selumetinib (Koselugo™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO193

Description

Selumetinib (Koselugo) is a mitogen-activated protein kinase (MEK) inhibitor for both MEK 1 and 2 that inhibits the phosphorylation of extracellular signal related kinase (ERK) and reducing neurofibroma numbers, volume, and proliferation.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
selumetinib (Koselugo)	10 mg capsules	Neurofibromatosis type 1 (NF1)	120 capsules/30 days
	25 mg capsules		

Initial Evaluation

I. Selumetinib (Koselugo) may be considered medically necessary when the following criteria are met:
   A. Member is between two and 18 years of age; **AND**
   B. Medication is prescribed by, or in consultation with, a neurosurgeon or neurologist; **AND**
   C. Documentation of baseline comprehensive ophthalmic assessments; **AND**
   D. Documentation of baseline assessment of left ventricular ejection fraction (LVEF); **AND**
   E. Member has NOT experienced disease progression (increase in tumor size or tumor spread) while on a MEK inhibitor [e.g., binimetinib (Mektovi®), cobimetinib (Cotellic®), trametinib (Mekinist®)]; **AND**
   F. A diagnosis of **Neurofibromatosis type 1 (NF1)** when the following are met:
      1. Member has inoperable and symptomatic plexiform neurofibromas (PN); **AND**
      2. Symptoms affect quality of life (e.g. pain, impaired physical function, compression of vital organs, respiratory impairment, visual dysfunction, and neurological dysfunction); **AND**
      3. Diagnosis confirmed by genetic testing; **OR**
         i. Member meets at least one criterion:
            a. Six or more light brown spots (café-au-lait macule – CALMs) equal to, or greater than, 5 mm in longest diameter in prepubertal

patients and 15 mm in longest diameter in post pubertal patient; **OR**

b. Freckling in the axillary or inguinal regions (Crowe sign); **OR**
c. Optic glioma (OPG); **OR**
d. Two or more iris hamartomas (Lisch nodules – dome-shaped gelatinous masses developing on the surface of the iris); **OR**
e. A distinctive osseous lesion, such as sphenoid wing dysplasia or long-bone dysplasia (with associated cortical thickening and medullary canal narrowing), with or without pseudoarthrosis; **OR**
f. A first-degree relative (parent, sibling, or child) with NF1.

II. Selumetinib (Koselugo) is considered investigational when used for all other conditions.

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited response to treatment defined by stabilization of disease or decrease in tumor size or tumor spread; **AND**
IV. Member has **NOT** exhibited ophthalmic toxicity (e.g. blurred vision, photophobia, cataracts, or ocular hypertension) nor experienced a decrease of 10% or more below baseline in LVEF during treatment.

Supporting Evidence

I. The safety and efficacy of selumetinib (Koselugo) in pediatric patients two years of age or older with NF1 who have inoperable PN was established in the SPRINT trial (a phase II, open-label, single arm, multicenter clinical trial).
II. Patients older than 18 years of age are being studied in a phase 2, open label, single site clinical trial, with the primary outcome being to determine an objective response rate. The study is still ongoing and therefore has no published safety and efficacy data to support the use in adult patients (those 18 years of age or older).

III. NF1 is a multifaceted disease state and selumetinib (Koselugo) has a complex dosing regimen and safety profile; therefore, it should be prescribed by, or in consultation with, a specialist in the treatment and management of NF1.

IV. Cardiomyopathy, defined as a decrease in left ventricular ejection fraction (LVEF) of 10% or more below baseline, occurred in 23% of the 74 pediatric patients who received selumetinib (Koselugo) in the clinical trial. The safety and efficacy, of use in those with a history of impaired LVEF or a baseline ejection fraction that is below the institutional LLN, has not been established.

V. Blurred vision, photophobia, cataracts, and ocular hypertension occurred in 15% of 74 pediatric patients receiving selumetinib (Koselugo). Blurred vision resulted in dose interruption in 2.7% of patients. Ocular toxicity resolved in 82% of 11 patients. Comprehensive ophthalmic assessments prior to initiating, and at regular intervals during treatment, for new or worsening visual changes is recommended.

