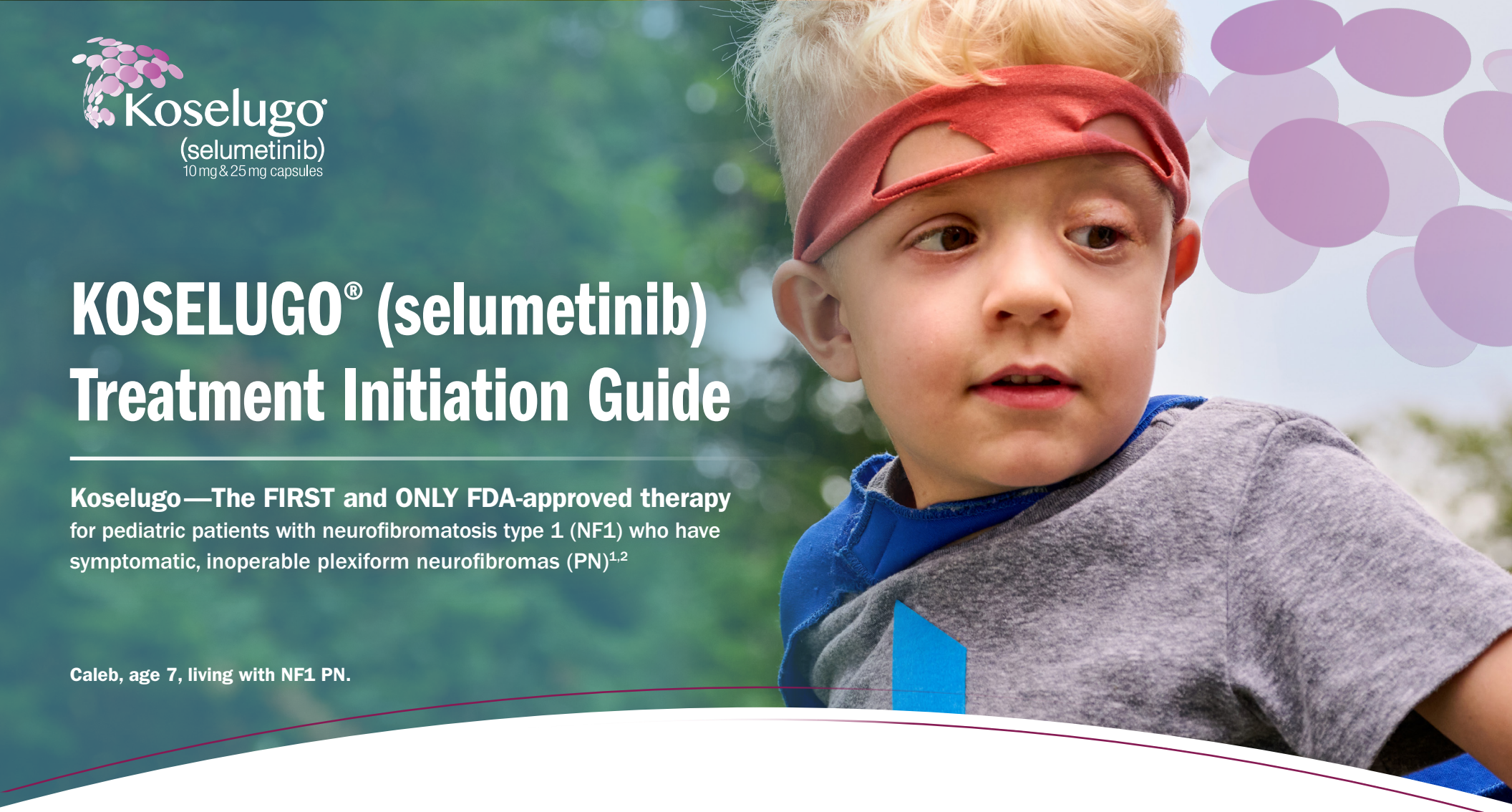
Koselugo
(selumetinib)
10 mg & 25 mg capsules

KOSELUGO® (selumetinib) Treatment Initiation Guide



Koselugo—The FIRST and ONLY FDA-approved therapy for pediatric patients with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN)[1,2]

Caleb, age 7, living with NF1 PN.

