Pharmacy Policy Bulletin: J-0905 Hedgehog Pathway Inhibitors – Commercial and Healthcare Reform	
Number: J-0905	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes with Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0905-008	**Original Date:** 06/04/2003
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Erivedge (vismodegib) • Odomzo (sonidegib) • Daurismo (glasdegib)

FDA-Approved Indication(s):	• Erivedge (vismodegib)
	  ○ Treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.
	• Odomzo (sonidegib)
	  ○ Treatment of adult patients with locally advanced basal cell carcinoma (laBCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.
	• Daurismo (glasdegib)
	  ○ In combination with low-dose cytarabine, for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

Background:	• Odomzo is an antineoplastic agent that inhibits the smoothened (SMO) receptor, a transmembrane protein involved in Hedgehog (Hh) signal transduction that is known to be important in normal embryonic growth, development, and cell maintenance. This signal transduction becomes less active in adults. Abnormal Hh signaling plays an important role in basal cell carcinoma • Erivedge is a small molecule that selectively inhibits the hedgehog signaling pathway. Erivedge functions as an inhibitor of the SMO signaling protein, the central mediator within the hedgehog pathway. Both ligand-dependent and mutation-driven SMO signaling are inhibited by direct binding of Erivedge to SMO, preventing the activation of downstream hedgehog target genes and transcription factors in the hedgehog pathway. • Daurismo is a self-administered hedgehog pathway inhibitor given orally for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy. It is intended for use with low-dose cytarabine (LDAC).

	○ Daurismo binds to and inhibits the smoothened (SMO) receptor, a transmembrane protein involved in hedgehog signal transduction. The hedgehog signaling pathway plays an essential role in embryogenesis, the process by which human embryos are developed. In adults, however, abnormal activation of this pathway is thought to contribute to the development and persistence of cancer stem cells. • Prescribing Considerations ○ Hedgehog pathway inhibitors should be prescribed under the supervision of a hematologist/oncologist. ○ Hedgehog pathway inhibitors can cause embryo-fetal toxicity and the pregnancy status of female patients should be evaluated prior to initiation. Advise males of the potential exposure through semen and to use condoms with a pregnant partner of a female partner of reproductive function during treatment. ○ Daurismo is associated with QTc prolongation and ventricular arrhythmias, including ventricular fibrillation and ventricular tachycardia. Electrocardiograms (ECGs) and electrolytes should be monitored.

Approval Criteria

I. Initial Authorization

A. Erivedge (vismodegib)

When a benefit, coverage of Erivedge may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of basal cell carcinoma (ICD-10: C44.01-C44.92) and meets one (1) of the following criteria **(a. or b.):**

a. Disease is classified as metastatic.

b. Disease is classified as locally advanced and all of the following criteria are met **(i. and ii.):**

i. Disease has recurred after surgery or the member is not a candidate for surgery.

ii. The member is not a candidate for radiation.

B. Odomzo (sonidegib)

When a benefit, coverage of Odomzo may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of locally advanced basal cell carcinoma (laBCC, ICD-10: C44.01-C44.92).

3. The member meets one (1) of the following criteria **(a. or b.)**:

a. The member has experienced recurrence following surgery or radiation therapy.

b. The member is not a candidate for surgery or radiation therapy.

C. Daurismo (glasdegib)

When a benefit, coverage of Daurismo may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 18 years of age or older.

2. The member was newly-diagnosed with acute myeloid leukemia (AML, ICD-10: C92).

3. The member is using Daurismo in combination with low-dose cytarabine.

4. The member has at least one (1) comorbidity that precludes use of intensive induction chemotherapy, defined as one (1) of the following **(a. through e.)**:

a. Age ≥ 75 years

b. Severe cardiac or pulmonary comorbidity

c. Reduced renal function

d. Hepatic impairment

e. The prescriber attests that the member is not a candidate for intensive induction therapy.

II. Reauthorization

When a benefit, reauthorization of a hedgehog pathway inhibitor may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:

1. Disease improvement

2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support their effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

For previous versions please see J-699 and J-850.

References:

1. Erivedge [package insert]. South San Francisco, CA: Genentech, Inc.; March 2023.

2. Odomzo [package insert]. Cranbury, NJ: Sun Pharmaceuticals Industries, Inc.; August 2023.

3. Daurismo [package insert]. New York, NY: Pfizer Labs, Division of Pfizer Inc.; March 2023.