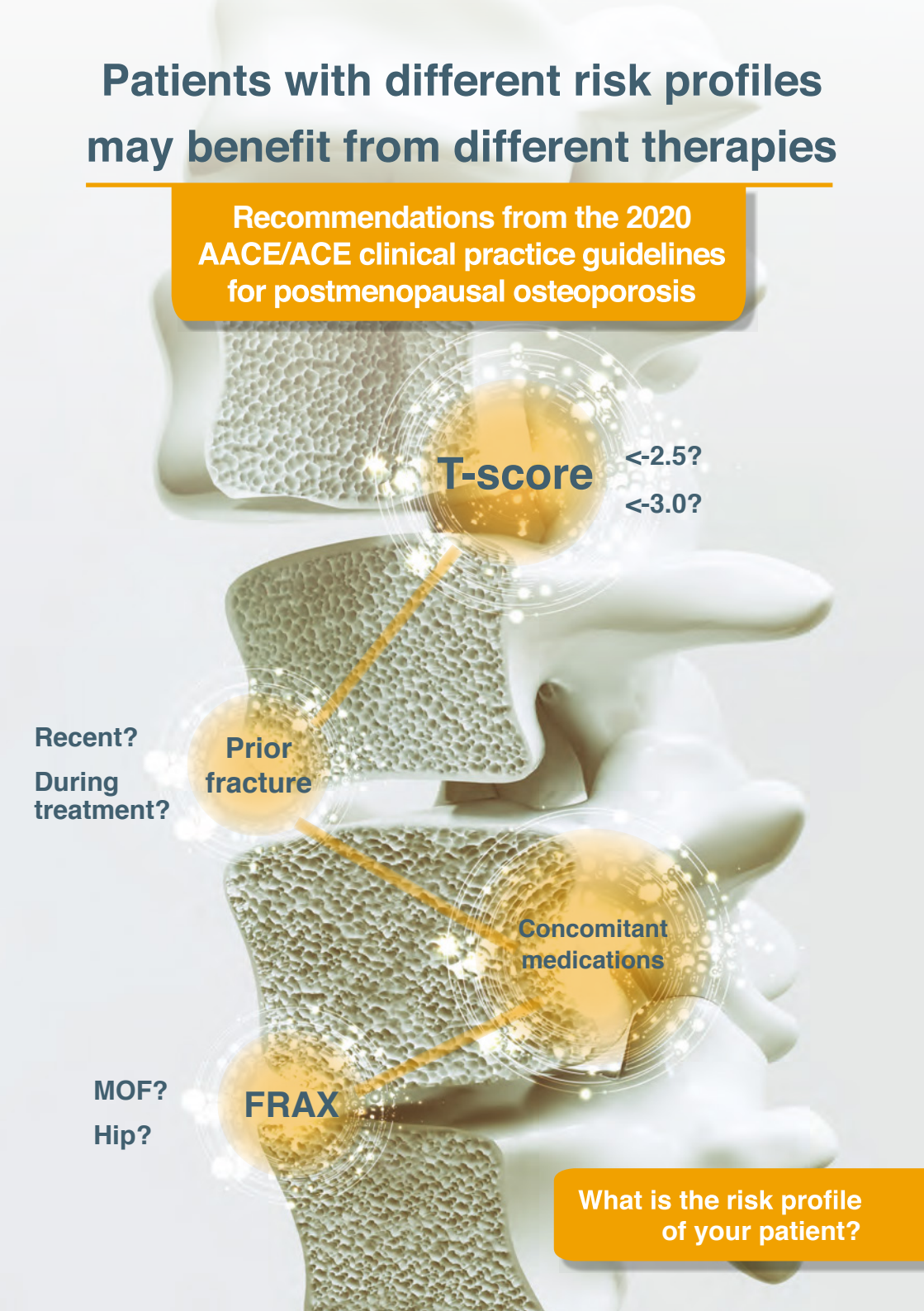
Patients with different risk profiles may benefit from different therapies

Recommendations from the 2020 AACE/ACE clinical practice guidelines for postmenopausal osteoporosis



What is the risk profile of your patient?

