A Guide to Common Prior Authorization (PA) Criteria for KOSELUGO® (selumetinib)

Koselugo® (selumetinib)
10 mg & 25 mg capsules

For the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN)[1]

Many commercial and public healthcare insurance plans or pharmacy benefit manufacturers (PBMs) require PA or precertification for use of Koselugo for the treatment of pediatric patients 2 years of age and older with NF1 who have symptomatic, inoperable PN.[1] Although requirements vary by plan, there are common criteria that may be used for Koselugo. Please verify the current requirements for Koselugo, including whether a PA is required, with each individual plan or PBM.

PA Process Tips

For personalized educational support on behalf of a specific patient, the patient must be enrolled in OneSource™, Alexion's patient support program, and provide consent for these optional services.

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.

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Common Commercial and Public Healthcare Insurance and PBM Criteria for PA

Below are criteria that may be required by healthcare insurance plans including commercial, Managed Medicaid, and Federal Employees Health Benefits Program (FEHBP), as well as PBMs.

Diagnosis Requirements

Health plans or PBMs typically require confirmation of:

- Diagnosis of NF1[2,3]
- Symptomatic and inoperable PNs

Some health plans or PBMs will require additional details related to the patient's diagnosis.

Age Limitations

- Most health plans or PBMs provide treatment to pediatric patients 2 years of age or older who have been diagnosed with NF1 PN

Some health plans or PBMs have additional age information.

Body Surface Area Requirements

- Patients may be required to have a body surface area ≥0.55m^2

Relevant Lab Results and Testing

Some health plans or PBMs require:

- Documentation (eg, office chart notes, lab results, or other clinical information) supporting that the patient has met all approval criteria

Some health plans or PBMs may require additional testing or lab values.

Additional Information

Health plans or PBMs typically do not mention prescriber requirements, although some may require that Koselugo is prescribed by or in consultation with a neurologist or oncologist.

Some health plans or PBMs will provide additional physician specialty prescribing requirements.

Some health plans or PBMs may provide dosing information or specify quantity limits.

Important Reminder

Health plans or PBMs can have different requirements, so it is important to complete a benefits investigation to understand the key clinical and coverage criteria that apply to each patient given their unique plan.

Medical necessity exceptions may be available even if your patient does not meet the policy criteria.

Reauthorization Criteria

In many cases, after a patient has received a PA, the patient will need a reauthorization (sometimes known as a renewal of authorization) after a specified time period.[4] At minimum, reauthorization criteria may require physician attestation. Documentation/evidence of stability (ie, absence of disease progression) or improvement of the patient on Koselugo may also be required.

Several health plans or PBMs have specific reauthorization criteria. These plans may require that patients demonstrate a positive clinical response defined by at least one of the following: decrease in or maintained reduction in tumor volume; decrease in or maintained reduction in tumor pain; improvement in symptoms from baseline.

Source: Information is based on a review of 2022 coverage and PA criteria for national and large regional US commercial, Federal Employee Program (FEP), Medicare Advantage-Prescription Drug (MA-PD), Managed Medicaid, and Pharmacy Benefit Manager (PBM) plans. Please check with the individual payer for specific coverage information because coverage policies change, and information can vary.

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Common Commercial and Public Healthcare Insurance and PBM Criteria for PA (continued)

Koselugo Dosing Information[1]

Body Surface Area (BSA)*	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

*The recommended dosage for patients with a BSA less than 0.55 m^2 has not been established.

Important Reminder

In order to facilitate a timely review of the PA request, be sure to submit all requisite documentation together with the fully completed PA/precertification form.

Providers are responsible for timely and accurate submission of PA requests. Alexion does not make any representation or guarantee concerning reimbursement or coverage for any service or item.

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.

IMPORTANT SAFETY INFORMATION (continued)

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. KOSELUGO® (selumetinib). Prescribing information. AstraZeneca Pharmaceuticals LP; 2021. **2.** Neurofibromatosis. Conference statement. National Institutes of Health Consensus Development Conference. *Arch Neurol*. 1988;45(5):575-578. **3.** 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. **4.** Drella M. Frequently asked questions about pharmacy prior authorization [blog]. Outsource Strategies International. December 2, 2019. Accessed January 27, 2023. https://www.outsourcestrategies.com/blog/frequently-asked-questions-about-pharmacy-prior-authorization.html

This resource is provided for informational purposes only and is not medical advice or guidance. It is not inclusive of all payer PA or precertification criteria for Koselugo for patients 2 years of age and older with NF1 who have symptomatic, inoperable PN. 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.

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