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RESEARCH**

APPLICATION NUMBER:

761436Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

BOSAYA (denosumab-kyqq) REMS

I. Administrative Information

Risk: Severe hypocalcemia

Application Number: BLA 761436

Application Holder: Biocon Biologics Inc

Initial REMS Approval: 09/2025

II. REMS Goal

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

Objective 1: Inform healthcare providers on:

- Risk of severe hypocalcemia in patients with advanced chronic kidney disease (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m²).
- Need to assess for the presence of chronic kidney disease-mineral bone disorder (CKD-MBD) before initiating BOSAYA in patients with advanced chronic kidney disease.

III. REMS Requirements

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

Target Audience	Communication Materials & Dissemination Plans
Healthcare providers who are likely to prescribe BOSAYA	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 BOSAYA 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 the correct address cannot be obtained, the attempt will be documented. 2. Email REMS Letter for Professional Societies within 60 calendar days of the date BOSAYA 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:

Target Audience	Communication Materials & Dissemination Plans
	a. American Academy of Family Physicians b. American Association of Clinical Endocrinologists c. American College of Physicians d. American College of Rheumatology e. American Society of Bone Mineral Research f. American Society of Clinical Oncology g. Bone Health and Osteoporosis Foundation h. Endocrine Society i. North American Menopause Society 3. Make available via a link from the BOSAYA REMS Website. 4. Disseminate through field-based sales and medical representatives from the date BOSAYA is first commercially distributed for the duration of the REMS. 5. Disseminate and prominently display at Professional Meetings where Biocon Biologics Inc. has a BOSAYA commercial presence from the date BOSAYA is first commercially distributed for the duration of the REMS. Patient Guide and Prescribing Information 1. Disseminate and prominently display at Professional Meetings where Biocon Biologics Inc. has a BOSAYA commercial presence from the date BOSAYA 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 BOSAYA 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 Prescribing Information 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 BOSAYA is first commercially distributed. 2. Maintain the REMS Website from the date BOSAYA 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 Assessment Timetable

Biocon Biologics Inc. must submit REMS Assessments at 18 months, 3 years, and 7 years from the date of the initial approval of the REMS (09/16/2025). To facilitate the inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Biocon Biologics 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 BOSAYA REMS:

Training and Educational Material

Patient:

1. [Patient Guide](#)

Communication Materials

2. [REMS Letter for Healthcare Providers](#)
3. [REMS Letter for Professional Societies](#)

Other Material

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

Bosaya® REMS

FDA Required REMS Safety Information / Important Safety Update

Dear Healthcare Provider:

The FDA has required this safety update as part of the Bosaya® REMS (Risk Evaluation and Mitigation Strategy) to inform healthcare providers about the following **serious risk of Bosaya®**:

Severe Hypocalcemia in Patients with Advanced Kidney Disease

Patients with advanced chronic kidney disease (eGFR < 30 mL/min/1.73 m²), including dialysis-dependent patients, are at greater risk of severe hypocalcemia following Bosaya® 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 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 Bosaya® 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 Bosaya® 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 Bosaya® 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 Bosaya®. Please review the Prescribing Information enclosed. All Bosaya® REMS materials are also available at www.bosayahcp.com

Reporting Adverse Events

To report Adverse Reactions with Bosaya®, please call Biocon Biologics Inc. at 1-833-986-1468, or report the event at FDA MedWatch.

Sincerely,

Biocon Biologics Inc.

Bosaya® REMS

FDA Required REMS Safety Information / Important Safety Update

Dear [Professional Society]:

The FDA has required Biocon Biologics Inc. to distribute this safety update to your organization as part of our Bosaya® REMS (Risk Evaluation and Mitigation Strategy). We request that you inform your members about the following **serious risk of Bosaya®**:

Severe Hypocalcemia in Patients with Advanced Kidney Disease

Patients with advanced chronic kidney disease (eGFR < 30 mL/min/1.73 m²), including dialysis-dependent patients, are at greater risk of severe hypocalcemia following Bosaya® 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 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 Bosaya® 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 Bosaya® 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 Bosaya® 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 Bosaya®. Please review the Prescribing Information enclosed.

All Bosaya® REMS materials are also available at www.bosayahcp.com

Reporting Adverse Events

To report Adverse Reactions with Bosaya®, please call Biocon Biologics Inc. at 1-833-986-1468, or report the event at FDA MedWatch.

Sincerely,
Biocon Biologics Inc.

Bosaya® REMS PATIENT GUIDE

What is Bosaya®?

Bosaya® (denosumab-kyqq) 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 of fracture

What is the serious risk of Bosaya®?

Patients with advanced chronic kidney disease, including dialysis-dependent patients, are at risk of severe hypocalcemia (low calcium levels in your blood) following Bosaya® 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 Bosaya® treatment:

- Talk to your doctor before starting Bosaya®.
- If you have low blood calcium before you start receiving Bosaya®, it may get worse during treatment.
- Your low blood calcium must be treated before you receive Bosaya®.
- Your doctor may prescribe calcium and vitamin D to help prevent low calcium levels in your blood while you take Bosaya®. 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), Bosaya® 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 Bosaya® 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 Bosaya® treatment with a healthcare provider with expertise in CKD-MBD.

Bosaya[®] (denosumab-kyqq) Risk Evaluation and Mitigation Strategy

What is the Bosaya[®] REMS?

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration to manage known or potential serious risks associated with a drug product.

The purpose of the Bosaya[®] REMS is to inform healthcare providers and patients about the following serious risk of:

► Severe Hypocalcemia in Patients with Advanced Kidney Disease

The Bosaya[®] REMS program materials are designed to inform healthcare providers and patients about this risk with Bosaya[®]. The Bosaya[®] REMS program materials include a REMS Letter for Healthcare Providers and a Patient Guide. It is important that you discuss with each patient the information included in the Patient Guide.

To learn more about the serious risk of Bosaya[®], read the [Important Safety Information](#) provided in this link and use the links on the right to access REMS supporting materials.

Reporting Adverse Events

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. Healthcare providers should report all suspected adverse events associated with Bosaya[®] to the FDA or to call Biocon Biologics Inc. at 1-833-986-1468.

Materials for Healthcare Providers

[↓ REMS Letter for Healthcare Providers](#)

[↓ Patient Guide](#)

[↓ Prescribing Information](#)

Materials for Patients

[↓ Patient Guide](#)

**Placeholder for
Bosaya[®] Logo**

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
09/16/2025 01:43:30 PM

CHRISTY L OSGOOD
09/16/2025 01:51:26 PM