Sample Letter of Medical Necessity for KOSELUGO® (selumetinib)

Capsules for Oral Use

Koselugo® (selumetinib) 10 mg & 25 mg capsules

Payers may request a letter of medical necessity to support coverage of Koselugo. The letter should explain why the drug is medically necessary for the specific patient and may include supporting documentation (eg, medical records, peer-reviewed literature, Prescribing Information, clinical treatment history, etc). The letter may be submitted as part of a prior authorization (PA) request, with the claim form, or in response to a payer's request for additional documentation. The letter should include patient-specific information, be on your letterhead, be signed by the prescriber, and be submitted to a payer to support a PA request or claim for Koselugo.

This sample letter of medical necessity is provided for informational purposes only and is not based on legal advice or official guidance from payers. It is not intended to increase or maximize reimbursement by any payer. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for Koselugo or that any payment received will cover providers' costs.

INDICATION

KOSELUGO® (selumetinib) 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).

IMPORTANT SAFETY INFORMATION

Cardiomyopathy. A decrease in left ventricular ejection fraction (LVEF) ≥10% below baseline occurred in 23% of 74 pediatric patients who received Koselugo in SPRINT. Four percent of patients experienced decreased LVEF below the institutional lower limit of normal (LLN). Grade 3 decreased LVEF occurred in one patient and resulted in dose reduction. All patients with decreased LVEF were asymptomatic and identified during routine echocardiography. Decreased LVEF resolved in 71% of these patients. Decreased LVEF resulting in permanent discontinuation of Koselugo occurred in a pediatric population with NF1 in an expanded access program. The safety of Koselugo has not been established in patients with a history of impaired LVEF or a baseline ejection fraction that is below the institutional LLN.

Assess ejection fraction by echocardiogram prior to initiating treatment, every 3 months during the first year of treatment, every 6 months thereafter, and as clinically indicated. Withhold, reduce dose, or permanently discontinue Koselugo based on severity of adverse reaction. In patients who interrupt Koselugo for decreased LVEF, obtain an echocardiogram or a cardiac MRI every 3 to 6 weeks. Upon resolution of decreased LVEF, obtain an echocardiogram or a cardiac MRI every 2 to 3 months.

ALEXION® AstraZeneca Rare Disease

Please see additional Important Safety Information on **page 4** and **US Full Prescribing Information** for KOSELUGO® (selumetinib).

[John Doe, MD]
[Address]
[City, State ZIP]
[(888) 555-5555]

[Date]
[Contact Name], [Title] [Name of Health Insurance Plan or PBM]
[Address]
[City, State ZIP]

Letter of Medical Necessity for KOSELUGO® (selumetinib)
[Request for Expedited Review Due to Medical Urgency]
Insured: [Name]; Policy Number: [Number]; Group Number: [Number]
Date(s) of service: [Date(s)]

Dear [Contact Name],

I am writing on behalf of my patient, [First Name] [Last Name], to request that [name of health insurance company or Pharmacy Benefit Manager (PBM)] approve coverage for [Patient's First Name] [Patient's Last Name]'s treatment with KOSELUGO® (selumetinib), a kinase inhibitor. 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).

Patient Medical Overview

[First Name] [Last Name] is a[n] [age]-year-old [gender] born [MM/DD/YYYY] who requires treatment with Koselugo after being diagnosed with NF1 PN on [date of diagnosis MM/DD/YYYY]. [Patient's First Name] [Patient's Last Name] has been in my care for NF1 PN since [MM/DD/YYYY].

Medical History (Including Diagnostic Criteria, Clinical Presentations, and Laboratory Results)

[See page 3 for further details] [Provide relevant NF1 PN diagnostic criteria and describe the symptomology related with PN. Describe the severity of your patient's current and historical disease progression based on your medical opinion. Provide all relevant laboratory results. Include specific clinical presentations, relevant patient-specific clinical scenarios demonstrating serious medical need, and previous treatments/management strategies for NF1 PN. Include attestation and/or evidence of the inoperable nature of the PNs, accompanied by a description of any consultation with surgical specialists and relevant chart notes supporting inoperable nature of PNs.]

Treatment Plan

I have prescribed the following, based on the recommended regimen for NF1 PN in the Prescribing Information for Koselugo:
[Describe the patient's prescribed dosage and frequency based on patient's diagnosis, body surface area, etc].

Summary

In my medical opinion, Koselugo is the most appropriate treatment for [Patient's First Name] [Patient's Last Name]'s NF1 PN based on the clinical efficacy and safety data.

Based on the above facts, I am confident you will agree that Koselugo is indicated and medically necessary for this patient. For your convenience, I am enclosing [list enclosures such as supporting clinical documentation, Prescribing Information, copy of patient's health insurance and/or pharmacy benefit card, etc].

If you have any further questions, please feel free to call me at [physician's phone number] to discuss.

Thank you in advance for your immediate attention to this request.

Sincerely,

[Physician's Name], MD
[Physician's Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures [Supporting clinical documentation, Prescribing Information, copy of patient's health insurance and/or pharmacy benefit card, etc]

Medical History (Including Diagnostic Criteria, Clinical Presentations, and Laboratory Results)

Below are some diagnostic criteria, clinical presentations, and laboratory results for NF1 PN—please include any relevant documentation that is applicable to your patient's clinical presentation or medical history as well as applicable laboratory or test results. Add any additional comments on patient's symptoms or clinical presentation.

Diagnostic Criteria for NF1 *(Attached if checked)*[1,2]

☐ (A) Patients who do not have a parent diagnosed with NF1 must satisfy two or more of the following criteria.

- ☐ 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 the axillary or inguinal region
- ☐ Two or more neurofibromas of any type or one PN (magnetic resonance imaging [MRI] or positron emission tomography-computed tomography [PET-CT] scan)
- ☐ Optic pathway glioma (MRI of PET-CT scan)
- ☐ Two or more iris Lisch nodules identified by slit lamp examination or two or more choroidal abnormalities—defined as bright, patchy nodules imaged by optical coherence tomography/near-infrared reflectance imaging
- ☐ A distinctive osseous lesion such as 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 (confirmed by genetic testing)

☐ (B) Patients with a parent diagnosed with NF1 according to (A) must satisfy one or more of the criteria in A.

Clinical Symptoms, Presentations, or Comorbidities

- ☐ Pain
- ☐ Disfigurement
- ☐ Airway compromise
- ☐ Bladder/bowel dysfunction
- ☐ Motor dysfunction
- ☐ Spinal cord compression
- ☐ Vision impairment
- ☐ Other: _____

Laboratory and Other Test Results *(Attached if checked)*

- ☐ Comprehensive ophthalmic examination
- ☐ Left ventricular ejection fraction (LVEF)
- ☐ Creatine phosphokinase (CPK)
- ☐ Pregnancy test for individuals of childbearing potential
- ☐ Other: _____

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Please see Indication & Important Safety Information on **page 1** and **page 4** and **US Full Prescribing Information** for KOSELUGO® (selumetinib).

IMPORTANT SAFETY INFORMATION (continued)

Ocular Toxicity. Blurred vision, photophobia, cataracts, and ocular hypertension occurred in 15% of 74 pediatric patients receiving Koselugo in SPRINT. Blurred vision resulted in dose interruption in 2.7% of patients. Ocular toxicity resolved in 82% of 11 patients. Retinal pigment epithelial detachment (RPED) occurred in the pediatric population during treatment with single agent Koselugo and resulted in permanent discontinuation.

Conduct ophthalmic assessments prior to initiating Koselugo, at regular intervals during treatment, and for new or worsening visual changes. Permanently discontinue Koselugo in patients with retinal vein occlusion (RVO). Withhold Koselugo in patients with RPED, conduct ophthalmic assessments every 3 weeks until resolution, and resume Koselugo at a reduced dose. For other ocular toxicities, withhold, reduce dose, or permanently discontinue Koselugo based on severity of adverse reaction.

Gastrointestinal Toxicity. Diarrhea occurred in 77% of 74 pediatric patients who received Koselugo in SPRINT, including Grade 3 in 15% of patients. Diarrhea resulting in permanent discontinuation occurred in 1.4% of patients. Diarrhea resulting in dose interruption or dose reduction occurred in 15% and 1.4% of patients, respectively. The median time to first onset of diarrhea was 17 days, and the median duration was 2 days.

