CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761362Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document Jubbonti (denosumab-bbdz) REMS

I. Administrative Information

Risks: Severe hypocalcemia
Application Number: BLA 761362
Application Holder: Sandoz Inc.
Initial REMS Approval: 03/2024

II. REMS Goal

The goal of the Jubbonti REMS is to mitigate the risk of severe hypocalcemia in patients with advanced chronic kidney disease (CKD) including dialysis-dependent patients associated with Jubbonti.

Objective 1: Inform healthcare providers on:

- Risk of severe hypocalcemia with advanced chronic kidney disease (estimated glomerular filtration rate [eGFR] < 30 ml/min/1.73 m^2)
- Need to assess for presence of chronic kidney disease-mineral bone disorder (CKD-MBD) before initiating Jubbonti in patients with advanced chronic kidney disease

III. REMS Requirements

To inform healthcare providers about the REMS and the risk and safe use of Jubbonti, Sandoz Inc. must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials & Dissemination Plans
Healthcare providers who are likely to prescribe Jubbonti	REMS Letters: **REMS Letter for Healthcare Providers**, **REMS Letter for Professional Societies** with attachment Prescribing Information. 1. Mail **REMS Letter for Healthcare Providers** within 60 calendar days of the date Jubbonti is first commercially distributed and again 12 months later. a. If returned, attempt to obtain updated address information and send a second letter by mail within 45 calendar days of the date the first letter is returned. If correct address cannot be obtained, the attempt will be documented. 2. Email **REMS Letter for Professional Societies** within 60 calendar days of the date Jubbonti is first commercially distributed and again 12 months later through the following professional societies and request the letter or content be provided to their members. If the first email is undeliverable, the REMS letter will be mailed within 30 calendar days. If the first email is marked as unopened, a second email will be sent within 7 calendar days. If the second email is undeliverable or marked as unopened, the REMS letter will be mailed within 30 calendar days. a. American Society of Bone Mineral Research b. American College of Rheumatology c. American Association of Clinical Endocrinologists d. Endocrine Society e. American Society of Clinical Oncology f. Bone Health and Osteoporosis Foundation g. North American Menopause Society h. American Academy of Family Physicians i. American College of Physicians 3. Make available via a link from the **REMS Website**. 4. Disseminate through field-based sales and medical representatives from the date Jubbonti is first commercially distributed for the duration of the REMS. 5. Disseminate and prominently display at Professional Meetings where Sandoz Inc. has a Jubbonti commercial presence from the date Jubbonti is first commercially distributed for the duration of the REMS. **Patient Guide** and Prescribing Information (PI) 1. Disseminate and prominently display at Professional Meetings where Sandoz Inc. has a Jubbonti commercial presence from the date Jubbonti is first commercially distributed for the duration of the REMS. 2. Disseminate through field-based sales and medical representatives during the initial and/or follow-up discussion with healthcare providers from the date Jubbonti is first commercially distributed for the duration of the REMS. Field-based sales and/or medical representatives to verbally review the risk messages contained in the **Patient Guide** and PI during the visit with the healthcare provider. **Website**

	1. Make the **REMS Website** fully operational and all REMS materials available through the website by the date Jubbonti is first commercially distributed. 2. Maintain the **REMS Website** from the date Jubbonti is first commercially distributed for the duration of the REMS. 3. Include a prominent REMS-specific link to the **REMS Website** on all product websites for consumers and healthcare providers. The **REMS Website** must not link back to the promotional product websites.

IV. REMS Assessments Timetable

Sandoz Inc. must submit REMS Assessments at 18 months, 3 years, and 7 years from the date of the initial REMS approval (03/05/2024). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting internal covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Sandoz Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the Jubbonti REMS**:**

Training and Educational Materials

Patient:

1. Patient Guide

Communication Materials

2. REMS Letter for Healthcare Providers
3. REMS Letter for Professional Societies

Other Materials

4. REMS Website

VI. Statutory Elements

This REMS is required under section 505-1 of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 355-1) and consists of the following elements:

1. Communication Plan
2. Timetable for Submission of Assessments

Jubbonti REMS Patient Guide

What is Jubbonti?

