Clinical Policy: Selumetinib (Koselugo)

Reference Number: CP.PHAR.464
Effective Date: 04.10.20
Last Review Date: 02.25
Line of Business: Commercial, HIM, 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 1 year 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.

It is the policy of health plans affiliated with Centene Corporation® 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 1 and 18 years at start of therapy (*see Appendix G*);
4. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member's body surface area is one of the following (a or b):
   a. Request for capsules: ≥ 0.55 m^2;
   b. Request for oral granules: ≥ 0.4 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. If request is for oral granules, documentation supports that member has difficulty swallowing whole capsules;
10. Dose does not exceed both of the following (a and b):
    a. 25 mg/m^2 (up to a maximum of 100 mg) per day;

b. 4 capsules or 14 oral granules per day.

Approval duration: 6 months

B. Off-Label NCCN Compendium Recommended Indications (must meet all):

1. Diagnosis of one of the following (a, b, or c):
   a. Circumscribed glioma that is one of the following (i or ii):
      i. Positive for BRAF fusion or BRAF V600E activating mutation;
      ii. NF-1 mutated;
   b. Pleomorphic xanthoastrocytoma (PXA);
   c. Langerhans cell histiocytosis, and one of the following (i, ii, or iii):
      i. Disease is positive for mitogen-activated protein (MAP) kinase pathway mutation;
      ii. Disease has no detectable/actionable mutation;
      iii. Provider attestation that testing is not available;
2. Prescribed by or in consultation with one of the following (a or b):
   a. For circumscribed glioma or PXA: an oncologist;
   b. For Langerhans cell histiocytosis: a hematologist or oncologist;
3. Prescribed as a single agent;
4. For circumscribed glioma or PXA, disease is recurrent or progressive;
5. For Langerhans cell histiocytosis, failure of one of the following, unless clinically significant adverse effects are experienced or both are contraindicated (a or b):
   a. Cotellic® (cobimetinib);
   b. Mekinist® (trametinib);
   **Prior authorization may be required for Mekinist and Cotellic*
6. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. If request is for oral granules, documentation supports that member has difficulty swallowing whole capsules;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 25 mg/m^2 (up to a maximum of 100 mg) per day;
      ii. 4 capsules or 14 oral granules 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: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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 oral granules, documentation supports that member has difficulty swallowing whole capsules;
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 25 mg/m^2 (up to a maximum of 100 mg) per day;
   b. 4 capsules or 14 oral granules per day.

Approval duration: 12 months

B. Off-Label NCCN Compendium Recommended Indications (must meet all)**:**

1. Currently receiving medication via Centene benefit, 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. If request is for oral granules, documentation supports that member has difficulty swallowing whole capsules;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed both of the following (i and ii):
      i. 25 mg/m^2 (up to a maximum of 100 mg) per day;
      ii. 4 capsules or 14 oral granule capsules per day;
   b. New 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MAP: mitogen-activated protein
NF1: neurofibromatosis type 1
PN: plexiform neurofibroma
PXA: pleomorphic xanthoastrocytoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Langerhans cell histiocytosis		
Cotellic® (cobimetinib)	60 mg (three tablets) PO QD for 21 days, then off for 7 days (28-day cycle)	60 mg/day
Mekinist® (trametinib)	Various	Varies

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Neurofibromatosis 1 Diagnostic Criterion

- A: The diagnostic criteria for NF1 are met in an individual who does not have a parent diagnosed with NF1 if two or more of the following are present:
  - Six or more café-au-lait macules over 5 mm in greatest diameter in prepubertal individuals and over 15 mm in greatest diameter in postpubertal individuals
  - Freckling in axilla or inguinal region

- Two or more neurofibromas of any type or one plexiform neurofibroma
- Optic glioma
- Two or more Lisch nodules
- A distinctive bony lesion (sphenoid dysplasia, anterolateral bowing of the tibia, or pseudarthrosis of a long bone)
- A heterozygous pathogenic NF1 variant with a variant allele fraction of 50% in apparently normal tissue such as white blood cells

- B: A child of a parent who meets the diagnostic criteria specified in A merits a diagnosis of NF1 if one or more of the criteria in A are present

Appendix E: Recommended Dosage of Capsules 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: Recommended Dosage of Oral Granules Based on Body Surface Area

Body Surface Area	Recommended Dosage
0.40 – 0.59 m^2	12.5 mg twice daily
0.60 – 0.69 m^2	15 mg twice daily
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 G: 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. The study consisted of 50 children ages 2-18, median age 10.2 (3.5-17.4). A pediatric extension was granted to include children aged ≥ 1 year based on data from bridging studies comparing the capsule and oral granule formulations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NF1	25 mg/m^2 PO BID Reduce to 20 mg/m^2 PO BID for patients with moderate hepatic impairment (Child-Pugh B). The recommended	100 mg/day

Indication	Dosing Regimen	Maximum Dose
	dosage for use in patients with severe hepatic impairment (Child-Pugh C) has not been established	

VI. Product Availability

- Capsules: 10 mg, 25 mg
- Oral granules (contained within capsules): 5 mg, 7.5 mg

VII. References

1. Koselugo Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2025. https://alexion.com/Documents/koselugo_uspi.pdf. Accessed September 17, 2025.
2. Selumetinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 4, 2024.
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 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. Erratum in: N Engl J Med. 2020 Sep 24;383(13):1290.
5. Legius E, Messiaen L, Wolkenstein P, Pancza P, et al; International Consensus Group on Neurofibromatosis Diagnostic Criteria (I-NF-DC); Huson SM, Evans DG, Plotkin SR. 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.
6. Miller DT, Freedenberg D, Schorry E, et al. Health supervision for children with Neurofibromatosis Type 1. *Pediatrics*. 2019;143(5):e20190660
7. Central Nervous System Cancers version 3.2024. National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed November 4, 2024.
8. Histiocytic Neoplasms version 2.2024. National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed November 4, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: clarified PNs are inoperable as per FDA label; references to HIM.PHAR.21 revised to HIM.PA.154; 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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications.	09.28.22	
1Q 2023 annual review: added off-label use for Langerhans cell histiocytosis per NCCN; modified off-label use for glioma to limit coverage to WHO grade 1 glioma as supported by NCCN; references reviewed and updated.	11.04.22	02.23
1Q 2024 annual review: for glioma, removed restriction to WHO grade 1 as supported by NCCN; added criteria for failure of Mekinist or Cotellic for Langerhans cell histiocytosis per NCCN and updated Appendix B; added approval duration of 6 months and 12 months respectively for initial and continuation criteria to off-label NCCN compendium recommended indications (Section I.B and II.B); updated Appendix D; references reviewed and updated	11.16.23	02.24
1Q 2025 annual review: for all indications, added weight-based limitation (25 mg/m^2) to max dose requirement per PI; for off-label NCCN compendium recommended indications, updated the following per NCCN: added PXA and NF-1 mutated circumscribed glioma as coverable diagnoses; specified that BRAF fusion or BRAF V600E activating mutation applies only to circumscribed glioma and that Langerhans cell histiocytosis must be MAP kinase positive or have no detectable/actionable mutation unless testing is not available; added that Koselugo must be prescribed as a single agent; references reviewed and updated.	11.04.24	02.25
RT4: revised criteria to reflect pediatric extension from age 2 years and older to age 1 year and older and added new dosage form (oral granules) with requirement for body surface area ≥ 0.4 m^2 per PI.	09.17.25	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.