vismodegib (Erivedge®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO198

Description

Vismodegib (Erivedge) is an orally administered hedgehog pathway inhibitor.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
vismodegib (Erivedge)	150 mg capsules	Basal cell carcinoma; metastatic or locally advanced	28 capsules/28 days

Initial Evaluation

I. Vismodegib (Erivedge) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist or dermatologist; **AND**
   C. Vismodegib (Erivedge) will NOT be used in combination with any other oncologic medication; **AND**
   D. Member has not progressed on any other oncologic medication (e.g. has not progressed on sonidegib [Odomzo]); **AND**
   E. A diagnosis of **basal cell carcinoma (BCC)** when the following are met:
      1. Member has metastatic (Stage IV) basal cell carcinoma; **OR**
      2. Member has locally advanced basal cell carcinoma; **AND**
         i. Basal cell carcinoma has recurred or progressed after radiation or surgery; **OR**
         ii. Member is not a candidate for either

II. Vismodegib (Erivedge) is considered investigational when used for all other conditions, including but not limited to:
   A. Ovarian Cancer
   B. Nevoid basal cell carcinoma syndrome
   C. Prostate Cancer

D. Acute leukemia
E. Lymphoma
F. Breast Cancer
G. Medulloblastoma
H. Multiple myeloma
I. Myelofibrosis
J. Graft versus host disease
K. Pancreatic cancer
L. Lung cancer
M. Hepatocellular carcinoma

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. Vismodegib (Erivedge) is prescribed by, or in consultation with, an oncologist or dermatologist; **AND**
IV. Member has a diagnosis of **metastatic or locally advanced basal cell carcinoma; AND**
V. Member has experienced a clinical response to therapy defined by improvement or stabilization of disease or decrease or stabilization of tumor size or spread; **AND**
VI. Provider attestation that the member, either male or female, has been counseled on the teratogenicity and embryo-fetal toxicity risks with vismodegib (Erivedge).

Supporting Evidence

I. The safety and efficacy of vismodegib (Erivedge) in basal-cell carcinoma was evaluated in the pivotal ERIVANCE trial; a multicenter, international, two-cohort, open-label, single-arm study of 104 patients with metastatic basal-cell carcinoma (BCC) and those with locally advanced BCC who had inoperable disease or who were not a candidate for surgery. Patients with locally advanced disease were required to have had prior radiation therapy, unless contraindicated or inappropriate.
II. The primary efficacy endpoint was the independently assessed objective response rate (ORR) based on RECIST guidelines for metastatic disease or a decrease of 30% or more in the externally visible or radiographic dimension or complete resolution of ulceration for locally advanced disease. The key secondary endpoint was duration of response (DOR). The study met its primary

endpoint in both cohorts with an ORR of 30% (95% confidence interval [CI], 16 to 48; P=0.001) in the group with metastatic BCC and 43% (95% CI, 30 to 56; P<0.001) in the group with locally advanced BCC. The median duration of objective response was 7.6 months for metastatic BCC (rang, 2.1 to 11.1) and locally advanced BCC (range, 1.0 to 12.9).

III. During the ERIVANCE trial, all patients experienced at least one adverse event (AE), with the majority classified as grade 1 or 2 in severity, and 25% experienced at least one serious adverse event. Of those who experienced a serious adverse event, seven patients experienced a fatal adverse event and 12% had an adverse event that led to discontinuation. Common adverse events included muscle spasms, dysgeusia, alopecia, fatigue and weight loss.

IV. Patients enrolled in the study were age 18 and older and concurrent antitumor (oncologic) therapy was not permitted. The safety and/or efficacy of use in pediatric and adolescent patients or in combination with other oncologic therapies has not been evaluated.

V. Vismodegib (Erivedge) carries a black box warning for Embryo-fetal toxicity, as this agent is known to cause embryo-fetal death or severe birth defects when administered to a pregnant woman. FDA-label advises women of reproductive potential and men to use effective contraception during therapy with vismodegib (Erivedge) and for 24 months after the final dose.

