Koselugo® (selumetinib)
(Oral)

Document Number: IC-0530

Last Review Date: 05/01/2020
Date of Origin: 05/01/2020
Dates Reviewed: 05/2020

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: 4 capsules per day
- Koselugo 25 mg capsules: 4 capsules per day

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

- 100 mg daily

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 2 years or older; **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 any of the following potential drug-drug interactions:
  - Coadministration with strong or moderate CYP3A4-Inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **OR**
  - Coadministration with strong or moderate CYP3A4 inhibitors (e.g., fluconazole, itraconazole, etc.) if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications; **OR**
  - 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) †/Φ [1,2,4]

- 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 below diagnostic criteria for NF1 listed below:
    - Six or more cafe-au-lait macules (≥ 0.5cm in pre-pubertal subjects or ≥ 1.5 cm in post-pubertal subjects)
    - 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**
- Patient 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)

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s); Φ 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 ≥ 10% and is not below the lower limit of normal (LLN)

V. Dosage/Administration

Indication	Dose
Neurofibromatosis Type-1	Administer 25 mg/m², orally on an empty stomach, twice daily until disease progression or unacceptable toxicity.

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
≥ 1.90 m^2	50 mg twice daily

** The recommended dosage for patients with a BSA less than 0.55 m² has not been established.*

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; April 2020. Accessed April 2020.
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 on April 23, 2020).

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D36.10	Benign neoplasm of peripheral nerves and autonomic nervous system, unspecified
Q85.01	Neurofibromatosis, type 1

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)
15	KY, OH	CGS Administrators, LLC