FDA=Food and Drug Administration.
Caleb and his family have been compensated by Alexion.

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).

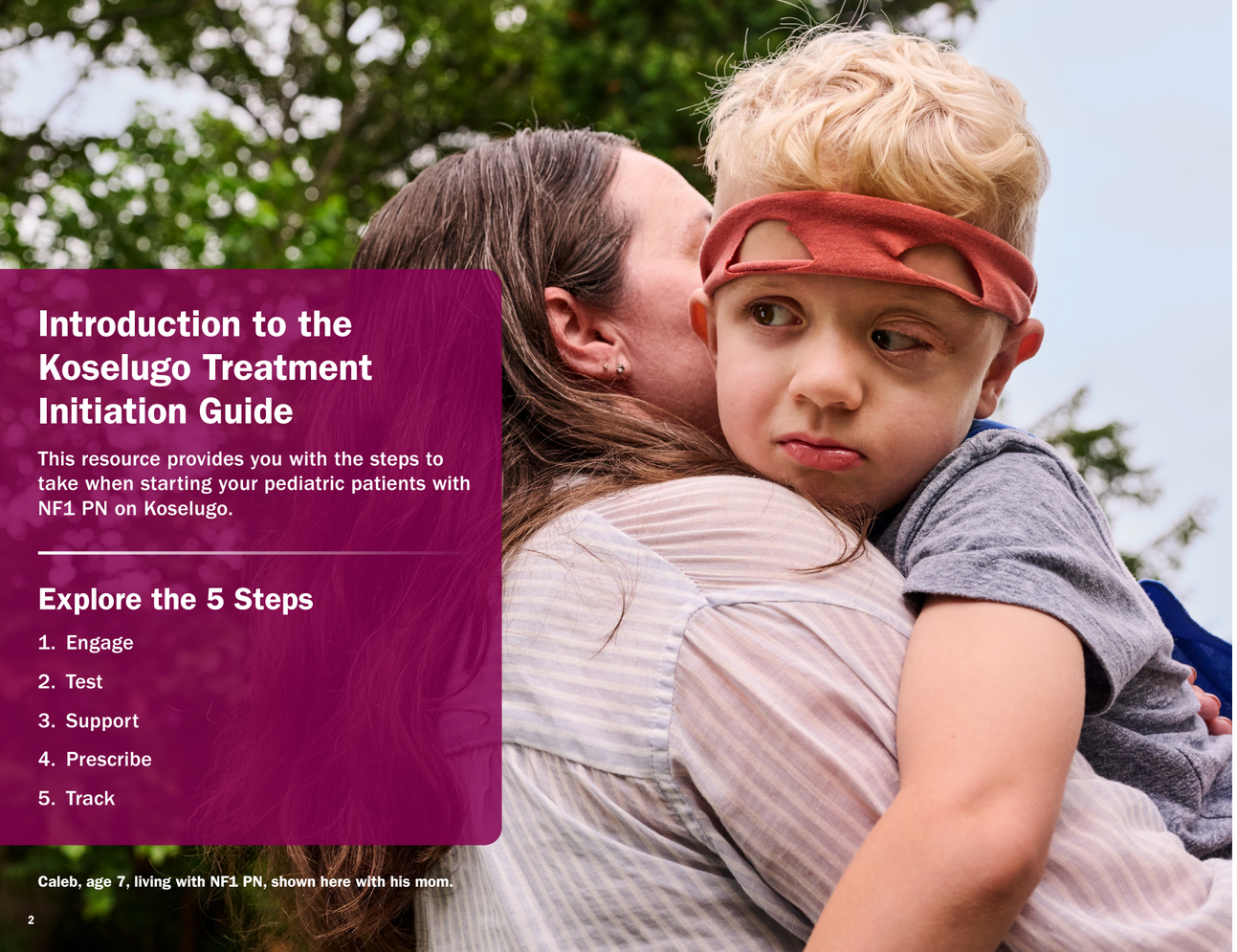
SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS associated with Koselugo include Cardiomyopathy, Ocular Toxicity, Gastrointestinal Toxicity, Skin Toxicity, Increased Creatine Phosphokinase, Increased Levels of Vitamin E and Risk of Bleeding, and Embryo-Fetal Toxicity.

