selumetinib (Koselugo™)

Policy # 00722
Original Effective Date: 12/14/2020
Current Effective Date: 12/14/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider selumetinib (Koselugo™)‡ for the treatment of neurofibromatosis type 1 to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for selumetinib (Koselugo) will be considered when the following criteria are met:

- Patient has a diagnosis of neurofibromatosis type 1; AND
- Patient is between 2-18 years of age; AND
- Patient has at least one plexiform neurofibroma (PN) that meets BOTH of the following:
    - Causes significant morbidity (e.g., disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment, bladder/bowel dysfunction); AND
    - Cannot be removed completely with surgery (e.g., risk for substantial morbidity due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN).

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of selumetinib (Koselugo) when patient selection criteria are not met to be **investigational.***

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Background/Overview

Koselugo is an oral kinase inhibitor indicated for the treatment of pediatric patients 2 years of age an older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas. It works by inhibiting the mitogen-activated protein kinases 1 and 2 (MEK1/2) and should be given twice daily at a dose of 25 mg/m^2. Adverse events with this treatment were common in the clinical trial and included vomiting, rash, abdominal pain, diarrhea, musculoskeletal pain, and others. However, there is currently no alternative treatment for these patients and the discontinuation rate in the clinical trial was low (12%).

NF1 is the most common of the neurofibromatoses, a group of tumor suppressor syndromes that predispose patients to an increased risk of nervous system tumors including neurofibromas, malignant peripheral nerve sheath tumors, and gliomas. Clinical features of NF1 include skin fold freckling, distinctive osseous lesions, optic pathway gliomas, neurofibromas (including plexiform neurofibromas), and others with a variety of features present in each patient. Up to 50% of patients with NF1 have plexiform neurofibromas which are benign nerve sheath tumors that can occur anywhere in the body and are often present at birth. These tumors tend to grow the fastest in the first decade of life and can continue to grow into adolescence and early adulthood. Plexiform neurofibromas may be asymptomatic and only detected with MRI, or may cause significant pain, disfigurement, bone destruction, and loss of nerve function. While surgery is indicated for the treatment of symptomatic plexiform neurofibromas, this approach is often challenging due to the involvement of underlying neurological structures. Prior to the approval of Koselugo, there were no drugs approved for the treatment of plexiform neurofibromas and no treatment guidelines are available to guide the medical management of them. However, early stage studies have been conducted with pegylated interferon α-2b, imatinib, and sirolimus.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Koselugo is approved for the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 who have symptomatic, inoperable plexiform neurofibromas.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Koselugo was evaluated in SPRINT Phase II Stratum 1, an open-label, multicenter, single arm trial. Eligible patients (n=50) were required to have neurofibromatosis type 1 with inoperable PN, 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. Patients were also required to have significant morbidity related to the target PN. Morbidities that were present in ≥20% of patients included disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment, and bladder/bowel dysfunction. Patients received Koselugo 25 mg/m^2 orally twice daily until disease progression or unacceptable toxicity.

The major efficacy outcome measure was overall response rate (ORR), defined as the percentage of patients with a complete response (defined as disappearance of the target PN) or confirmed partial response (defined as ≥20% reduction in PN volume confirmed at a subsequent tumor assessment within 3-6 months). Tumor response was evaluated at baseline and while on treatment after every 4 cycles for 2 years, and then every 6 cycles. The overall response rate was found to be 66% which included 0 complete responses and 33 partial responses.

References

1. Koselugo [package insert]. AstraZeneca Pharmaceuticals LP. Wilmington, DE. May 2020.
2. Koselugo Drug Evaluation. Express Scripts. April 2020.

Policy History

Original Effective Date: 12/14/2020
Current Effective Date: 12/14/2020
11/05/2020 Medical Policy Committee review

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11/11/2020 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 11/2021

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.