Koselugo™
(selumetinib)
10 mg & 25 mg capsules

Koselugo Treatment Initiation Guide

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Contact

Start the Discussion

During your remote or telemedicine appointment, talk to your appropriate patient's family about Koselugo™ (selumetinib):

- Please discuss with your patient the variety of options for appointments, such as telemedicine or local healthcare provider offices. Review the testing required prior to and during treatment with Koselugo, initial treatment plan, and then follow up with the family about ongoing treatment with Koselugo. Virtual and local healthcare appointments are increasingly available in most institutions
- Discuss the overall commitment that will be required of the patient's family in terms of time, initial and periodic testing, monitoring adverse events, number of visits, and frequency of communication with the clinic. Be sure to review the *Warnings and Precautions* in the Koselugo Prescribing Information
- Discuss adverse events that may occur and remind caregivers to report all instances of adverse events to you. Depending on the seriousness of adverse events, a dose reduction, treatment interruption, or discontinuation may be considered
- Review the SPRINT Patient Treatment Journey included in the *Therapy Management Guide* (ask your AstraZeneca Rare Disease Sales Specialist for a copy of this resource) to help patients and caregivers understand the median time to response and onset of adverse events that were reported in the SPRINT study

INDICATION

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).

SELECT 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 were 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, identified during routine echocardiography. It resolved in 71% of patients. Decreased LVEF resulting in permanent discontinuation of Koselugo occurred in a pediatric population with NF1 in an expanded access program.

Assess ejection fraction by echocardiogram prior to starting treatment and periodically during treatment. Withhold, reduce dose, or permanently discontinue Koselugo based on severity of adverse reaction. **For additional details about patient LVEF, see accompanying Important Safety Information.**

Please read additional Important Safety Information on pages 4, 6, and 7. Please see full Prescribing Information, including Patient Information, by clicking here or at KoselugoHCP.com.

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Test

Baseline Exams

- Ensure that proper baseline exams are completed
- Coordinate testing even if it requires working with local healthcare clinics

REQUIRED TESTS BEFORE KOSELUGO IS ADMINISTERED:

Echocardiogram/Cardiac MRI

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 to greater than or equal to the institutional LLN, obtain an echocardiogram or a cardiac MRI every 2 to 3 months or as directed by the cardiologist.

Ophthalmologic Assessments

Conduct comprehensive ophthalmic assessments prior to initiating Koselugo, at regular intervals during treatment, and for new or worsening visual changes. Permanently discontinue Koselugo in patients with 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 the adverse reaction.

CPK Evaluation

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.

Pregnancy

Assess the pregnancy status of females of reproductive age prior to initiating therapy. 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.

CPK=creatine phosphokinase; LLN=lower limit of normal; LVEF=left ventricular ejection fraction; MRI=magnetic resonance imaging; RPED=retinal pigment epithelial detachment; RVO=retinal vein occlusion.

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Support

AstraZeneca Access 360™

Contact Access 360™ at www.MyAccess360.com or 1-844-ASK-A360 to ensure that your patient is able to receive a benefits investigation and AstraZeneca support.

This personal support program aims to:

- Connect patients to affordability programs
- Streamline access and reimbursement for Koselugo

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Prescribe

Pharmacy Options

Prescribe Koselugo and arrange for the patient to receive the product in one of two ways:

Onco360 (Specialty Pharmacy Provider)

— OR —

Your in-house pharmacy via an authorized Specialty Distributor:

- AmerisourceBergen (ASD Healthcare, Oncology Supply)
- Cardinal Health Specialty Distribution
- CuraScript SD
- McKesson Specialty (McKesson Specialty Health, McKesson Plasma and Biologics)

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Track

Treatment Journey

Encourage your patient's family to track their treatment journey.

- Offer them a *Koselugo Treatment Tracking Journal* to record potential adverse reactions (download at **KoselugoHCP.com**)
- Agree upon a schedule and maintain open communication via clinic visits, video chats, phone calls, texts, or other means to monitor treatment
- Encourage families to share their journal notes with you and your staff
- Please refer to the accompanying full Prescribing Information for additional information on the testing requirements prior to and during treatment with Koselugo

Help Your Patients Start Treatment on Koselugo

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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.

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.

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Patient Information:

Initial Treatment Plan ____ weight ____ height ____ BSA m^2

Patient Name

Patient D.O.B.

Gender ☐ male ☐ female ☐ not specified

Primary Language ☐ English ☐ Spanish ☐ Other

Parent/Caregiver Name

Relationship to Patient

Parent/Caregiver Phone Number

Site of Target PN

Volume of PN at Baseline

Symptoms at Baseline:

Previous Surgeries ☐ yes ☐ no

Starting Dose:

CPK Evaluation

Month / Date / Year

Facility/Provider		Baseline Date			Value
Facility/Provider		Exam Date 1			Value
Facility/Provider		Exam Date 2			Value

Echocardiogram/Cardiac MRI

Month / Date / Year

Facility/Provider		Baseline Date			Value
Facility/Provider		Exam Date 1			Value
Facility/Provider		Exam Date 2			Value

Ophthalmologic Assessments

Month / Date / Year

Facility/Provider		Baseline Date			Value
Facility/Provider		Exam Date 1			Value
Facility/Provider		Exam Date 2			Value
Facility/Provider		Exam Date 3			Value
Facility/Provider		Exam Date 4			Value

Pregnancy Test
(females with reproductive potential)

Month / Date / Year

Facility/Provider		Exam Date 1			Value

Exam

Month / Date / Year

Facility/Provider		Baseline Date			Value
Facility/Provider		Exam Date 1			Value

Exam

Month / Date / Year

Facility/Provider		Baseline Date			Value
Facility/Provider		Exam Date 1			Value

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IMPORTANT SAFETY INFORMATION (Cont'd)

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.

Please read additional Important Safety Information on pages 4 and 7. Please see full Prescribing Information, including Patient Information, by clicking here or at KoselugoHCP.com.

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Consider these 5 steps when starting your appropriate patients on Koselugo:

IMPORTANT SAFETY INFORMATION (Cont'd)

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.

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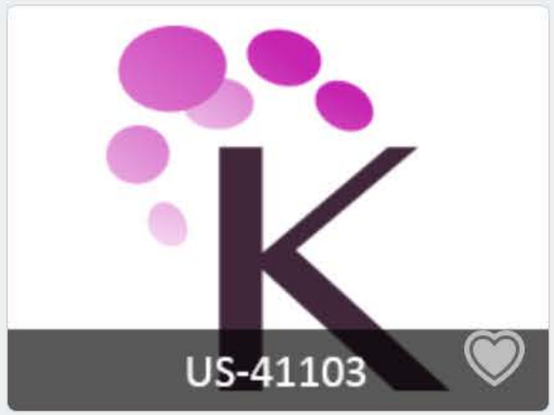

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