VI. Long-term safety and efficacy of vismodegib (Erivedge) was evaluated in a follow-up study of the ERIVANCE trial for 39 months after the final data cutoff date of the primary analysis. The primary end point was ORR, with key secondary endpoints including DOR and overall survival (OS). Of the 104 patients enrolled at baseline, 96 discontinued for the following reasons: disease progression (27.9%), patient decision to withdraw (26.0%), and AEs (21.9%). The ORR for the mBCC cohort was 48.5% [95% CI, 30.8-66.2] and 60.3% in the laBCC cohort [47.2-71.7]. Median DOR was 14.8 months for the mBCC cohort [7.4-16.6] with a median OS of 33.4 months; Median DOR was 26.2 months [9.0-37.6] and OS was not estimable.

VII. No new safety concerns arose during the follow-up study. Again, all patients enrolled in the study experienced one or more treatment emergent adverse events (TEAEs). The incidence of TEAEs increased between the time of the primary analysis and the final data cutoff date for the follow-up study and correlated with patients who had 12 or more months of exposure to vismodegib (Erivedge). Patients who received treatment for 12 months or more had higher rates of muscle spasms, alopecia, dysgeusia, weight decreased, fatigue, and nausea. Deaths occurring during the study were considered by the investigator to be related to vismodegib (Erivedge).

VIII. Vismodegib (Erivedge) is currently recommended by NCCN guidelines for use in recurrent or advanced disease, with the caveat to be used in the FDA-approved indication of metastatic or locally advanced disease, with a category 2A recommendation.

IX. Vismodegib (Erivedge) is FDA-approved for adults with metastatic and locally advanced basal cell carcinoma. Vismodegib (Erivedge) has an overlapping indication with sonidegib (Odomzo), and if disease progression has occurred on or after one of these therapies, there is currently insufficient evidence regarding safety and/or efficacy of the other. One published piece of literature evaluated sonidegib (Odomzo) in those that were resistant to vismodegib (Erivedge);

however, this trial included only nine subjects all of which showed no response to sonidegib (Odomzo) or were not evaluable for safety and/or efficacy. Available evidence disfavors use of sequential Hedgehog pathway inhibitors.

Investigational or Not Medically Necessary Uses

I. Vismodegib (Erivedge) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Ovarian Cancer
   B. Nevoid basal cell carcinoma syndrome
   C. Prostate Cancer
   D. Acute leukemia
   E. Lymphoma
   F. Breast Cancer
   G. Medulloblastoma
   H. Multiple myeloma
   I. Myelofibrosis
   J. Graft versus host disease
   K. Pancreatic cancer
   L. Lung cancer
   M. Hepatocellular carcinoma

References

1. Vismodegib (Erivedge) [Prescribing Information]. Genentech USA, INC. South San Franicos, CA. January 2012.
2. Sekulic A, et al. Efficacy and Safety of Vismodegib in Advanced Basal-Cell Carcinoma. *N Engl J Med.* 2012 June 07; 366(23):2171-2179. Doi:10.1056/NEJMoal1113713.
3. Sekulic A, et al. Long-term safety and efficacy of vismodegib in patients with advanced basal cell carcinoma: final update of the pivotal ERIVANCE BCC study. *BMC Cancer* (2017) 17:332. Doi:10.1186/s 12885-017-3286-5/
4. National Comprehensive Cancer Network. NCCN Guidelines: Basal Cell Skin Cancer. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf
5. Danial C., Sarin K. Oro A., et al. An investigator-initiated open-label trial of sonidegib in advanced basal cell carcinoma patients resistant to vismodegib. Clin Cancer Res. 2016;22: 1325-1329.

Policy Implementation/Update:

Action and Summary of Changes	Date

Transition to policy format, addition of supporting evidence, addition of requirement attesting agent will NOT be used in combination with any other oncologic medication, removal of teratogenicity counseling attestation.	10/2020
Previous review	01/2013 12/2012
Criteria created	07/2012