



KOSELUGO (selumetinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

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) $\geq 10\%$ 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



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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).

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.