

Submitted by:

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NCCN Guidelines Panel: Non-Melanoma Skin Cancers

On behalf of Genentech, I respectfully request the NCCN Non-Melanoma Skin Cancers Guideline Panel to review the enclosed data for Erivedge™ (vismodegib) capsule for the treatment of adults with metastatic basal cell carcinoma (mBCC) or with locally advanced basal cell carcinoma (laBCC) that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

Specific Changes: Consider updating the NCCN Guidelines for Basal Cell Carcinoma with the available data on the use of Erivedge for the treatment of adults with mBCC or with laBCC that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

FDA Clearance: On January 30, 2012, Genentech, a member of the Roche Group, received FDA approval for Erivedge capsule for treatment of adults with mBCC, or with laBCC that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.² Please refer to the enclosed Erivedge prescribing information for the full FDA-approved indication and safety information.

Rationale: The FDA approval of Erivedge is based on results from the pivotal study, ERIVANCE BCC (SHH4476g), in patients with histologically-confirmed, radiographically measureable mBCC or patients with laBCC in which lesions had recurred after radiotherapy, unless radiotherapy was contraindicated or inappropriate, and where the lesions were either unresectable or surgical resection would result in substantial deformity.^{1,3,4} ERIVANCE BCC is an international, single-arm, multicenter, two-cohort, open-label Phase II study evaluating the efficacy and safety of Erivedge in patients with mBCC or laBCC. Erivedge shrank lesions, as measured by objective response rate (ORR) assessed by independent review, the primary endpoint of the study, in 30 percent of patients with mBCC and 43 percent of patients with laBCC. The most common adverse reactions (incidence of ≥ 10%) are muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, diarrhea, decreased appetite, constipation, arthralgias, vomiting, and ageusia.¹

There is additional data on the use of Erivedge in patients with Basal Cell Nevus Syndrome (Gorlin Syndrome), which is a genetic condition that predisposes patients to multiple basal cell carcinomas.^{5,6}

The following enclosures are included for your review (copyright-paid where applicable):

- Sekulic A, Migden MR, Oro AE, et al. A pivotal study evaluating efficacy and safety of the hedgehog pathway inhibitor vismodegib (GDC-0449) in patients with locally advanced or metastatic basal cell carcinoma. Presented at: European Association of Dermato-Oncology; 2011; Nantes, France. EADO Oral Presentation. <http://www.eado.org/>

- Sekulic A, Migden MR, Oro AE, et al. A pivotal study evaluating efficacy and safety of the hedgehog pathway inhibitor vismodegib (GDC-0449) in patients with locally advanced or metastatic basal cell carcinoma. *Melanoma Res* 2011;21(e-Suppl):e9. Presented at: European Association of Dermato-Oncology; 2011; Nantes, France. EADO Abstract #CO14. <http://www.eado.org/>
- Tang JY, Epstein Jr EH. An investigator-initiated, phase II, randomized, double-blind, placebo-controlled trial of GDC-0449 for prevention of BCCs in patients with basal cell nevus syndrome (BCNS). Presented at: American Academy of Dermatology; 2011; New Orleans, LA. AAD Oral Abstract. <http://www.aad.org/>
- Tang JY, MacKay-Wiggan J, Aszterbaum M, Bickers DR, Epstein Jr EH. Phase II randomized, double-blind, placebo-controlled trial of GDC-0449 for prevention of BCCs in basal cell nevus syndrome (BCNS) patients. Presented at: American Academy of Dermatology; 2011; New Orleans, LA. AAD Oral Presentation. <http://www.aad.org/>
- Erivedge™ Prescribing Information

Cited References:

1. Erivedge™ Prescribing Information
2. FDA Approves Erivedge (Vismodegib) Capsule, the First Medicine for Adults with Advanced Basal Cell Carcinoma. [press release]. South San Francisco: Genentech, A Member of the Roche Group; January 30, 2012. Accessed January 30, 2012 from <http://www.gene.com/gene/news/press-releases/display.do?method=detail&id=13827>
3. Sekulic A, Migden MR, Oro AE, et al. A pivotal study evaluating efficacy and safety of the hedgehog pathway inhibitor vismodegib (GDC-0449) in patients with locally advanced or metastatic basal cell carcinoma. Presented at: European Association of Dermato-Oncology; 2011; Nantes, France. EADO Oral Presentation. <http://www.eado.org/>
4. Sekulic A, Migden MR, Oro AE, et al. A pivotal study evaluating efficacy and safety of the hedgehog pathway inhibitor vismodegib (GDC-0449) in patients with locally advanced or metastatic basal cell carcinoma. *Melanoma Res* 2011;21(e-Suppl):e9. Presented at: European Association of Dermato-Oncology; 2011; Nantes, France. EADO Abstract #CO14. <http://www.eado.org/>
5. Tang JY, Epstein Jr EH. An investigator-initiated, phase II, randomized, double-blind, placebo-controlled trial of GDC-0449 for prevention of BCCs in patients with basal cell nevus syndrome (BCNS). Presented at: American Academy of Dermatology; 2011; New Orleans, LA. AAD Oral Abstract. <http://www.aad.org/>
6. Tang JY, MacKay-Wiggan J, Aszterbaum M, Bickers DR, Epstein Jr EH. Phase II randomized, double-blind, placebo-controlled trial of GDC-0449 for prevention of BCCs in basal cell nevus syndrome (BCNS) patients. Presented at: American Academy of Dermatology; 2011; New Orleans, LA. AAD Oral Presentation. <http://www.aad.org/>