2.2 Design Modifications for Adverse Reactions

Screen ODOMZO for:
- Severe or imminent mucocutaneous adverse reactions.
- First occurrence of skin ulceration between 2.5 and 12.0 months after start of treatment with ODOMZO.
- Baseline serum CK greater than 5.0 times ULN with worsening renal function.
- Baseline serum CK greater than 10 times ULN.
- Baseline serum CK greater than 40 times ULN.
- Baseline serum CK greater than 100 times ULN.

Mucocutaneous Reactions

2.3 Dosage Modifications for Adverse Reactions

If ODOMZO is stopped because of severe or imminent mucocutaneous adverse reaction, treatment can continue with the following dosage modifications:

1. Reduce dose of ODOMZO to 200 mg every 28 days.
2. Reduce dose of ODOMZO by 50% (i.e., 100 mg every 28 days).
3. Reduce dose of ODOMZO to 50 mg every 28 days.

If the mucocutaneous adverse reaction does not improve with the above modifications, if ODOMZO is stopped because of severe or imminent mucocutaneous adverse reactions, treatment can continue with the following dosage modifications:

1. Reduce dose of ODOMZO to 200 mg every 28 days.
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**12. CLINICAL PHARMACOLOGY**

**12.1 Mechanism of Action**

Sonidegib is an inhibitor of the hedgehog (Hh) protein.

**12.2 Pharmacodynamics**

**Dosage and Administration**

**Dosage**

**Adults**

As a single dose of 800 mg orally daily, sonidegib does not impair QTc interval.

**Pharmacokinetics**

Sonidegib inhibited dose-proportional increases in the area under the curve (AUC) and the maximum concentration (Cmax) over the dose range of 10 to 150 mg. Sonidegib was not absorbed when given with food (800 mg sonidegib was coadministered with a complete meal).

**Elimination**

Sonidegib is primarily metabolized by CYP3A. The main circulating compound was unchanged sonidegib (36% of the dose).

**Side Effects**

**13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Sonidegib resulted in a lack of fertility when administered to female rats at ≥20 mg/kg/day (approximately 1.3 times the recommended human dose based on BSA). In addition, in rat reproductive toxicity studies, sonidegib was not genotoxic.

**13.2 Animal Toxicology and Pharmacology**

Body tissues and organs with significant increases in tissue weights were unchanged and normal after administration of sonidegib 200 mg once daily for 12 months in rats. Moderate CYP3A inducer: (erythromycin) for 4 months.

**14. CLINICAL STUDIES**

The safety and effectiveness of ODOMZO were evaluated in a single, multicenter, double-blind, multiple cohort clinical trial conducted in patients with locally advanced basal cell carcinoma (laBCC) (n=194) or metastatic basal cell carcinoma (MBC) (n=52) [see Dosage and Administration (2.1)]. Patients randomized to receive ODOMZO 200 mg daily were followed for at least 30 months unless patients with laBCC randomized to receive ODOMZO 200 mg daily were followed for at least 20 months after the last dose. The safety and effectiveness of ODOMZO were also evaluated in a phase 3, double-blind, placebo-controlled, randomized, multicenter clinical trial conducted in patients with locally advanced basal cell carcinoma (laBCC) (n=194) or metastatic basal cell carcinoma (MBC) (n=52) [see Dosage and Administration (2.1)].

**15. ADVERSE REACTIONS**

Sonidegib treatment was associated with hyperglycemia, muscle pain, dyspepsia, diarrhea, arthralgia, abdominal pain, and headache. Sonidegib treatment was associated with hyperglycemia, muscle pain, dyspepsia, diarrhea, arthralgia, abdominal pain, and headache.

**16. OVERDOSAGE**

Sonidegib is primarily metabolized by CYP3A. A single oral dose of 60 mg/kg was administered to healthy volunteers and was associated with a mean steady-state Cmin of 0.11 mg/L and Cmax of 0.74 mg/L.

**17. PATIENT COUNSELING**

Inform patients that they may experience a temperature rise and/or temperature elevation.

**How should I store ODOMZO?**

**How should I take ODOMZO?**

**What is the most important information I should know about ODOMZO?**

**What should I avoid while taking ODOMZO?**

**What is the most important information I should know about ODOMZO?**

**What are possible side effects of ODOMZO?**

**What should I do if I miss a dose?**

**Keep ODOMZO and all medicines out of the reach of children.**

**What is the most important information I should know about ODOMZO?**

**What are the ingredients in ODOMZO?**

**Active ingredient:**

Sonidegib is a prescription medicine used to treat adults with a type of skin cancer, called basal cell carcinoma, that has come back after surgery or radiation therapy or that cannot be treated with surgery or radiation. It is not known if ODOMZO is safe and effective in children.

**What should I do if I miss a dose of ODOMZO?**

**What are the ingredients in ODOMZO?**

**Active ingredient:**

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