VI. There is no published data from a head-to-head study between selumetinib (Koselugo) and other MEK inhibitors [e.g., binimetinib (Mektovi®), cobimetinib (Cotellic®), trametinib (Mekinist®)] to show effectiveness for the treatment of pediatric patients two years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).
There is no data to show one MEK inhibitor could overcome common mechanisms of resistance of MEK inhibitors.

VII. The safety and efficacy of selumetinib (Koselugo) was evaluated in patients with NF1 who have inoperable (defined as a PN that could not be completely removed without risk for substantial morbidity due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN) and symptomatic [defined as PNs that may located around the orbit, face, upper and lower limbs, back, thorax, abdomen, neck brachial plexus and/or lumbosacral plexus, which result in clinical symptoms such as disfigurement, motor dysfunction (weakness and restricted range of motion), pain, respiratory impairment, visual dysfunction, and neurological dysfunction] PNs.

VIII. Per the American Academy of Pediatrics, National Institutes of Health (NIH) consensus development conference regarding NF1, to establish a diagnosis of NF1, two out of seven criteria have to have been met: **1.** Six or more light brown spots on skin (café-au-lait macule – CALMs) equal to, or greater than, 5 mm in longest diameter in prepubertal patients and 15 mm in longest diameter in post pubertal patient. **2.** Two or more neurofibromas of any type or 1 plexiform neurofibroma. **3.** Freckling in the axillary or inguinal regions (Crowe sign). **4.** Optic glioma (OPG). **5**. Two or more iris hamartomas (Lisch nodules – dome-shaped gelatinous masses developing on the surface of the iris). **6**. A distinctive osseous lesion, such as sphenoid wing dysplasia (partial or complete absence of the greater wing of the sphenoid) or long-bone dysplasia (with associated cortical thickening and medullary canal narrowing), with or without pseudoarthrosis (unsuccessful spinal fusion). **7.** A first-degree relative (parent, sibling, or child) with NF1

A. NF1 genetic testing may be performed for purposes of diagnosis, but if a child fulfills diagnostic criteria for NF1, molecular genetic confirmation is usually unnecessary. Molecular diagnosis of NF1 is available based on DNA analysis for a pathogenic variant in the NF1 gene. Only 4 genotype-phenotype correlations have been established (deletion of the entire NF1 gene, specific 3-base deletion in exon 22, Amino acid substitution at codon 1809, some missense or splicing variants are associated with "spinal NF1,").

Investigational or Not Medically Necessary Uses

I. Selumetinib (Koselugo) has not been FDA-approved, or sufficiently studied for safety and efficacy for other conditions except neurofibromatosis type 1 (NF1) with inoperable PNs.

References

1. Koselugo [Prescribing Information]. AstraZeneca Pharmaceuticals LP: Wilmington, DE. April 2020.
2. David T. Miller, MD, PhD, FAAP, Debra Freedenberg, MD, PhD, FAAP, Elizabeth Schorry, MD, et al. American Academy of Pediatrics (AAP) COUNCIL ON GENETICS, AAP AMERICAN COLLEGE OF MEDICAL GENETICS AND GENOMICS. Health Supervision for Children with Neurofibromatosis Type 1. Pediatrics. May 2019. 143(5). e20190660
3. Andrea M. Gross, M.D., Pamela L. Wolters, Ph.D., Eva Dombi, M.D., et al. Selumetinib in Children with Inoperable Plexiform Neurofibromas. N Engl J Med 2020; 382:1430-1442.
4. National Cancer Institute (NCI). MEK 1/2 Inhibitor Selumetinib (AZD6244 Hydrogen Sulfate) in Adults With Neurofibromatosis Type 1 (NF1) and Inoperable Plexiform Neurofibromas. ClinicalTrials.gov NCT02407405
5. Ly KI, Blakeley JO. The Diagnosis and Management of Neurofibromatosis Type 1. Med Clin North Am. Nov 2019; 103(6):1035-1054
6. Boyd, K. P., Korf, B. R., & Theos, A. Neurofibromatosis type 1. Journal of the American Academy of Dermatology. 2009. 61(1), 1–16

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	08/2020