



## How will I receive romidepsin for injection?

- Romidepsin for injection will be given to you by your healthcare provider or nurse as an intravenous injection into your vein usually over 4 hours.
- Romidepsin for injection is usually given on Day 1, Day 8, and Day 15 of a 28-day cycle of treatment.
- Your healthcare provider will decide how long you will receive treatment with romidepsin for injection.
- Your healthcare provider will check your blood cell counts and other blood tests regularly during your treatment with romidepsin for injection to check for side effects of romidepsin for injection. Your healthcare provider may decide to do other tests to check your health as needed.
- Your healthcare provider may stop your treatment, change when you get your treatment, or change the dose of your treatment if you have certain side effects while receiving romidepsin for injection.

## What are the possible side effects of romidepsin for injection?

### Romidepsin for injection may cause serious side effects, including:

- **Low blood cell counts:** Your healthcare provider will regularly do blood tests to check your blood counts.
  - **Low platelets:** can cause unusual bleeding or bruising under the skin. Talk to your healthcare provider right away if this happens.
  - **Low red blood cells:** may make you feel tired and you may get tired easily. You may look pale and feel short of breath. Tell your healthcare provider if you have these symptoms.
  - **Low white blood cells:** can cause you to get infections, which may be serious.

- **Serious infections.** People receiving romidepsin for injection can develop serious infections that can sometimes lead to death. These infections can happen during and after treatment with romidepsin for injection. Your risk of infection may be higher if you have had chemotherapy in the past. Tell your healthcare provider right away if you have any of these symptoms of infection:

- Fever
- cough
- shortness of breath with or without chest pain
- burning with urination
- flu-like symptoms
- muscle aches
- worsening skin problems

- **Changes in your heartbeat.** Your healthcare provider may check your heart by doing an ECG (electrocardiogram) and blood tests to check your potassium and magnesium levels, before you start romidepsin for injection treatment. Tell your healthcare provider if you feel an abnormal heartbeat, feel dizzy or faint, have chest pain or shortness of breath.

- **Tumor Lysis Syndrome (TLS).** TLS is a problem of the rapid breakdown of cancer cells that can happen during your treatment with romidepsin for injection. You should drink plenty of fluids in the 3 days after you receive treatment with romidepsin for injection. Your healthcare provider may do blood tests to check for TLS and may give you medicine to prevent or treat TLS.

The most common side effects of romidepsin for injection include:

- nausea, tiredness, vomiting, loss of appetite, changes in sense of taste, constipation, and itching.

These are not all the possible side effects of romidepsin for injection. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

## General information about the safe and effective use of romidepsin for injection

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet.

This Patient Information leaflet summarizes the most important information about romidepsin for injection. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Romidepsin for injection that is written for health professionals.

## What are the ingredients in romidepsin for injection?

**Active ingredient:** romidepsin

**Inactive ingredients:** povidone, hydrochloric acid as a pH adjuster. The diluent contains 80% propylene glycol and 20% dehydrated alcohol.

This Patient Information has been approved by the U.S. Food and Drug Administration.

**FRESENIUS**  
**KABI**

Lake Zurich, IL 60047

www.fresenius-kabi.com/us

Revised: September 2021

4 5 1 3 5 3 C

distribution by 44% and 52%, respectively. The increase in exposure seen after co-administration with rifampin is likely due to rifampin's inhibition of an undetermined hepatic uptake process that is predominant for the disposition of romidepsin.

Drugs that inhibit P-glycoprotein: Drugs that inhibit p-glycoprotein may increase the concentration of romidepsin.

### Specific Populations

#### Effect of Age, Gender, Race or Renal Impairment

The pharmacokinetics of romidepsin was not influenced by age (27 to 83 yrs), gender, race (white vs. black) or mild (estimated creatinine clearance 50–80 mL/min), moderate (estimated creatinine clearance 30–50 mL/min), or severe (estimated creatinine clearance <30 mL/min) renal impairment. The effect of end-stage renal disease (estimated creatine clearance less than 15 mL/min) on romidepsin pharmacokinetics has not been studied.

