Koselugo (selumetinib)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Koselugo (selumetinib) policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PNs).

POLICY

Criteria for Initial Approval

A. Koselugo (selumetinib) may be considered **medically necessary** when the following criteria is met:
   1. The member is 2 years of age or older
   2. Must be prescribed by, or in consultation with, an oncologist, hematologist, neurologist, or geneticist
   3. Member has a confirmed diagnosis of neurofibromatosis type 1 (NF1)
   4. The member has at least one symptomatic, inoperable plexiform neurofibroma (PN), as defined by all of the following:
      - The member is experiencing functional impairment or significant morbidity related to the PN (e.g. motor dysfunction, airway dysfunction, bladder or bowel dysfunction, visual impairment, pain, disfigurement)
      - PN can 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

Approval will be for **6 months.**

Continuation of Therapy

A. The continued treatment of Koselugo (selumetinib) may be considered **medically necessary** for the treatment of patients with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas when the following criteria is met:
   1. There is no evidence of disease progression
   2. The member has experienced a positive clinical response to therapy as defined by at least one of the following:
      - Decrease in or maintained reduction in tumor volume
      - Decrease in or maintained reduction in tumor pain
      - Improvement in symptoms from baseline

Approval will be for **12 months.**

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

4 capsules per day

CLINICAL RATIONALE

Koselugo (selumetinib) is a kinase inhibitor that targets mitogen-activated protein kinase (MAPK) 1 and 2 (MEK1/2) and 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). MEK is a critical component of the RAS-regulated RAF-MEK-ERK pathway, which is often activated in different types of cancers.

NF1 is an autosomal dominant genetic disorder, affecting approximately 1 in 3,000 individuals, although as many as 50% of cases may result from spontaneous mutations. NF1 arises from loss-of-function variants in the tumor-suppressor gene NF1 and is characterized by changes in skin pigmentation, other nontumor manifestations, and growth of tumors along nerves in the skin, brain, and other areas of the body. PNs are benign nerve sheath tumors that typically present in early childhood, can be asymptomatic or cause pain and morbidity due to compression of adjacent structures. Persistent pain at the site of the PN may indicate transformation into a malignant peripheral nerve sheath tumor, which along with cardiovascular complications, are the major causes of reduced life expectancy in people with NF1.

PNs occur in up to 50% of people with NF1. While approximately 50% occur in the head and neck area, PNs can occur in any area of the body, causing substantial complications such as disfigurement, motor dysfunction, airway obstruction, vision obstruction, and bowel and bladder dysfunction. Management has traditionally been surgical, as PNs are not radiosensitive, and only limited benefit has been seen with chemotherapy; however, PNs are usually difficult to remove in their entirety due to interdigitation into normal tissues and peripheral nerves.

Koselugo was studied in the Phase 1/2 clinical trial, SPRINT, which was divided into two strata, one for patients with at least one neurofibroma-related complication, and the second for patients with no clinically significant complications but the potential for the development of a complication. The FDA approval of Koselugo was based upon results from the SPRINT Phase 2 Stratum 1 open-label, multicenter, single arm trial where patients were required to have NF1 with inoperable PN defined as one 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. Patients were also required to have significant morbidity related to the target PN. The was to confirm the objective response rate of plexiform neurofibromas to selumetinib (primary objective) and to assess whether treatment was associated with clinical benefit (key secondary objectives). An objective response rate which was defined as the percentage of patients with a confirmed complete or partial response of ≥ 20% tumor volume reduction.

Of the fifty pediatric patients (median age, 10.2 years; range, 3.5 to 17.4) included in the Stratum 1 study, 35 patients (70%) had a confirmed partial response and 28 (56%) of these patients had a durable response (lasting ≥1 year). The median change in neurofibroma volume at best response was −27.9% (range, −55.1 to 2.2). The median time to first response and best response were 8 and 16 cycles, respectively. The median progression-free survival (PFS) was not reached, but at 3 years the PFS rate was 84% compared with 15% in an NCI natural-history study of age-matched controls with NF1. Patients also showed reduced pain and improved functioning.

Adverse drug reactions in pediatric patients receiving selumetinib were frequent and varied. Serious adverse events occurred in 24% of patients; those occurring in two or more patients were anemia, hypoxia and diarrhea. Permanent discontinuation resulting from adverse events occurred in 12% of patients, and included increased creatinine, weight gain, diarrhea, paronychia, malignant peripheral nerve sheath tumor, acute kidney injury, and skin ulcer. Dose interruptions as a result of adverse reactions occurred in 80% of patients while dose reductions after adverse events occurred in 24% of patients, and those occurring in more than 5% of patients included vomiting, paronychia, diarrhea, nausea, abdominal pain, rash, skin infection, influenza-like illness, pyrexia and weight gain. The most common adverse reactions reported in ≥ 40% of patients were: vomiting, abdominal pain, rash, blood creatine phosphokinase increased, diarrhea, nausea, dry skin, asthenic events, fatigue, musculoskeletal pain, pyrexia, acneiform rash, hypoalbuminemia, and stomatitis. Long-term safety evaluations are continuing as a part of this trial.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

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POLICY HISTORY

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