Advise patients to start an anti-diarrheal agent (eg, loperamide) and to increase fluid intake immediately after the first episode of diarrhea. Withhold, reduce dose, or permanently discontinue Koselugo based on severity of adverse reaction.

Skin Toxicity. Rash occurred in 91% of 74 pediatric patients who received Koselugo in SPRINT. The most frequent rashes included dermatitis acneiform (54%), maculopapular rash (39%), and eczema (28%). Grade 3 rash occurred in 8% of patients. Rash resulted in dose interruption in 11% of patients and dose reduction in 4% of patients. Monitor for severe skin rashes. Withhold, reduce dose, or permanently discontinue Koselugo based on severity of adverse reaction.

Increased Creatine Phosphokinase (CPK). Increased CPK occurred in 76% of 74 pediatric patients who received Koselugo in SPRINT, including Grade 3 or 4 in 9% of patients. Increased CPK resulted in dose reduction in 7% of patients. Increased CPK concurrent with myalgia occurred in 8% of patients, including one patient who permanently discontinued Koselugo for myalgia.

Obtain serum CPK prior to initiating Koselugo, periodically during treatment, and as clinically indicated. If increased CPK occurs, evaluate patients for rhabdomyolysis or other causes. Withhold, reduce dose, or permanently discontinue Koselugo based on severity of adverse reaction.

Increased Levels of Vitamin E and Risk of Bleeding. Koselugo capsules contain vitamin E (10 mg capsules contain 32 mg vitamin E as the excipient, D-alpha-tocopheryl polyethylene glycol 1000 succinate [TPGS], while Koselugo 25 mg capsules contain 36 mg vitamin E as TPGS). Vitamin E can inhibit platelet aggregation and antagonize vitamin K-dependent clotting factors. Daily vitamin E intake that exceeds the recommended or safe limits may increase the risk of bleeding. Supplemental vitamin E is not recommended if daily vitamin E intake (including the amount of vitamin E in Koselugo and supplement) will exceed the recommended or safe limits.

An increased risk of bleeding may occur in patients who are coadministered vitamin-K antagonists or anti-platelet antagonists with Koselugo. Monitor for bleeding in these patients and increase international normalized ratio (INR) monitoring in patients taking a vitamin-K antagonist. Perform anticoagulant assessments more frequently and adjust the dose of vitamin K antagonists or anti-platelet agents as appropriate.

Embryo-Fetal Toxicity. Based on findings from animal studies, Koselugo can cause fetal harm when administered to a pregnant woman. In animal studies, administration of selumetinib to mice during organogenesis caused reduced fetal weight, adverse structural defects, and effects on embryo-fetal survival at approximate exposures >5 times the human exposure at the clinical dose of 25 mg/m^2 twice daily. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Koselugo and for 1 week after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Koselugo and for 1 week after the last dose.

Breastfeeding. Due to the potential for adverse reactions in a breastfed child, advise women not to breastfeed during treatment with Koselugo and for 1 week after the last dose.

Concomitant use of Koselugo with a strong or moderate CYP3A4 inhibitor or fluconazole increased selumetinib plasma concentrations, which may increase the risk of adverse reactions. Avoid coadministration of strong or moderate CYP3A4 inhibitors or fluconazole with Koselugo. If coadministration with strong or moderate CYP3A4 inhibitors or fluconazole cannot be avoided, reduce Koselugo dosage.

Concomitant use of Koselugo with a strong or moderate CYP3A4 inducer decreased selumetinib plasma concentrations, which may reduce Koselugo efficacy. Avoid concomitant use of strong or moderate CYP3A4 inducers with Koselugo.

The most common adverse reactions ≥40% are: vomiting, rash (all), abdominal pain, diarrhea, nausea, dry skin, musculoskeletal pain, fatigue, pyrexia, acneiform rash, stomatitis, headache, paronychia, and pruritus.

References: **1.** Neurofibromatosis. Conference statement. National Institutes of Health Consensus Development Conference. *Arch Neurol*. 1988;45(5):575-578. **2.** Legius E, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. *Genet Med*. 2021;23(8):1506-1513.

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