#### Hepatic Impairment

Romidepsin clearance decreased with increased severity of hepatic impairment. In patients with cancer, the geometric mean *C*<sub>max</sub> values after administration of 14, 7, and 5 mg/m<sup>2</sup> romidepsin in patients with mild (B1: bilirubin ≤ULN; AST >ULN; B2: bilirubin > ULN but ≤1.5 x ULN and any AST), moderate (bilirubin >1.5 x ULN to ≤3 x ULN and any AST), and severe (bilirubin >3 x ULN and any AST) hepatic impairment were approximately 111%, 96%, and 86% of the corresponding value after administration of 14 mg/m<sup>2</sup> romidepsin in patients with normal (bilirubin ≤upper limit of normal (ULN) and aspartate aminotransferase (AST) ≤ULN) hepatic function, respectively. The geometric mean AUC<sub>0-∞</sub> values in patients with mild, moderate, and severe hepatic impairment were approximately 144%, 114%, and 116% of the corresponding value in patients with normal hepatic function, respectively. Among these 4 cohorts, moderate interpatient variability was noted for the exposure parameters *C*<sub>max</sub> and AUC<sub>0-∞</sub>, as the coefficient of variation (CV) ranged from 30% to 54%.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been performed with romidepsin. Romidepsin was not mutagenic in vitro in the bacterial reverse mutation assay (Ames test) or the mouse lymphoma assay. Romidepsin was not clastogenic in an in vivo rat bone marrow micronucleus assay when tested to the maximum tolerated dose (MTD) of 1 mg/kg in males and 3 mg/kg in females (6 and 18 mg/m<sup>2</sup> in males and females, respectively). These doses were up to 1.3-fold the recommended human dose, based on body surface area.

Based on nonclinical findings, male and female fertility may be compromised by treatment with romidepsin. In a 26-week toxicology study, romidepsin administration resulted in testicular degeneration in rats at 0.33 mg/kg/dose (2 mg/m<sup>2</sup>/dose) following the clinical dosing schedule. This dose resulted in AUC<sub>0-∞</sub> values that were approximately 2% the exposure level in patients receiving the recommended dose of 14 mg/m<sup>2</sup>/dose. A similar effect was seen in mice after 4 weeks of drug administration at higher doses. Seminal vesicle and prostate organ weights were decreased in a separate study in rats after 4 weeks of daily drug administration at 0.1 mg/kg/day (0.6 mg/m<sup>2</sup>/day), approximately 30% the estimated human daily dose based on body surface area. Romidepsin showed high affinity for binding to estrogen receptors in pharmacology studies. In a 26-week toxicology study in rats, atrophy was seen in the ovary, uterus, vagina and mammary gland of females administered doses as low as 0.1 mg/kg/dose (0.6 mg/m<sup>2</sup>/dose) following the clinical dosing schedule. This dose resulted in AUC<sub>0-∞</sub> values that were 0.3% of those in patients receiving the recommended dose of 14 mg/m<sup>2</sup>/dose. Maturation arrest of ovarian follicles and decreased weight of ovaries were observed in a separate study in rats after 4 weeks of daily drug administration at 0.1 mg/kg/day (0.6 mg/m<sup>2</sup>/day). This dose is approximately 30% the estimated human daily dose based on body surface area.

## 14 CLINICAL STUDIES

Romidepsin was evaluated in 2 multicenter, single-arm clinical studies in patients with CTCL (Study 1 [NCT00106431] and Study 2 [NCT00073451]). Overall, 167 patients with CTCL were treated in the US, Europe, and Australia. Study 1 included 96 patients with confirmed CTCL after failure of at least 1 prior systemic therapy. Study 2 included 71 patients with a primary diagnosis of CTCL who received at least 2 prior skin directed therapies or one or more systemic therapies. Patients were treated with romidepsin at a starting dose of 14 mg/m<sup>2</sup> infused over 4 hours on days 1, 8, and 15 every 28 days.

In both studies, patients could be treated until disease progression at the discretion of the investigator and local regulators. Objective disease response was evaluated according to a composite endpoint that included assessments of skin involvement, lymph node and visceral involvement, and abnormal circulating T-cells ("Sézary cells").

The primary efficacy endpoint for both studies was overall objective disease response rate (ORR) based on the investigator assessments, and was defined as the proportion of patients with confirmed complete response (CR) or partial response (PR). CR was defined as no evidence of disease and PR as ≥ 50% improvement in disease.

Secondary endpoints in both studies included duration of response and time to response.

### Baseline Patient Characteristics

Demographic and disease characteristics of the patients in Study 1 and Study 2 are provided in Table 3.

