Original Effective Date: 07/23/2020
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Last P&T Approval/Version: 01/31/2024
Next Review Due By: 01/2025
Policy Number: C19330-A

Koselugo (selumetinib)

PRODUCTS AFFECTED

Koselugo (selumetinib)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Neurofibromatosis type 1 (NF1) plexiform neurofibromas (PN)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. NEUROFIBROMATOSIS TYPE 1 PLEXIFORM NEUROFIBROMAS:
1. Documented diagnosis of Neurofibromatosis type 1 (NF1) plexiform neurofibromas (PN) AND
2. Documentation member has at least one measurable PN, defined as a lesion ≥ 3 cm measured in one dimension

AND

3. Prescriber attests that complete resection of PN is not considered to be feasible without substantial risk or morbidity (e.g., due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN)
AND
4. Prescriber attests that member is able to swallow capsules whole and take medication on an empty stomach including 2 hours prior to administration and 1 hour after
AND
5. Prescriber attests a recent review of member's current medication has been completed and there is no concomitant use of Vitamin E preparations, and strong or moderate CYP3A4 inducers (e.g., butalbital, carbamazepine, rifampin, etc.)
AND
6. Documentation that member is symptomatic (i.e., experiencing pain, motor dysfunction, and visual loss)
AND
7. Prescriber attests to all of the following:
   a. Baseline ophthalmic assessment has been done and prescriber agrees to monitor for ocular toxicities AND
   b. Baseline left ventricular ejection fraction (LVEF) has been assessed and prescriber agrees to monitor LVEF regularly throughout treatment with Koselugo AND
   c. Monitoring for severe skin rashes AND
   d. Member has been counseled regarding how to treat loose stools AND
   e. Member has been counseled not to exceed the recommended daily intake of Vitamin E AND
   f. Baseline creatine phosphokinase (CPK) has been assessed and prescriber agrees to monitor CPK periodically during treatment and as clinically indicated
AND
8. Prescriber attests to (or clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Koselugo (selumetinib) include: avoid concomitant use of strong and moderate CYP3A4 inducers, concomitant use of St. John's wort, pregnancy (including female partners of reproductive potential with male patients)]
AND
9. Documentation member's BSA is at least 0.55 m2

CONTINUATION OF THERAPY:

A. NEUROFIBROMATOSIS TYPE 1 PLEXIFORM NEUROFIBROMAS:

1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance) unless therapy held for toxicity
AND
2. Documentation of positive clinical response as demonstrated by no evidence of disease progression or unacceptable toxicity (See Appendix)
AND
3. Prescriber attests that member continues to be able to swallow capsules whole and take medication on an empty stomach including 2 hours prior to administration and 1 hour after
AND
4. Prescriber attests to all of the following:
   a. Continued ophthalmic assessment to monitor for ocular toxicities AND
   b. Monitoring left ventricular ejection fraction (LVEF) AND
   c. Monitoring for severe skin rashes AND
   d. Member has been counseled how to treat loose stools AND
   e. Member has been counseled not to exceed the recommended daily intake of Vitamin E AND
   f. Monitoring creatine phosphokinase (CPK)

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with an oncologist or a neurologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
2 years of age and older

QUANTITY:
25mg/m2 twice a day (See Appendix)

Maximum Quantity Limits – Minimum quantity of both strengths necessary to make dose

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Antineoplastic - MEK Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Recommended Dosage Based on Body Surface Area

Body Surface Area*	Recommended Dosage
0.55 – 0.69 m2	20 mg in the morning and 10 mg in the evening
0.70 – 0.89 m2	20 mg twice daily
0.90 – 1.09 m2	25 mg twice daily
1.10 – 1.29 m2	30 mg twice daily
1.30 – 1.49 m2	35 mg twice daily
1.50 – 1.69 m2	40 mg twice daily
1.70 – 1.89 m2	45 mg twice daily
≥ 1.90 m2	50 mg twice daily

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

Adverse Reactions requiring permanent discontinuation of Koselugo:

- Cardiomyopathy: Symptomatic decreased LVEF
- Cardiomyopathy: Grade 3 or 4 decreased LVEF
- Ocular Toxicity: Retinal vein occlusion (RVO)
- Gastrointestinal Toxicity: Grade 4 diarrhea
- Gastrointestinal Toxicity: Grade 3 or 4 colitis
- Increased Creatine Phosphokinase (CPK): Rhabdomyolysis

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Neurofibromatosis type 1 (NF1) is a rare, progressive condition caused by a mutation or flaw in the NF1 gene. It occurs in approximately 1 out of 2,600–3,000 infants. About 50% of cases are due to an inherited autosomal dominant genetic disorder, while the other 50% of cases are due to sporadic genetic mutations. Plexiform neurofibromas (PN) are tumors involving the nerve sheaths which can grow anywhere in the body, including the face, extremities, areas around the spine and deep in the body where they may affect organs. NF1 is usually diagnosed in early childhood. It is characterized by changes in skin pigmentation, neurologic and skeletal impairments, and risk for development of benign and malignant tumors throughout life. The risk of developing a cancer is estimated to be about 7%. Between 30% and 50% of patients born with NF1 develop one or more PNs. An Italian study by Maria Masocco in the Orphanet Journal of Rare Diseases (2011) noted the mean age for NF1-associated death was approximately 20 years lower than that for the general population.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Koselugo (selumetinib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Koselugo (selumetinib) include: avoid concomitant use of strong and moderate CYP3A4 inducers, concomitant use of St. John's wort, pregnancy (including female partners of reproductive potential with male patients).

OTHER SPECIAL CONSIDERATIONS:

Verify the pregnancy status of females of reproductive potential prior to initiating Koselugo. Advise females of reproductive potential to use effective contraception during treatment and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Koselugo and for 1 week after the last dose.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

Koselugo CAPS 10MG
Koselugo CAPS 25MG

REFERENCES

1. Koselugo (selumetinib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2021.
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3. Gross AM, Wolters P, Baldwin A, et al. SPRINT: Phase II study of the MEK 1/2 inhibitor selumetinib (AZD6244, ARRY-142886) in children with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN) [Abstract]. J Clin Oncol 2018; 36(Suppl15):10503.
4. Dombi, et al. Activity of Selumetinib in Neurofibromatosis Type 1–Related Plexiform Neurofibromas. NEJM. 2016;375:2550–2560. doi: 10.1056/NEJMoa1605943
5. Boyd, et al. Neurofibromatosis Type 1. J Am Acad Dermatol. 2009;61:1—-16.doi: 10.1016/j.jaad.2008.12.051
6. National Institutes of Health. In NIH trial, selumetinib shrinks tumors, provides clinical benefit for children with NF1. News Release; www.nih.gov. Published March 18, 2020. Accessed April17, 2020.
7. Masocco, et al. Mortality associated with neurofibromatosis type 1: A study based on Italian death certificates (1995-2006). Orphanet J Rare Dis. 2011;6:11. doi: 10.1186/1750-1172-6-11
8. Jensen SE, Patel ZS, Listernick R, et al. Lifespan Development: Symptoms Experienced by Individuals with Neurofibromatosis Type 1 Associated Plexiform Neurofibromas from Childhood into Adulthood. J Clin Psychol Med Settings 2019; 26:259.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Appendix	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Age Restrictions Quantity Appendix Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file