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Coverage Policy Number **IP0038**

Selumetinib

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Overview

This policy supports medical necessity review for selumetinib (**Koselugo**™) for non-oncology uses. The use of selumetinib (Koselugo) for oncology uses is addressed in a separate coverage policy. Please refer to the related coverage policy link above (Oncology Medications).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Selumetinib (Koselugo) is considered medically necessary for the treatment of Neurofibromatosis Type 1 when the individual meets ALL of the following criteria:

1. **ONE** of the following (A or B):
   A. 2 to 18 years of age
   B. 19 years of age or older AND has been previously started on therapy with Koselugo prior to becoming 19 years of age

2. Documentation of symptomatic, inoperable plexiform neurofibromas prior to starting Koselugo

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of Selumetinib (Koselugo) is considered medically necessary for Neurofibromatosis Type 1 when initial criteria are met AND benficial response is demonstrated as determined by the prescriber.

Authorization Duration

Initial approval duration: up to 12 months

Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other non-oncology use is considered experimental, investigational, or unproven.

Background

Overview
Koselugo, a kinase inhibitor, is indicated for the treatment of pediatric patients ≥ 2 years of age with **neurofibromatosis type 1** (NF1) who have symptomatic, inoperable plexiform neurofibromas.[1]

Koselugo is a mitogen-activated protein kinase kinases 1 and 2 (MEK1/2) inhibitor.[1]

Disease Overview
Neurofibromatoses are a group of tumor suppressor syndromes that predisposes patients to an increased risk of nervous system tumors including neurofibromas, malignant peripheral nerve sheath tumors, and gliomas.[5,6] NF1 is the most common of the neurofibromatoses, occurring in approximately one in 2,500 to 3,000 individuals worldwide.[7,8] NF1 is an autosomal dominate disorder, with 50% of children of affected parents inheriting the mutated NF1 tumor-suppressor gene.[5,7] However, up to 50% of the cases occur spontaneously in patients without a family history of NF1.[5-9]

Plexiform neurofibromas are benign nerve sheath tumors that can occur anywhere in the body,[8] affect up to 50% of patients with NF1,[5] and are often present at birth.[7,8] These tumors tend to grow the fastest in the first decade of life,[7,8] and can continue to grow into adolescence and early adulthood.[7] Plexiform neurofibromas may be asymptomatic and only detected with MRI,[5,8] or may cause significant pain,[5,7] disfigurement,[5] bone destruction,[7] and loss of nerve function.[5] Due to the risk of transformation to malignant peripheral nerve sheath tumors, patients with any change in the signs or symptoms of plexiform neurofibromas should be assessed for malignant transformation.[5,8]

Other Uses with Supportive Evidence
In a Phase II, open-label trial, the efficacy of Koselugo was assessed in patients 3 to 21 years of age with recurrent, refractory, or progressive pilocytic astrocytoma with either *KIAA1549-BRAF* fusion or *BRAF V600E* mutation.[2] Koselugo 25 mg/m^2/dose was administered twice daily for up 2 years if the patient did not have progressive disease or unacceptable adverse events. A total of 25 patients were enrolled with a median age of 9.2 years, and 52% were female. A partial response was achieved in 36% of patients, 36% of patients had stable disease, and 28% had disease progression. The 2 year progression-free survival was 70% and 44% of patients have not progressed after a median of 36.4 months of follow-up.

Guidelines
The National Comprehensive Cancer Network central nervous system cancers (version 2.2021 – September 8, 2021) clinical practice guidelines recommend Koselugo for the treatment of *BRAF* fusion or *BRAF V600E* activating mutation positive recurrent or progressive pilocytic astrocytoma, as a single agent.[3,4]

References

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6. Ly KI, Blakeley JO. The diagnosis and management of neurofibromatosis type 1. *Med Clin N Am*. 2019;103:1035-1054.
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