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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	May 8, 2020
Subject:	Koselugo	**Page:**	1 of 5

Last Review Date: December 13, 2024

Koselugo

Description

Koselugo (selumetinib)

Background
Koselugo (selumetinib) is an inhibitor of mitogen-activated protein kinases 1 and 2 (MEK1/2). MEK1/2 proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway. Both MEK and ERK are critical components of the RAS-regulated RAF-MEK-ERK pathway, which is often activated in different types of cancers. Koselugo inhibits ERK phosphorylation and reduces neurofibroma numbers, volume, and proliferation (1).

Regulatory Status
FDA-approved indication: Koselugo is a kinase inhibitor 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) (1).

Koselugo carries warnings for cardiomyopathy, ocular toxicity, gastrointestinal toxicity, skin toxicity, increased creatinine phosphokinase (CPK), and increased vitamin E levels and risk of bleeding (1).

Cardiomyopathy, defined as a decrease in left ventricular ejection fraction (LVEF) ≥ 10% below baseline, has occurred in patients treated with Koselugo. Ejection fraction should be assessed prior to initiating treatment, every 3 months during the first year of treatment, every 6 months thereafter, and as clinically indicated (1).

Ocular toxicities have also been reported in patients treated with Koselugo. This includes blurred vision, photophobia, cataracts, ocular hypertension, and serious toxicities such as retinal vein occlusion and retinal pigment epithelial detachment. Comprehensive ophthalmic assessments should be conducted prior to initiating Koselugo, at regular intervals during treatment, and for new or worsening visual changes (1).

Koselugo can cause fetal harm when administered to a pregnant woman. Pregnant women should be advised of the potential risk to a fetus. Females of reproductive potential should be advised to use effective contraception during treatment with Koselugo and for 1 week after the last dose. Males with female partners of reproductive potential should be advised to use effective contraception during treatment with Koselugo and for 1 week after the last dose (1).

The safety and effectiveness of Koselugo in pediatric patients less than 2 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Koselugo may be considered **medically necessary** if the conditions indicated below are met.

Koselugo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 2 years of age or older

Diagnosis

Patient must have the following:

Neurofibromatosis Type 1 (NF1)

AND ALL of the following**:**

a. Patient is symptomatic
b. Patient has plexiform neurofibromas (PN) that are inoperable

c. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Koselugo and for 1 week after the last dose
d. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Koselugo and for 1 week after the last dose
e. Baseline ophthalmic assessment has been done and prescriber agrees to monitor for ocular toxicities
f. Baseline left ventricular ejection fraction (LVEF) has been assessed and prescriber agrees to monitor LVEF

Prior – Approval *Renewal* Requirements

Age 2 years of age or older

Diagnosis

Patient must have the following:

Neurofibromatosis Type 1 (NF1)

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Koselugo and for 1 week after the last dose
c. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Koselugo and for 1 week after the last dose
d. Prescriber agrees to monitor for ocular toxicities
e. Prescriber agrees to monitor left ventricular ejection fraction (LVEF)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 720 capsules per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Koselugo (selumetinib) is a kinase inhibitor indicated for the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1). Koselugo carries warnings for cardiomyopathy, ocular toxicity, gastrointestinal toxicity, skin toxicity, increased creatinine phosphokinase (CPK), and increased vitamin E levels and risk of bleeding. Koselugo can cause fetal harm when administered to a pregnant woman. The safety and effectiveness of Koselugo in pediatric patients less than 2 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Koselugo while maintaining optimal therapeutic outcomes.

References

1. Koselugo [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2024.
2. NCCN Drugs & Biologics Compendium® Selumetinib 2024. National Comprehensive Cancer Network, Inc. Accessed on October 24, 2024.

Policy History

Date	Action
May 2020	Addition to PA
June 2020	Annual review
September 2020	Annual review and reference update
June 2021	Annual editorial review
June 2022	Annual review and reference update
June 2023	Annual review and reference update
September 2023	Annual review and reference update
June 2024	Annual review and reference update

September 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.