Your patient is at high or very high risk of fracture if they meet ≥1 of the below criteria:

		HIGH RISK	VERY HIGH RISK
BMD T-SCORE		• T-score ≤-2.5 to -3.0[1] • T-score -1.0 to -2.5, refer to FRAX[1] • T-score -1.0 to -2.5 **and** fragility fracture of proximal humerus, pelvis or distal forearm	• T-score <-3.0[1]
FRACTURE HISTORY	**PRIOR FRACTURE**	• >12 months (hip or spine) with osteopenia (T-score ≤-1.0 to -2.5)[1]	• Recent (≤12 months)[1]
	MULTIPLE FRACTURE	N/A	• Yes[1]
	FRACTURE DURING TREATMENT*	N/A	• Yes[1]
FRAX		• FRAX probability ≥20% (MOF) or ≥3% (hip)[1] • FRAX probability estimates are country-specific[1] • Local data suggest a FRAX (BMD) risk of 9.95% (MOF) is an appropriate intervention threshold for Hong Kong[2]	• FRAX probability >30% (MOF), >4.5% (hip)[1]
		• Correct calcium and vitamin D levels[1] • Address causes of secondary osteoporosis[1] • Provide education on lifestyle measures, fall prevention and benefits and risk of medication[1]	
INITIAL TREATMENT		• Bisphosphonate[1] • Denosumab[1]	• Romosozumab (1 year)[1] • Teriparatide (≤2 years)[1] • Denosumab[1] • Zoledronic acid[1] Anabolic and dual-acting agents that enhance bone formation are preferred as initial therapy in very high risk patients[1]
MONITORING		• Yearly (including BMD) for response to therapy and change in fracture risk[1]	• Yearly (including BMD) for response to therapy and change in fracture risk[1]

SUBSEQUENT TREATMENT		• For bisphosphonate
		  • Review after 3 years (IV) or 5 years (oral)[1]
		  • A drug holiday may be considered if no fractures occurred, BMD is stable or increasing and fracture risk is low[1]
		  • Consider anabolic agent or romosozumab if bone loss or fracture occurs[1]
		• For denosumab
		  • Drug holiday is **NOT** recommended[1]
		  • If discontinued, switch to another antiresorptive agent[1]
			• Consider denosumab or bisphosphonates after anabolic agent or romosozumab[1]
			• If denosumab is discontinued, switch to another antiresorptive agent[1]
			• Zoledronic acid is recommended to be continued for 6 years if BMD stable; consider anabolic agent or romosozumab if bone loss or fracture occurs[1]

*Osteoporosis medication or medication harmful to bone (e.g. glucocorticoids).

EVIDENCE FOR FRACTURE RISK REDUCTION[1]

TREATMENT	VERTEBRAL[1]	NON-VERTEBRAL[1]	HIP[1]	Suitable patient profile...
Dual-action (both antiresorptive & bone-forming)				
ROMOSOZUMAB	✓	✓*	✓*	• Very high fracture risk, preferably as initial therapy[1] • Patients with very low BMD[1] • Recent (≤12 months) fracture[1] • Fracture/bone loss while on previous antiresorptive therapy or medication harmful to bone[1]
Anabolic agents				
TERIPARATIDE	✓	✓	Not demonstrated†	
Antiresorptives (injectable)				
DENOSUMAB	✓	✓	✓	• High to very high fracture risk[1] • As follow-up therapies for patients treated with dual-action and anabolic agents[1] • Injectable antiresorptives may be suitable for patients with intolerance/ poor compliance with oral bisphosphonates[1] • E.g., denosumab can be used in patients with renal insufficiency[1]
ZOLEDRONIC ACID	✓	✓	✓	
Antiresorptives (oral)				
ALENDRONATE	✓	✓	✓	• High fracture risk • Prior fracture >12 months/ no prior fracture[1]

*Clinical fracture reduction was shown in both trials. Non-vertebral and hip fracture reductions were shown at month 24 for patients receiving 12 months of romosozumab followed by 12 months of alendronate compared with patients receiving 24 months of alendronate.
†The lack of demonstrable effect at these sites should be considered in context that the studies may not have been adequately powered.

Abbreviations: AACE, American Association of Clinical Endocrinologists; ACE, American College of Endocrinology; BMD, bone mineral density; FRAX, fracture risk assessment; IV, intravenous; MOF, major osteoporotic fracture; N/A, not applicable.

