Clinical Policy: Selumetinib (Koselugo)

Reference Number: ERX.SPA.370
Effective Date: 04.10.20
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Selumetinib (Koselugo™) is a mitogen-activated protein kinase enzyme 1/2 inhibitor.

FDA Approved Indication(s)
Koselugo is 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).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Koselugo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Neurofibromatosis Type 1 (must meet all)**:**
1. Diagnosis of NF1;
2. Prescribed by or in consultation with an oncologist or neurologist;
3. Age between 2 and 18 years at start of therapy (*see Appendix F*);
4. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has body surface area ≥ 0.55 m^2;
6. Member has at least one inoperable and measurable PN, defined as a lesion ≥ 3 cm measured in one dimension;
7. Member meets one of the following (a or b):
   a. Positive genetic testing for NF1;
   b. Member has at least one other diagnostic criterion for NF1 (*see Appendix D*);
8. 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);
9. Dose does not exceed 100 mg (4 capsules) per day.

Approval duration: 6 months

B. Glioma (off-label) (must meet all)**:**
1. Diagnosis of WHO Grade 1 or 2 pilocytic astrocytoma;
2. Prescribed by or in consultation with an oncologist;
3. Disease is recurrent or progressive;
4. Documentation of BRAF fusion or BRAF V600E activating mutation;
5. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg (4 capsules) per day.

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Neurofibromatosis Type 1 (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Koselugo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy as evidenced by decreased or maintained volume of PN(s) from baseline;
3. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 100 mg (4 capsules) per day.

Approval duration: 12 months

B. Glioma (off-label) (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Koselugo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg (4 capsules) per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NF1: neurofibromatosis type 1
PN: plexiform neurofibroma
WHO: World Health Organization

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: National Institutes of Health: NF1 Diagnostic Criterion
- Six or more café-au-lait macules (greater than or equal to 0.5 cm in prepubertal subjects or greater than or equal to 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

Appendix E: Recommended Dosage Based on Body Surface Area

Body Surface Area	Recommended Dosage
0.55 – 0.69 m^2	20 mg in the morning and 10 mg in the evening
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

Appendix F: General Information
- FDA approval was based on SPRINT II (NCT01362803): Phase II Stratum 1 clinical trial. Eligible patients were 2-18 years of age with NF1 who had inoperable PN. Study consisted of 50 children ages 2-18, median age 10.2 (3.5-17.4).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NF1	25 mg/m^2 PO BID	100 mg/day

VI. Product Availability
Capsules: 10 mg, 25 mg

VII. References
1. Koselugo Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213756s000lbl.pdfAccessed November 24, 2021.
2. Selumetinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 24, 2021.
3. Dombi E, Baldwin A, Marcus L, et al. Activity of selumetinib in neurofibromatosis type-1 related plexiform neurofibromas. N Engl J Med. 2016; 375(26): 2550-2560.
4. Gross AM, Wolters P, Baldwin A et al. SPRINT: Phase II study of the MEK ½ inhibitor selumetinib (AZD6244, ARRY142886) in children with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN). Journal of Clinical Oncology. 2018; 36(15): 10503. Available from: http://ascopubs.org/doi/abs/10.1200/JCO.2018.36.15_suppl.10503. Accessed January 9, 2020.
5. National Institutes of Health Consensus Development Conference Statement: neurofibromatosis. Bethesda, Md., USA, July 13-15, 1987. Neurofibromatosis 1:172-178, 1988
6. Miller DT, Freedenberg D, Schorry E, et al. Health Supervision for Children With Neurofibromatosis Type 1. Pediatrics. 2019;143(5):e20190660

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	01.21.20	02.20
Drug is now FDA approved - criteria updated per FDA labeling; modified prescriber restriction to indicate that Koselugo can be prescribed by neurologist and oncologist; expanded age restriction; added Appendix E: Recommended Dosage Based on Body Surface Area; references reviewed and updated.	04.21.20	05.20
1Q 2021 annual review: clarified PNs are inoperable as per FDA label; added Appendix F; references reviewed and updated.	11.25.20	02.21
1Q 2022 annual review: added off-label use for low grade glioma per CNS cancers NCCN guidelines version 2.2021; added requirement for use of generic product if available; references reviewed and updated.	11.16.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.