INDICATIONS

STOBOCLO® (denosumab-bmwo) is a RANK ligand (RANKL) inhibitor indicated for treatment:

- of **postmenopausal women** with osteoporosis at high risk for fracture
- to **increase bone mass in men** with osteoporosis at high risk for fracture or in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- of **glucocorticoid-induced osteoporosis** in men and women at high risk for fracture
- to **increase bone mass in women** at high risk for fracture receiving an adjuvant aromatase inhibitor therapy for breast cancer

IMPORTANT SAFETY INFORMATION

WARNING: 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 the administration of denosumab products. Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported

The presence of chronic kidney disease-mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia in these patients

Prior to initiating STOBOCLO in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with STOBOCLO in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD

Contraindications:

- Hypocalcemia: Pre-existing hypocalcemia must be corrected before initiating therapy.
- Pregnancy: Denosumab products may cause fetal harm when administered to a pregnant woman.
- Hypersensitivity: Known hypersensitivity to denosumab products.

Severe Hypocalcemia and Mineral Metabolism Changes. Severe hypocalcemia can occur. Ensure adequate calcium and vitamin D supplementation.

Drug Products with Same Active Ingredient. Patients receiving STOBOCLO should not receive other denosumab products concomitantly.

Hypersensitivity. Clinically significant hypersensitivity including anaphylaxis has been reported with denosumab products. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of STOBOCLO.

Osteonecrosis of the Jaw (ONJ). ONJ can occur in patients on STOBOCLO, particularly after tooth extraction and/or local infection with delayed healing. A routine oral exam is recommended before starting STOBOCLO, with a dental evaluation and preventive care for high-risk patients. Good oral hygiene should be maintained, and ONJ-risk drugs may heighten ONJ likelihood, especially with extended STOBOCLO exposure. For invasive dental procedures, individualize treatment based on clinical judgment. If ONJ develops, consult a dentist or oral surgeon. Extensive surgery may worsen ONJ, consider discontinuing STOBOCLO based on a benefit-risk assessment.

Atypical Subtrochanteric and Diaphyseal Femoral Fractures. Atypical low energy or low trauma fractures of the shaft have been reported in patients receiving denosumab products. During STOBOCLO treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Patients with thigh or groin pain should be evaluated for an atypical femur fracture, including assessment for potential fractures in the contralateral limb. Interruption of STOBOCLO therapy should be considered, pending a benefit-risk assessment, on an individual basis.

Multiple Vertebral Fractures (MVF) Following Discontinuation of Treatment. Following discontinuation of denosumab treatment, fracture risk increases, including the risk of multiple vertebral fractures. Prior vertebral fracture was a predictor of multiple vertebral fractures after denosumab discontinuation. Evaluate an individual's benefit-risk before initiating treatment with STOBOCLO. If STOBOCLO treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

Serious Infections. In a trial of women with postmenopausal osteoporosis, serious infections were more frequent with denosumab than placebo, including skin, abdominal, urinary, ear infections, and endocarditis. Overall infection rates were similar between groups. Advise patients to seek medical attention for severe infection symptoms like cellulitis. Those on immunosuppressants or with weakened immune systems may face higher risks. Assess the benefit-risk profile before starting STOBOCLO, and reconsider its use if serious infections develop.

Dermatologic Adverse Reactions. Epidermal and dermal adverse events such as dermatitis, eczema, and rashes have been reported in patients treated with denosumab. Consider discontinuing STOBOCLO if severe symptoms develop.

Musculoskeletal Pain. In postmarketing experience, severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking denosumab products. Consider discontinuing use if severe symptoms develop.

Suppression of Bone Turnover. In clinical trials in women with postmenopausal osteoporosis, denosumab significantly suppressed bone remodeling, with unknown long-term effects that may lead to osteonecrosis of the jaw, atypical fractures, or delayed fracture healing; patients should be monitored for these outcomes.

Hypercalcemia in Pediatric Patients with Osteogenesis Imperfecta. STOBOCLO is not indicated for use in pediatric patients. Hypercalcemia has been reported in pediatric patients with osteogenesis imperfecta treated with denosumab products. Some cases required hospitalization.

Adverse Reactions:

- **Postmenopausal osteoporosis:** Most common adverse reactions (> 5%) were: back pain, pain in extremity, hypercholesterolemia, musculoskeletal pain, and cystitis. Pancreatitis has been reported in clinical trials.
- **Male osteoporosis:** Most common adverse reactions (> 5%) were: back pain, arthralgia, and nasopharyngitis.
- **Glucocorticoid-induced osteoporosis:** Most common adverse reactions (> 3%) were: back pain, hypertension, bronchitis, and headache.
- **Bone loss due to hormone ablation for cancer:** Most common adverse reactions (≥10%) were: arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials.