Beleodaq®

(belinostat) for injection

500 mg per vial for intravenous infusion

Please see full Important Safety Information on pages 2-3.
Please see accompanying full Prescribing Information or visit www.BELEODAQ.com for full Prescribing Information.

Indications and Usage

BELEODAQ® (belinostat) is a histone deacetylase inhibitor indicated for the treatment of adult patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

BELEODAQ Important Safety Information

Warnings and Precautions

- **Hematologic Toxicity:** BELEODAQ can cause thrombocytopenia, leukopenia (neutropenia and lymphopenia), and/or anemia; monitor blood counts weekly during treatment and modify dosage as necessary.
- **Infections:** Serious and sometimes fatal infections, including pneumonia and sepsis, have occurred with BELEODAQ. Do not administer BELEODAQ to patients with an active infection. Patients with a history of extensive or intensive chemotherapy may be at a higher risk of life-threatening infections.
- **Hepatotoxicity:** BELEODAQ can cause fatal hepatotoxicity and liver function test abnormalities. Monitor liver function tests before treatment and before the start of each cycle. Interrupt or adjust dosage until recovery, or permanently discontinue BELEODAQ based on the severity of the hepatic toxicity.
- **Tumor Lysis Syndrome:** Tumor lysis syndrome has occurred in BELEODAQ-treated patients in the clinical trial of patients with relapsed or refractory PTCL. Monitor patients with advanced stage disease and/or high tumor burden, and take appropriate precautions.
- **Gastrointestinal Toxicity:** Nausea, vomiting, and diarrhea occur with BELEODAQ and may require the use of antiemetic and antidiarrheal medications.
- **Embryo-Fetal Toxicity:** BELEODAQ can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the risk to a fetus. Advise females of reproductive potential to use an effective method of contraception during treatment with BELEODAQ and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with BELEODAQ and for 3 months after the last dose.

Adverse Reactions

- The most common adverse reactions observed in more than 25% of patients with relapsed or refractory PTCL in the trial, who were treated with BELEODAQ, were nausea (42%), fatigue (37%), pyrexia (35%), anemia (32%), and vomiting (29%).
- Sixty-one patients (47.3%) experienced serious adverse reactions while taking BELEODAQ or within 30 days after their last dose of BELEODAQ. The most common serious adverse reactions (>2%) were pneumonia, pyrexia, infection, anemia, increased creatinine, thrombocytopenia, and multi-organ failure.

Drug Interactions

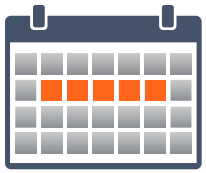
- BELEODAQ is primarily metabolized by *UGT1A1*. Avoid concomitant administration of BELEODAQ with strong inhibitors of *UGT1A1*.

Use in Specific Populations

- **Lactation:** Due to the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with BELEODAQ and for 2 weeks after the last dose.
- **Pregnancy Testing:** BELEODAQ can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended for females of reproductive potential prior to initiating BELEODAQ.
- **Pediatric Use:** The safety and effectiveness of BELEODAQ in pediatric patients have not been established.

Please see full Prescribing Information for BELEODAQ.

BELEODAQ is administered as a short, 30-minute intravenous infusion



- The recommended dosage of BELEODAQ is 1000 mg/m^2 administered over 30 minutes by intravenous (IV) infusion once daily on days 1-5 of a 21-day cycle. Cycles can be repeated every 21 days until disease progression or unacceptable toxicity
- Treatment discontinuation or interruption with or without dosage reductions by 25% may be needed to manage adverse reactions

How supplied

- BELEODAQ is supplied in single-vial cartons; each 30 mL clear vial contains sterile, lyophilized powder equivalent to 500 mg of belinostat
- NDC 72893-002-01; individual carton of BELEODAQ 30 mL single-dose vial containing 500 mg of belinostat

Storage and handling

- Store BELEODAQ at room temperature 20°C to 25°C (68°F to 77°F)
- Excursions are permitted between 15°C and 30°C (59°F and 86°F). Retain BELEODAQ in its original packaging until ready for use (see US Pharmacopeia [USP] controlled room temperature)
- BELEODAQ is a cytotoxic drug. Follow special handling and disposal procedures

Use in Specific Populations

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Reconstitution and infusion instructions