**Table 3. Baseline Patient Characteristics (CTCL Population)**

Characteristic	Study 1 (N=96)	Study 2 (N=71)
Age		
N	96	71
Mean (SD)	57 (12)	56 (13)
Median (Range)	57 (21, 89)	57 (28, 84)
Sex, n (%)		
Men	59 (61)	48 (68)
Women	37 (39)	23 (32)
Race, n (%)		
White	90 (94)	55 (77)
Black	5 (5)	15 (21)
Other/Not Reported	1 (1)	1 (1)

**Table 3. Baseline Patient Characteristics (CTCL Population) (Continued)**

Characteristic	Study 1 (N=96)	Study 2 (N=71)
Stage of Disease at Study Entry, n (%)		
IA	0 (0)	1 (1)
IB	15 (16)	6 (9)
IIA	13 (14)	2 (3)
IIB	21 (22)	14 (20)
III	23 (24)	9 (13)
IVA	24 (25)	27 (38)
IVB	0 (0)	12 (17)
Number of Prior Skin-Directed Therapies		
Median (Range)	2 (0, 6)	1 (0, 3)
Number of Prior Systemic Therapies		
Median (Range)	2 (1, 8)	2 (0, 7)

### Clinical Results

Efficacy outcomes for CTCL patients are provided in Table 4. Median time to first response was 2 months (range 1 to 6) in both studies. Median time to CR was 4 months in Study 1 and 6 months in Study 2 (range 2 to 9).

**Table 4. Clinical Results for CTCL Patients**

Response Rate	Study 1 (N=96)	Study 2 (N=71)
ORR (CR + PR), n (%) [95% Confidence Interval]	33 (34) [25, 45]	25 (35) [25, 49]
CR, n (%) [95% Confidence Interval]	6 (6) [2, 13]	4 (6) [2, 14]
PR, n (%) [95% Confidence Interval]	27 (28) [19, 38]	21 (30) [20, 43]
<b>Duration of Response (months)</b>		
N	33	25
Median (range)	15 (1, 20*)	11 (1, 66*)

\*Denotes censored value.

## 15 REFERENCES

1. OSHA Hazardous Drugs. *OSHA*. [Accessed on 09/11/2018, from http://www.osha.gov/SLTC/hazardousdrugs/index.html]

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### How Supplied

Romidepsin for injection is supplied as a kit including a sterile, lyophilized powder in a 10 mg single-dose vial containing 11 mg of romidepsin, 22 mg of the bulking agent, povidone, USP, and hydrochloric acid, NF, as a pH adjuster. In addition, each kit includes a single-dose sterile vial with 2.2 mL deliverable volume of the diluent composed of 80% propylene glycol, USP, and 20% dehydrated alcohol, USP.

Product No.	NDC No.	
704928	63323-926-88	Romidepsin Kit containing 1 vial of romidepsin and 1 vial of diluent for romidepsin per carton.

### Storage and Handling

Romidepsin for injection is supplied as a kit containing 2 vials in a single carton. The carton must be stored at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Romidepsin is a hazardous drug. Follow applicable special handling and disposal procedures.<sup>1</sup>

The container closure is not made with natural rubber latex.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

- **Low Blood Counts**  
Advise patients that treatment with romidepsin can cause low blood counts and that frequent monitoring of hematologic parameters is required. Patients should be instructed to report fever or other signs of infection, significant fatigue, shortness of breath, or bleeding [see *Warnings and Precautions* (5.1)].
- **Infections**  
Advise patients that infections may occur during treatment with romidepsin. Advise patients to report fever, cough, shortness of breath with or without chest pain, burning on urination, flu-like symptoms, muscle aches, or worsening skin problems. Advise patients to report any previous history of hepatitis B before starting romidepsin [see *Warnings and Precautions* (5.2)].
- **Tumor Lysis Syndrome**  
Advise patients of the risk of tumor lysis syndrome (especially those with advanced stage disease and/or high tumor burden) to maintain high fluid intake for at least 72 hours after each dose [see *Warnings and Precautions* (5.4)].
- **Nausea and Vomiting**  
Advise patients that nausea and vomiting are common following treatment with romidepsin. Prophylactic antiemetics are recommended for all patients. Advise patients to report these symptoms so that appropriate treatment can be instituted [see *Adverse Reactions* (6.1)].
- **Embryo-Fetal Toxicity**  
Advise patients that romidepsin can cause fetal harm when administered during pregnancy [see *Warnings and Precautions* (5.5) and *Use in Specific Populations* (8.1)].
- **Contraception**  
Advise females of reproductive potential to use effective contraception during treatment with romidepsin and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with romidepsin and for 1 month after the last dose [see *Use in Specific Populations* (8.3)].

- **Lactation**

Advise lactating women not to breastfeed during treatment with romidepsin and for 1 week after the last dose [see *Use in Specific Populations* (8.2)].

- **Infertility**

Advise females and males of reproductive potential that romidepsin may cause infertility [see *Nonclinical Toxicology* (13.1)].

**FRESENIUS**  
**KABI**

Lake Zurich, IL 60047

www.fresenius-kabi.com/us

4 5 1 3 5 2 E