

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Erivedge® (vismodegib capsules – Genentech)

TAC REVIEW DATE: 10/10/2018

OVERVIEW

Erivedge is indicated for the treatment of adults with metastatic basal cell carcinoma (BCC), or with locally advanced BCC that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.¹ It is an inhibitor of the hedgehog signaling pathway, where it binds to and inhibits Smoothened, a transmembrane protein involved in Hedgehog signal transduction.

Disease Overview

Localized BCC is most commonly treated with surgery or radiation therapy (RT) and BCC is usually cured by local therapy.² Few options exist in the scenario of disease progression; however, hedgehog pathway inhibitors have provided a new option for patients with advanced disease and in those who are not amenable to local therapy. The sonic hedgehog signaling pathway has emerged as playing a pivotal role in the parthenogenesis of BCC. Mutations in the patched (PTCH) gene on chromosome 9q, which codes for the sonic hedgehog receptor, are the underlying cause of nevoid BCC syndrome and are frequently present in sporadic BCC.

Guidelines

National Comprehensive Cancer Network (NCCN) guidelines for BCC (version 1.2019) note that surgical approaches offer the most effective and efficient means for accomplishing a cure; radiation therapy may be chosen as the primary treatment in order to achieve optimal overall results.² For residual disease when surgery and radiation therapy are contraindicated and for recurrent disease with nodal or distant metastases, a hedgehog pathway inhibitor or clinical trials should be considered.

Safety

Erivedge has a Boxed Warning stating that it may cause fetal harm when administered to a pregnant woman.¹ Pregnancy status should be verified prior to initiation of therapy. Female patients should use contraception during and for 24 months after the final dose. Male patients should use contraception to avoid exposure to a partner of childbearing potential during and for 3 months after the final dose.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Erivedge. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Erivedge is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Basal Cell Carcinoma (BCC), Metastatic.** Approve for 3 years.
- 2. Basal Cell Carcinoma (BCC), Locally Advanced.** Approve for 3 years if the patients meets ONE of the following conditions (A or B):
 - A) Initial Therapy.** Approve if the patient meets ONE of the following (i or ii)
 - i.** The patient’s basal cell carcinoma has recurred following surgery or radiation therapy; OR
 - ii.** The patient meets BOTH of the following (a and b):
 - a)** The patient is not a candidate for surgery; AND
 - b)** According to the prescribing physician, the patient is not a candidate for radiation therapy.
 - B) Patients Currently Receiving Erivedge.** Approve.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Erivedge has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Basal Cell Carcinoma (Locally Advanced or Metastatic), in Patients with Disease Progression While on Odomzo® (sonidegib capsules).** [Note: This does not apply to patients already started on Erivedge. Refer to criteria for BCC, Locally Advanced for Patients Currently Receiving Erivedge.] There are no data to support the use of Erivedge in patients who have experienced disease progression on Odomzo. Previous use of a hedgehog inhibitor was not allowed in the pivotal study for Odomzo.³ Patients who develop resistance to one of the hedgehog pathway inhibitors are not expected to respond to another hedgehog pathway inhibitor. There is an open-label study which evaluated patients (n = 9) with advanced BCC who had progressed on Erivedge that showed resistance to Odomzo, another hedgehog signaling pathway used in BCC.⁷ This criterion was developed based on the professional opinion of specialized physicians.
- 2. Metastatic Colorectal Cancer (mCRC).** Erivedge is not recognized in the treatment recommendations for colon cancer from the NCCN (version 3.2018 –).⁴ In combination with standard of care treatment for first-line mCRC, Erivedge did not confer incremental clinical benefit as measured by progression-free survival (PFS) compared with standard care therapy alone. A Phase II study was designed to assess whether Erivedge would prolong PFS when combined with standard of care therapy (FOLFOX [leucovorin, fluorouracil, oxaliplatin] or FOLFIRI [leucovorin, fluorouracil, irinotecan] in combination with Avastin® [bevacizumab injection]) in patients requiring first-line treatment for mCRC.³ Adults with histologically confirmed mCRC and Eastern Cooperative Oncology Group (ECOG) performance score (PS) of 0 or 1 were randomized 1:1 to Erivedge or placebo (n = 199). Median PFS was 9.3 months vs. 10.1 months, respectively (hazard ratio [HR] 1.25; 95% confidence interval [CI]: 0.89, 1.76; P = 0.28). At data cutoff, 45 patients had died, yielding a 12-month Kaplan Meier overall survival (OS) rate of 81.4% and 80.1% for Erivedge and placebo, respectively.
- 3. Ovarian Cancer.** The NCCN guidelines for Ovarian Cancer (version 2.2018) do not address the use of Erivedge for the management of ovarian cancer.⁶ The prespecified magnitude of PFS was not achieved in a Phase II, randomized, double-blind, placebo-controlled trial in adults with

histologically confirmed epithelial ovarian carcinoma, primary peritoneal carcinoma, or fallopian tube carcinoma. The study was conducted to determine an estimate of clinical benefit of maintenance therapy with Erivedge in the setting of second or third complete remission as measured by PFS using radiographic assessment.⁵ Eligible patients had received chemotherapy (platinum based and/or non-platinum based) for recurrent disease and had achieved complete response (CR) after their most recent chemotherapy regimen; all patients had baseline ECOG PS of 1 or less (n = 104). PFS from time of randomization for patients treated with Erivedge was 7.5 months compared with 5.8 months for placebo (HR 0.79; 95% CI: 0.46, 1.35; P = 0.39). When assessed by remission status, a similar non-statistically significant improvement in PFS was noted among patients in second CR (n = 84); the median PFS in patients treated with Erivedge was 7.5 months vs. 5.6 months for placebo (HR 0.44; 95% CI: 0.36, 1.20; P = 0.17). For patients in third CR (n = 20), median PFS was shorter with Erivedge (5.6 months) than placebo (7.5 months) [HR 1.79; 95% CI: 0.50, 6.48; P = 0.37).

- Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

- Erivedge® capsules [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; September 2017.
- The NCCN Basal Cell Skin Cancer Clinical Practice Guidelines in Oncology (Version 1.2019 – August 31, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on October 4, 2018.
- Berlin JD, Bendell JC, Hart LL, et al. A randomized phase II trial of vismodegib versus placebo with FOLFOX or FOLFIRI and bevacizumab in patients with previously untreated metastatic colorectal cancer. *Clin Cancer Res.* 2013;19(1):258-267.
- NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 3.2018 – August 7, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 18, 2018.
- Kaye SB, Fehrenbacher L, Holloway R, et al. A Phase II, randomized, placebo-controlled study of vismodegib as maintenance therapy in patients with ovarian cancer in second or third complete remission. *Clin Cancer Res.* 2012;18(23):6509-6518.
- NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 18, 2018.
- Danial C, Sarin KY, Oro AE, Chang AL. An investigator-initiated open-label trial of sonidegib in advanced basal cell carcinoma patients resistant to vismodegib. *Clin Cancer Res.* 2016;22(6):1325-1329.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No changes to criteria.	09/14/2016
Annual revision	No changes to criteria.	09/13/2017
Annual revision	Patients Already Started on Erivedge: This criterion only applies to BCC, locally advanced disease; reformat to address in the criteria section for this condition.	10/10/2018

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; BCC – Basal cell carcinoma.