

Vismodegib (Erivedge™)**Criteria for Use****November 2013**

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <http://vaww.pbm.va.gov> for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive vismodegib.*

- AST and ALT > 3 X the upper limit of normal or total bilirubin >1.5 X the upper limit of normal (or >3 X the upper limit of normal for patients with Gilbert disease)
- Creatinine clearance <30 mL/min
- Patient who is unable to swallow intact capsule
- Patients currently receiving systemic therapy for basal cell carcinoma
- Patient refuses transfer of care to VA Dermatologist or Oncologist
- Pregnancy or lactation

Inclusion Criteria *The answers to ALL of the following must be fulfilled in order to meet criteria.*

- Goals of care and role of Palliative Care consult has been discussed and documented.
- Diagnosis of metastatic basal cell carcinoma, or locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation or a diagnosis of basal-cell nevus (Gorlin) syndrome
- ECOG Performance Status 0-2 (see attached)
- pregnancy must be excluded prior to receiving vismodegib and patient provided contraceptive counseling on potential risk vs. benefit of taking vismodegib if patient were to become pregnant. Female patients of childbearing potential and men with female partners of childbearing potential are required to use 2 methods of contraception. (see Issues for Consideration)

Dosage and Administration

Recommended dose is one 150mg capsule orally once daily until disease progression or unacceptable toxicity. May be taken with or without food. Capsules should remain whole and not opened or crushed. Caution if given concomitantly with drugs that alter the pH of the upper GI tract (see Issues for Consideration)

Monitoring

- Metastatic disease: Assess radiographically at baseline and then every 2 months.
- Locally advanced disease:
 - if measurable disease assessed radiographically, assess at baseline and then every 2 months
 - if disease is not measurable radiographically, assess by physical exam (digital photography) at baseline and every 2 months
- Assess renal and hepatic function periodically due to lack of data in safety and effectiveness in patients with either renal or hepatic impairment

Issues for Consideration

- Vismodegib may cause fetal death or severe birth defects. Both female and male patients should be advised of the risk for fetal death or severe birth defects and the need for contraception during and after treatment. Female patients should use a highly effective form of contraception starting before the first dose and continuing for 7 months after the last dose. Male patients with female partners of childbearing potential should use condoms during vismodegib therapy and for 2 months after the last dose. If a female patient is pregnant or becomes pregnant or if a female partner of childbearing potential of a male patient is exposed to vismodegib via semen, they should be informed of the risk to the fetus. Exposure to vismodegib during pregnancy should be reported to the Genentech Adverse Event Line at 1-888-835-2555. Women exposed to vismodegib during pregnancy can participate in a pharmacovigilance program by contacting Genentech at the same number.
- Blood Donation: advise patients not to donate blood or blood components during vismodegib therapy and for at least 7 months after the last dose of vismodegib.
- Drugs that alter the pH of the upper GI tract (e.g. proton pump inhibitors, H₂ antagonists, and antacids) may alter the solubility of

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vismodegib and reduce bioavailability. No formal studies have been conducted to evaluate the effect of gastric pH on systemic exposure of vismodegib. If vismodegib is given concomitantly with drugs that alter the gastric pH systemic exposure of vismodegib may be decreased and the effect on efficacy is unknown. Increasing the dose of vismodegib is not likely to compensate for the loss of exposure.

Discontinuation Criteria

- Progressive disease (assess every 2 months): an increase in size of 20% or more in externally visible or radiographic dimension, new ulceration, or a new lesion. If there are multiple measurable lesions, the sum of the longest diameters should be used.
- Unacceptable toxicity

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ECOG PERFORMANCE STATUS*

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.