PDL DRUG REVIEW

Proprietary Name: Odomzo®
Common Name: sonidegib
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Erivedge	Non-Recommended with Conditions

Summary

Pharmacology/Usage: Sonidegib, the active ingredient of Odomzo®, is a Smoothened homologue (Smo) antagonist that inhibits the Hedgehog (Hh) signaling pathway. Sonidegib is an inhibitor of the Hedgehog pathway, as it binds to and inhibits Smo, a transmembrane protein involved in Hh signal transduction.

Indication: For the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

There is no pregnancy category listed with Odomzo®; however, per the risk summary, Odomzo® can cause fetal harm when administered to pregnant women based on its mechanism of action and data from animal reproduction studies. There is currently no data on the use in pregnant women. It is recommended to advise pregnant women of the potential risk to a fetus. As such, Odomzo® has a box warning regarding the increased risk of embryo-fetal toxicity, as it can cause embryo-fetal death or severe birth defects if administered to a pregnant woman. Odomzo® is fetotoxic and teratogenic in animals. It is recommended to advise females of reproductive potential to use effective contraception during treatment and for ≥20 months after the last dose. Males with female partners should use condoms, even after a vasectomy, during treatment with Odomzo® and for ≥8 months after the last dose.

It is also recommended to advise patients not to donate blood or blood products while taking Odomzo® and for ≥20 months after the last dose of Odomzo® as the blood/blood products might be given to a female of reproductive potential.

The safety and efficacy of use in children under the age of 18 years have not been established.

Dosage Forms: Capsules: 200mg

Recommended Dosage: Take 200mg PO QD on an empty stomach until disease progression or unacceptable toxicity. Serum creatine kinase levels and renal function tests should be obtained prior to starting Odomzo® treatment. In addition, it is recommended to verify the pregnancy status of females of reproductive potential prior to starting treatment.

Dose adjustments are not required in those with renal impairment or in those with mild hepatic impairment. The use of Odomzo® has not been studied in patients with moderate or severe hepatic impairment.

It is recommended to interrupt Odomzo® therapy for the following: Severe/intolerable musculoskeletal adverse reactions; 1st occurrence of serum creatine kinase elevation between 2.5 and 10 times upper limit of normal (ULN); or Recurrent serum creatine kinase elevation between 2.5 and 5 times ULN.

It is recommended to permanently discontinue Odomzo® treatment for the following: Serum creatine kinase (CK) elevations greater than 2.5 times ULN with worsening renal function; Serum CK elevation greater than 10 times ULN; Recurrent serum CK elevation greater than 5 times ULN; or Recurrent severe/intolerable musculoskeletal adverse reactions.

Drug Interactions: The concomitant use of Odomzo® should be avoided with the following: strong CYP3A inhibitors (including but not limited to saquinavir, telithromycin, ketoconazole, itraconazole, voriconazole, posaconazole, and nefazodone), moderate CYP3A inhibitors (including but not limited to atazanavir, diltiazem, and fluconazole), and strong/moderate CYP3A inducers (including but not limited to carbamazepine, efavirenz, modafinil, phenobarbital, phenytoin, rifabutin, rifampin, and St. John's Wort). If a moderate CYP3A inhibitor must be used with Odomzo®, administer the moderate CYP3A inhibitor for less than 14 days and closely monitor for adverse reactions (especially musculoskeletal adverse reactions).

Common Adverse Drug Reactions: *There was no placebo data to compare with Odomzo®. The following are reported adverse events in patients treated with Odomzo® in a clinical trial.* The most frequently reported adverse events included muscle spasms (54%), musculoskeletal pain (32%), myalgia (19%), alopecia (53%), pruritus (10%), dysgeusia (46%), headache (15%), fatigue (41%), pain (14%), nausea (39%), diarrhea (32%), abdominal pain (18%), vomiting (11%), decreased weight (30%), and decreased appetite (23%). Key laboratory abnormalities included increased serum creatinine (92%), increased serum creatine kinase (61%), hyperglycemia (51%), increased lipase (43%), increased alanine aminotransferase (19%), increased aspartate aminotransferase (19%), increased amylase (16%), anemia (32%), and lymphopenia (28%).

Contraindications: None listed

Manufacturer: Novartis

Analysis: The safety and efficacy of Odomzo® were assessed in a small double-blind multiple-cohort randomized Phase 2 study that included patients (N=230) with locally advanced BCC (laBCC) or metastatic BBC (mBCC) who were randomized to Odomzo® 800mg or 200mg once daily until disease progression or intolerable toxicity. The primary outcome was objective response rate (ORR) as determined by blinded central review according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) in patients with laBCC or RECIST version 1.1 for patients with mBBC. A key secondary outcome was duration of response.

Patients randomized to the 200mg strength that had laBCC (N=66) were followed for at least 12 months, unless discontinued earlier. The ORR in this population was 58%, consisting of 3 (5%) complete responses and 35 (53%) partial responses. In a prespecified analysis using an alternative definition of complete response (CR), defined as at least a partial response (PR) according to MRI and/or photography and no evidence of tumor on biopsy of the residual lesion, generated a CR rate of 20%. Of the 38 with an objective response, 18% (N=7) had subsequent disease progression with 4 of these 7 having maintained a response of ≥6 months. The remaining 31 patients have ongoing responses ranging from 1.9+ to 18.6+ months, and the median duration of response has not been reached.

There were 128 patients randomized to Odomzo® 800mg who had laBCC. There was no evidence of better antitumor activity per the ORR in patients with laBCC randomized to receive Odomzo® 800mg daily and followed for at least 12 months.

In the primary efficacy analysis, 36% (N=20/55) in the 200mg group and 34% (N=39/116) in the 800mg dose group achieved objective response. Fewer adverse events leading to dose interruptions or reductions occurred in the 200mg group as compared to the 800mg group.[2]

Place in Therapy: Odomzo® is a hedgehog pathway inhibitor that is indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or for those who are not candidates for surgery or radiation therapy. One noted reference source suggests an inhibitor of hedgehog pathway, such as vismodegib or sonidegib, "...for patients with metastatic or locally advanced basal cell carcinoma that is not amenable to treatment with surgery or radiation therapy."[3]

It is recommended that Odomzo® require clinical prior authorization to ensure it is used only in appropriate clinical circumstances.

PDL Placement:

☐ **Recommended**

☒ **Non-Recommended with Conditions**

References

[1] Odomzo [package insert]. East Hanover, New Jersey; Novartis Pharmaceuticals Corp; 2015.

[2] Migden MR, Guminski A, Gutzmer R, et al. Treatment with two different doses of sonidegib in patients with locally advanced or metastatic basal cell carcinoma (BOLT): a multicenter, randomized, double-blind phase 2 trial. Lancet Oncol. 2015; 16(6): 716-28.

[3] UpToDate for desktop. Systemic treatment of advanced cutaneous squamous and basal cell carcinomas. Accessed January 2015.