- Aseptically reconstitute each vial of BELEODAQ by adding 9 mL of sterile water for injection, USP, into the BELEODAQ vial with a suitable syringe to achieve a concentration of 50 mg of belinostat per mL
- Swirl the contents of the vial until there are no visible particles in the resulting solution
- The reconstituted product may be stored for up to 12 hours at ambient temperature (15°C to 25°C; 59°F to 77°F)

- Aseptically withdraw the volume needed for the required dosage (based on the 50 mg/mL concentration and the patient's body surface area [BSA; m^2]) and transfer to an infusion bag containing 250 mL of 0.9% sodium chloride injection
- The infusion bag with drug solution may be stored at ambient room temperature (15°C to 25°C; 59°F to 77°F) for up to 36 hours, including infusion time
- Visually inspect the solution for particulate matter. Do not use if cloudiness or particulates are observed

- Connect the infusion bag containing drug solution to an infusion set with a 0.22 µm inline filter for administration
- Infuse intravenously over 30 minutes. If infusion site pain or other symptoms potentially attributable to the infusion occur, the infusion time may be extended to 45 minutes

Preparation and Administration Precautions

- As with other potentially cytotoxic anticancer agents, exercise care in the handling and preparation of solutions prepared with BELEODAQ

Drug Interactions

- BELEODAQ is primarily metabolized by *UGT1A1*. Avoid concomitant administration of BELEODAQ with strong inhibitors of *UGT1A1*.

Please see full Important Safety Information on pages 2-3 and full Prescribing Information for BELEODAQ.

Modify BELEODAQ treatment by adjusting dosage as needed

Modifying the dosage may allow for the possibility of continued treatment in some patients

Dosage modifications for hematologic toxicities

- Base dosage adjustments for thrombocytopenia and neutropenia on the nadir (lowest value) for platelet and absolute neutrophil count (ANC) in the preceding cycle of therapy
- ANC should be ≥1000/µL, and the platelet count should be ≥50,000/µL prior to the start of each cycle and prior to resuming treatment following discontinuation because of toxicity
  - Resume subsequent treatment with BELEODAQ according to the guidelines described in the table to the right
  - Discontinue BELEODAQ in patients who have recurrent ANC nadirs <500/µL and/or recurrent platelet count nadirs <25,000/µL after 2 dosage reductions

Toxicity and dosage modification
Platelet count ≥25,000/µL and **nadir ANC** ≥500/µL
NO CHANGE
Nadir ANC <500/µL (any platelet count)
DECREASE DOSAGE BY **25%** (750 mg/m²)
Platelet count <25,000/µL (any nadir ANC)
DECREASE DOSAGE BY **25%** (750 mg/m²)

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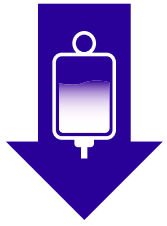
Dosage modifications for nonhematologic toxicities

Toxicities must be NCI-CTCAE grade 2 or less prior to retreatment

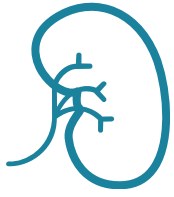
Any CTCAE grade 3 or 4 AE*	Recurrence of CTCAE grade 3 or 4 AE after 2 dosage reductions
DECREASE DOSAGE BY **25%** (750 mg/m²)	DISCONTINUE BELEODAQ

*For nausea, vomiting, and diarrhea, only dose modify if the duration is >7 days with supportive management.



Dosage modifications for patients with reduced *UGT1A1* activity

Reduce the starting dose of BELEODAQ to **750 mg/m²** in patients known to be homozygous for the *UGT1A1*28* allele



Use in patients with renal impairment

BELEODAQ exposure **is not altered in patients** with creatinine clearance (CrCl) >39 mL/min

There are insufficient data to recommend a dose of BELEODAQ in patients with CrCl ≤39 mL/min

Monitor complete blood counts at baseline and weekly. Perform serum chemistry tests, including renal and hepatic functions, prior to the start of the first dose of each cycle.

BELEODAQ is administered as a short, 30-minute intravenous infusion

No pretreatment is required

Dosage

The **recommended dosage of BELEODAQ** is 1000 mg/m^2

Infusion Time

Short, **30-minute** infusion

Dosing Schedule

5 days on, **16 days** off*

*Repeat every 21 days until disease progression or unacceptable toxicity.

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Reference

BELEODAQ® [Prescribing Information], Acrotech Biopharma, LLC. January 2020.

ACROTECH® BIOPHARMA

BEL-0177

www.acrotechbiopharma.com

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