant neoplasm of overlapping sites of brain |
| C71.9 | Malignant neoplasm of brain, unspecified |
| C72.0 | Malignant neoplasm of spinal cord |
| C72.9 | Malignant neoplasm of central nervous system, unspecified |
| C96.0 | Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis |
| C96.2 | Malignant mast cell neoplasm |
| C96.5 | Multifocal and unisystemic Langerhans-cell histiocytosis |
| C96.6 | Unifocal Langerhans-cell histiocytosis |
| C96.Z | Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue |
| C96.9 | Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified |
| D36.10 | Benign neoplasm of peripheral nerves and autonomic nervous system, unspecified |
| D43.0 | Neoplasm of uncertain behavior of brain, supratentorial |
| D43.1 | Neoplasm of uncertain behavior of brain, infratentorial |
| D43.2 | Neoplasm of uncertain behavior of brain, unspecified |
| D43.4 | Neoplasm of uncertain behavior of spinal cord |
| D43.9 | Neoplasm of uncertain behavior of central nervous system, unspecified |
| Q85.01 | Neurofibromatosis, type 1 |
| Z85.841 | Personal history of malignant neoplasm of brain |

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| **Jurisdiction** | **Applicable State/US Territory** | **Contractor** |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| **Jurisdiction** | **Applicable State/US Territory** | **Contractor** |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |