

Koselugo® (selumetinib) (Oral)

Document Number: IC-0530

Last Review Date: 10/22/2021

Date of Origin: 05/01/2020

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

I. Length of Authorization

Coverage is provided for six months and may be renewed.

II. Dosing Limits

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

- Koselugo 10 mg capsules: 8 capsules per day
- Koselugo 25 mg capsules: 5 capsules per day

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

CNS Cancer

- 125 mg daily

All other indications

- 100 mg daily

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 2 years or older (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; **AND**
- Patient will avoid concomitant therapy with all of the following:
 - Coadministration with strong or moderate CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
 - Coadministration with strong or moderate CYP3A4 inhibitors (e.g., fluconazole, itraconazole, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications; **AND**

- Patient will not receive vitamin E supplementation greater than 100% of the daily recommended dose; **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**
- Patient serum creatinine phosphokinase (CPK) will be measured at baseline and periodically during treatment as clinically indicated; **AND**
- Will not be used in combination with other MEK inhibitors (e.g., binimetinib, cobimetinib, trametinib, etc.); **AND**

Neurofibromatosis Type-1 (NF1) † ⊕¹⁻⁴

- Patient has a confirmed diagnosis of NF1 as defined by either of the following:
 - Patient has positive genetic testing for NF1 as evidenced by heterozygous pathogenic variants in *NF1*-gene; **OR**
 - Patient at least one of the diagnostic criteria for NF1 listed below:
 - Six or more cafe-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 axilla or groin
 - Optic glioma
 - Two or more Lisch nodules
 - A distinctive bony lesion (dysplasia of the sphenoid bone or dysplasia or thinning of long bone cortex)
 - A 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**
- Patients PN are inoperable (i.e., PN could not 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 Cancers ‡⁵⁻⁶

- Patient is at least 18 years or older; **AND**
- Used as single-agent therapy; **AND**
- Used for BRAF fusion or BRAF V600E activating mutation positive recurrent or progressive pilocytic astrocytoma; **AND**
- Patient has had prior fractionated external beam radiation therapy (EBRT)

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

IV. Renewal Criteria ¹

Coverage can 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 the following: cardiomyopathy, ocular toxicities (e.g., retinal vein occlusion or retinal pigment epithelial detachment), severe diarrhea, severe skin rashes, rhabdomyolysis, bleeding, etc. **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease from baseline \geq 10% and is not below the lower limit of normal (LLN)

CNS Cancer ⁶

- Patient has not received more than twenty-six 28-day course treatments

V. Dosage/Administration

Indication	Dose																			
Neurofibromatosis Type-1	Administer 25 mg/m ² , orally on an empty stomach, twice daily until disease progression or unacceptable toxicity.																			
		<table border="1"> <thead> <tr> <th>Body Surface Area*</th> <th>Recommended Dosage</th> </tr> </thead> <tbody> <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>\geq 1.90 m²</td> <td>50 mg twice daily</td> </tr> </tbody> </table>	Body Surface Area*	Recommended Dosage	0.55 – 0.69 m ²	20 mg in AM; 10 mg in PM	0.70 – 0.89 m ²	20 mg twice daily	0.90 – 1.09 m ²	25 mg twice daily	1.10 – 1.29 m ²	30 mg twice daily	1.30 – 1.49 m ²	35 mg twice daily	1.50 – 1.69 m ²	40 mg twice daily	1.70 – 1.89 m ²	45 mg twice daily	\geq 1.90 m ²	50 mg twice daily
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* The recommended dosage for patients with a BSA less than 0.55 m ² has not been established.																				
<u>Note:</u> reduce the dose to 20 mg/m ² twice daily for patients with moderate hepatic impairment.																				
CNS Cancers	Administer 25 mg/m ² twice daily in 28-day courses for up to 26 courses																			

VI. Billing Code/Availability Information

HCPCS code:

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

NDC:

- 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; May 2021. Accessed September 2021.
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, 2021. 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 September 2021.
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. NCT01029101.

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

ICD-10	ICD-10 Description
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.9	Malignant neoplasm of central nervous system, 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: <http://www.cms.gov/medicare-coverage-database/search/advanced-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.
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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
15	KY, OH	CGS Administrators, LLC