Jubbonti (denosumab-bbdz) is a prescription medicine used to:

- Treat osteoporosis (thinning and weakening of bone) in women after menopause ("change of life") who:
  - Are at high risk for fracture (broken bone)
  - Cannot use another osteoporosis medicine or other osteoporosis medicines did not work well
- Treat to increase bone mass in men with osteoporosis who are at high risk for fracture
- Treat bone loss in men who are at high risk for fracture receiving certain treatments for prostate cancer that has not spread to other parts of the body
- Treat bone loss in women who are at high risk for fracture receiving certain treatments for breast cancer that has not spread to other parts of the body
- Treat osteoporosis in men and women who will be taking corticosteroid medicines (such as prednisone) for at least 6 months and are at high risk for fracture

What is the serious risk of Jubbonti?

Patients with advanced chronic kidney disease, including dialysis-dependent patients, are at risk of severe hypocalcemia (low calcium levels in your blood) following Jubbonti administration.

Most people with low blood calcium levels do not have symptoms, but some people may have symptoms which include:

- Spasms, twitches, or cramps in your muscles
- Numbness or tingling in your fingers, toes, or around your mouth

Call your doctor right away if you think you may be having any of these symptoms.

What to expect before and during Jubbonti treatment:

- Talk to your doctor before starting Jubbonti.
- If you have low blood calcium before you start receiving Jubbonti, it may get worse during treatment.
- Your low blood calcium must be treated before you receive Jubbonti.
- Your doctor may prescribe calcium and vitamin D to help prevent low calcium levels in your blood while you take Jubbonti. Take calcium and vitamin D as your doctor tells you to.
- If you have advanced chronic kidney disease (may or may not be on kidney dialysis), Jubbonti may increase your risk for severe low calcium levels in your blood, leading to hospitalization, life-threatening events, and death.
- A mineral and bone disorder associated with kidney disease called chronic kidney disease-mineral bone disorder (CKD-MBD) may increase your risk for severe low calcium levels in blood. Before you start Jubbonti and during treatment, your doctor may need to do certain blood tests to check for CKD-MBD.

If you have advanced chronic kidney disease, your doctor may coordinate your Jubbonti treatment with a health care provider with expertise in CKD-MBD.

jubbonti®
(denosumab-bbdz) injection
60 mg/mL

Reference ID: 5340340

jubbonti®
(denosumab-bbdz) injection
60 mg/mL

Jubbonti REMS

FDA Required REMS Safety Information

Month YYYY

Important Safety Update

Dear Healthcare Provider:

The FDA has required this safety update as part of the Jubbonti REMS (**R**isk **E**valuation and **M**itigation **S**trategy) to inform healthcare providers about the following **serious risk of Jubbonti**.

Severe Hypocalcemia in Patients with Advanced Kidney Disease

Patients with advanced chronic kidney disease (eGFR < 30 mL/min/1.73 m^2), including dialysis-dependent patients, are at greater risk of severe hypocalcemia following Jubbonti administration.

- Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported.
- To minimize the risk of hypocalcemia in patients with advanced chronic kidney disease (CKD):
  - Evaluate for the presence of chronic kidney disease mineral and bone disorder (CKD-MBD) with intact parathyroid hormone (iPTH), serum calcium, 25(OH) vitamin D, and 1,25 $(OH)_2$ vitamin D prior to decisions regarding Jubbonti treatment.
  - Consider assessing bone turnover status (serum markers of bone turnover or bone biopsy) to evaluate the underlying bone disease that may be present.
  - Monitor serum calcium weekly for the first month after Jubbonti administration and monthly thereafter.
  - Coordinate care with healthcare providers with expertise in CKD-MBD for patients with advanced chronic kidney disease.

Role of the Healthcare Provider

- ✓ **Provide** each patient with a copy of the **Patient Guide**.
- ✓ **Review** information in the **Patient Guide** with each patient, including the serious risk of Jubbonti and the symptoms of severe hypocalcemia.
- ✓ **Advise** each patient to seek prompt medical attention if they have signs or symptoms of severe hypocalcemia.

This letter does not contain the complete safety profile for Jubbonti. Please review the Prescribing Information enclosed. All Jubbonti REMS materials are also available at www.jubbontirems.com or by contacting your local Sandoz Sales Representative.

Reporting Adverse Events

To report Adverse Reactions with Jubbonti, please call Sandoz Inc. at 1-800-525-8747, or report the event at FDA MedWatch.

Sincerely,

Shaloo Pandhi,
Global Head Patient Safety
Sandoz

jubbonti®
(denosumab-bbdz) injection
60 mg/mL

Jubbonti REMS

FDA Required REMS Safety Information

Month YYYY

Important Safety Update

Dear [Professional Society]:

The FDA has required Sandoz to distribute this safety update to your organization as part of our Jubbonti REMS (**R**isk **E**valuation and **M**itigation **S**trategy). We request that you inform your members about the following **serious risk of Jubbonti**.

Severe Hypocalcemia in Patients with Advanced Kidney Disease

Patients with advanced chronic kidney disease (eGFR < 30 mL/min/1.73 m^2), including dialysis-dependent patients, are at a greater risk of severe hypocalcemia following Jubbonti administration.

- Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported.
- To minimize the risk of hypocalcemia in patients with advanced chronic kidney disease (CKD):
  - Evaluate for the presence of chronic kidney disease mineral and bone disorder (CKD-MBD) with intact parathyroid hormone (iPTH), serum calcium, 25(OH) vitamin D, and 1,25 $(OH)_2$ vitamin D prior to decisions regarding Jubbonti treatment.
  - Consider assessing bone turnover status (serum markers of bone turnover or bone biopsy) to evaluate the underlying bone disease that may be present.
  - Monitor serum calcium weekly for the first month after Jubbonti administration and monthly thereafter.
  - Coordinate care with healthcare providers with expertise in CKD-MBD for patients with advanced chronic kidney disease.

Role of the Healthcare Provider

- ✓ **Provide** each patient with a copy of the **Patient Guide**.
- ✓ **Review** information in the **Patient Guide** with each patient, including the serious risk of Jubbonti and the symptoms of severe hypocalcemia.
- ✓ **Advise** each patient to seek prompt medical attention if they have signs or symptoms of severe hypocalcemia.

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Sincerely,

Shaloo Pandhi,
Global Head Patient Safety
Sandoz

jubbonti®
(denosumab-bbdz) injection
60 mg/mL

Jubbonti REMS

What is the Jubbonti REMS?

The Jubbonti REMS (**R**isk **E**valuation and **M**itigation **S**trategy) is a safety program required by the Food and Drug Administration. The purpose of the Jubbonti REMS is to inform healthcare providers and patients about the risk of severe hypocalcemia in patients with advanced chronic kidney disease, including dialysis-dependent patients, following Jubbonti administration.

The Jubbonti REMS materials are designed to inform healthcare providers and their patients about the risk of severe hypocalcemia associated with Jubbonti and include the below materials. It is important that you discuss with your patients the information included in the **Patient Guide**.

- REMS Letter for Healthcare Providers
- Prescribing Information
- Patient Guide

Resources

For Healthcare Providers

- REMS Letter for Healthcare Providers
- Prescribing Information
- Patient Guide

For Patients

- Patient Guide

To learn more about Jubbonti, read the Important Safety Information and use the links to access the Jubbonti REMS materials.

Reporting Adverse Events

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jubbonti®
(denosumab-bbdz) injection
60 mg/mL

Jubbonti REMS

Contact Us

If you have a question about the REMS, clinical inquiry, or would like to report an adverse event related to Jubbonti, call 1-800-525-8747.

→ Click here to report an adverse event online

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

THERESA E KEHOE
03/05/2024 08:01:26 AM

LALEH AMIRI KORDESTANI
03/05/2024 08:03:22 AM