ADVERSE REACTIONS (≥40%) include vomiting, rash (all), abdominal pain, diarrhea, nausea, dry skin, fatigue, musculoskeletal pain, pyrexia, acneiform rash, stomatitis, headache, paronychia, and pruritus.

DRUG INTERACTIONS include strong/moderate CYP3A4 Inhibitors or Fluconazole and CYP3A4 Inducers.

Please see full Important Safety Information on pages 8 and 9 and scan the QR code, or visit bit.ly/KoselugoPI, to see accompanying full Prescribing Information for Koselugo.



Introduction to the Koselugo Treatment Initiation Guide

This resource provides you with the steps to take when starting your pediatric patients with NF1 PN on Koselugo.

Explore the 5 Steps

1. Engage
2. Test
3. Support
4. Prescribe
5. Track

Caleb, age 7, living with NF1 PN, shown here with his mom.

1 Engage

Start the Conversation and Set Expectations

During your appointment, talk to your appropriate patients and their caregivers about Koselugo:

- Discuss what starting on Koselugo looks like, manage expectations, and review the testing requirements. Share the different types of support offered, and the importance of communication and tracking their treatment journey.
- Talk about the overall commitment that will be required of the patients and their families in terms of:
  - **Monitoring adverse reactions**
  - **Number of visits**
  - **Frequency of communication with the clinic**

Set Efficacy Expectations:

Share the **overall response rate,** median time to **onset of response, duration of response,** and other **general efficacy information.**

Set Safety Expectations:

Discuss possible **adverse reactions,** the **median time to onset of ARs,** and dosing adjustments that may be required depending on severity. **Remind caregivers to report all instances of ARs to you.**

Be sure to review *Warnings and Precautions* in the Koselugo Prescribing Information.

AR=adverse reaction.

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Koselugo® (selumetinib) 10 mg & 25 mg capsules

2 Test

Baseline and Routine Exams[1]

Ensure that proper testing is completed prior to starting and during treatment

Testing requirements

REQUIRED TESTING	Before treatment	3 months into treatment	6 months into treatment	9 months into treatment	12 months into treatment	>12 months into treatment
Ejection fraction by echocardiogram	✓	✓	✓	✓	✓	Every 6 months thereafter, and as clinically indicated
Ophthalmic assessment	✓	Conduct comprehensive ophthalmic assessments at regular intervals during treatment and for new or worsening visual changes.				
Serum CPK	✓	Obtain serum CPK periodically during treatment and as clinically indicated.				
Pregnancy test	✓	Advise females of reproductive potential and 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.

Please refer to the accompanying full Prescribing Information for additional information on the testing requirements prior to and during treatment with Koselugo.

2 Test (cont'd)

Additional Evaluation Guidelines[1]:

Ejection Fraction by Echocardiogram: 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.

Ophthalmic Assessment: Permanently discontinue Koselugo in patients with RVO. Withhold Koselugo in patients with RPED, follow up with optical coherence tomography 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.

Serum CPK: 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 Test: Assess the pregnancy status of females of reproductive age. Advise pregnant women of the potential risk to a fetus.

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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3 Support

OneSource™

Koselugo comes with a team.

OneSource is a free, personalized patient support program offered by Alexion.

Patient Education Manager (PEM)

Available to help your patients understand more about Koselugo and NF1.

Case Manager

Helps answer any questions your patients may have about Koselugo, their insurance coverage, and more.

To learn more or to contact a dedicated PEM or Case Manager, patients and caregivers can call **1-888-765-4747,** Monday through Friday, 8:30 AM – 8 PM ET, or visit **AlexionOneSource.com.**

Discover OneSource for yourself. Scan the code to learn more.

4 Prescribe

Onco360

Onco360, Alexion's sole contracted specialty pharmacy, is a nationwide independent specialty pharmacy.

Onco360 supports Koselugo patients during their treatment by providing ongoing, personalized support, including insurance benefit validation, financial assistance sourcing, expert clinical counseling, medication adherence, and side effect management. Additional capabilities include:

- 24/7 access to certified oncology pharmacists and nurses
- Caregiver and patient counseling on administration and adherence
- Coordination with your patients' insurance companies
- Digital capabilities including refill reminders, text messaging, and a mobile application

To learn more about Onco360, visit **https://onco360.com/koselugo-for-nf1/** or call **1-877-662-6633**.

ALEXION ACCESS NAVIGATOR **Visit www.alexionaccessnavigator.com/koselugo to find out more.**

5 Track

Treatment Journey

Encourage patients' families to play an active role in the Koselugo treatment journey.

Refer your patients and their caregivers to **Koselugo.com** for helpful resources

Agree upon a schedule and **maintain open communication** via clinic visits, video chats, phone calls, texts, or other means to monitor treatment

Check in with patients and their caregivers to **monitor progress** and **manage expectations**

Encourage patients and caregivers to **monitor adverse reactions and share their Koselugo journey** updates with you and your staff

It is important to monitor your patients and reassess dosage based on their BSA changes.[1]

BSA=body surface area.

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Indication & Important Safety Information

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

WARNINGS AND PRECAUTIONS

Cardiomyopathy. A decrease in left ventricular ejection fraction (LVEF) ≥10% below baseline occurred in pediatric patients who received Koselugo in SPRINT with some experiencing decreased LVEF below the institutional lower limit of normal (LLN), including one patient with Grade 3. All patients with decreased LVEF were asymptomatic and identified during routine echocardiography. 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. 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.

Gastrointestinal Toxicity. Diarrhea occurred, including Grade 3. Diarrhea resulting in permanent discontinuation, dose interruption or dose reduction occurred. 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. The most frequent rashes included dermatitis acneiform (54%), maculopapular rash (39%), and eczema (28%). Grade 3 rash occurred, in addition to rash resulting in dose interruption or dose reduction. 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, including Grade 3 or 4 resulting in dose reduction. Increased CPK concurrent with myalgia occurred, 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 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 which can inhibit platelet aggregation and antagonize vitamin K-dependent clotting factors. 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 due to increased risk of bleeding. 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) 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 during pregnancy. 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 patients of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with Koselugo and for 1 week after the last dose.

ADVERSE REACTIONS

Common adverse reactions ≥40% include vomiting, rash (all), abdominal pain, diarrhea, nausea, dry skin, musculoskeletal pain, fatigue, pyrexia, acneiform rash, stomatitis, headache, paronychia, and pruritus.

DRUG INTERACTIONS

Effect of Other Drugs on Koselugo

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 with Koselugo. If coadministration 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 with Koselugo.

SPECIAL POPULATIONS

Pregnancy & Lactation. Verify the pregnancy status of patients of reproductive potential prior to initiating Koselugo. Due to the potential for adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with Koselugo and for 1 week after the last dose.

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca 1-800-236-9933 or at https://us-aereporting.astrazeneca.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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Consider These 5 Steps When Initiating Koselugo

Koselugo: The FIRST and ONLY FDA-approved therapy proven to shrink NF1 PN in pediatric patients[1,2]

1 Engage

Start the conversation with your patients and their caregivers about Koselugo

2 Test

Ensure your patients are properly **tested before and during treatment**

3 Support

Provide eligible caregivers the information to get in contact with OneSource™

4 Prescribe

Prescribe Koselugo to your eligible NF1 PN patients

5 Track

Encourage patients and their families to **track their treatment journey** and share their progress with you

Help your patients start and stay on treatment with Koselugo. Learn more at KoselugoHCP.com

NF1=neurofibromatosis type 1; PN=plexiform neurofibromas.

SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS associated with Koselugo include Cardiomyopathy, Ocular Toxicity, Gastrointestinal Toxicity, Skin Toxicity, Increased Creatine Phosphokinase, Increased Levels of Vitamin E and Risk of Bleeding, and Embryo-Fetal Toxicity.

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References: 1. Koselugo. Package insert. AstraZeneca Pharmaceuticals LP. **2.** Koselugo (selumetinib) approved in US for paediatric patients with neurofibromatosis type 1 plexiform neurofibromas. AstraZeneca. Published April 13, 2020. Accessed November 10, 2023. https://www.astrazeneca.com/media-centre/press-releases/2020/koselugo-selumetinib-approved-in-us-for-paediatric-patients-with-neurofibromatosis-type-1-plexiform-neurofibromas.html#

ALEXION AstraZeneca Rare Disease

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