References: 1. Camacho P, et al. *Endocr Pract* 2020;26:1–46. **2.** Cheung E, et al. *Osteoporos Int* 2014;25:1017–1023.

Prolia® (Denosumab) Abbreviated Prescribing Information
Prolia® (denosumab) Solution for Injection in Pre-filled Syringe 60 mg/mL

INDICATIONS Prolia is indicated for: i) treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy; ii) treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy; iii) treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia also reduced the incidence of vertebral fractures; iv) treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

DOSAGE AND ADMINISTRATION The recommended dose of Prolia is 60 mg administered as a single subcutaneous injection once every 6 months. Administer Prolia via subcutaneous injection in the upper arm, the upper thigh, or the abdomen. All patients should receive calcium 1000 mg daily and at least 400 IU vitamin D daily.

CONTRAINDICATIONS Hypocalcemia and pregnancy, as well as hypersensitivity to any component of the product.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE *Hypersensitivity:* Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritis, and urticaria. *Hypocalcemia and Mineral Metabolism:* Hypocalcemia may be exacerbated by the use of Prolia. Pre-existing hypocalcemia must be corrected prior to initiating therapy with Prolia. Hypocalcemia following Prolia administration is a significant risk in patients with severe renal impairment [creatinine clearance < 30 mL/min] or receiving dialysis. Adequately supplement all patients with calcium and vitamin D. *Osteonecrosis of the Jaw (ONJ):* ONJ has been reported in patients receiving Prolia. The start of treatment or of a new course of treatment should be delayed in patients with unhealed open soft tissue lesions in the mouth. A dental examination with preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with Prolia in patients with concomitant risk factors. All patients should be encouraged to maintain good oral hygiene, undergo routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling, or non-healing of sores or discharge during treatment with Prolia. While on treatment, invasive dental procedures should be performed with caution and avoided in close proximity to Prolia treatment. *Atypical Subtrochanteric and Diaphyseal Femoral Fractures:* Atypical low-energy or low trauma fractures of the shaft have been reported in patients receiving Prolia. Patients should be advised to report new or unusual thigh, hip, or groin pain. *Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolia Treatment:* Following discontinuation of Prolia treatment, fracture risk increases, including the risk of multiple vertebral fractures. If Prolia treatment is discontinued, consider transitioning to an alternative antiresorptive therapy. *Serious Infections:* Serious infections leading to hospitalization were reported in clinical trial. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis. *Dermatologic Adverse Reactions:* Dermatitis, eczema, and rashes. Most of these events were not specific to the injection site. Consider discontinuing Prolia if severe symptoms develop. *Musculoskeletal Pain:* Severe and occasionally incapacitating bone, joint, and/or muscle pain. Consider discontinuing use if severe symptoms develop. *Suppression of Bone Turnover:* In clinical trials treatment with Prolia resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. *Osteonecrosis of the external auditory canal:* Osteonecrosis of the external auditory canal has been reported with denosumab. Possible risk factors include steroid use and chemotherapy and/or local risk factors such as infection or trauma.

INTERACTIONS In subjects with postmenopausal osteoporosis, Prolia (60 mg subcutaneous injection) did not affect the pharmacokinetics of midazolam, which is metabolized by cytochrome P450 3A4 (CYP3A4), indicating that it should not affect the pharmacokinetics of drugs metabolized by this enzyme in this population.

PREGNANCY AND LACTATION *Pregnancy:* Category X. *Breast-feeding:* It is not known whether Prolia is excreted into human milk.

PEDIATRIC, GERIATRIC AND RENAL IMPAIRMENT *Pediatric:* Prolia is not recommended in pediatric patients. *Geriatric:* No overall differences in safety or efficacy were observed in clinical studies between elderly patients and younger patients and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. *Renal Impairment:* No dose adjustment is necessary in patients with renal impairment.

UNDESIRABLE EFFECTS The most common adverse reactions reported with Prolia in patients with postmenopausal osteoporosis are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. The most common adverse reactions reported with Prolia in men with osteoporosis are back pain, arthralgia, and nasopharyngitis. The most common (per patient incidence ≥ 10%) adverse reactions reported with Prolia in patients with bone loss receiving androgen deprivation therapy for prostate cancer or adjuvant aromatase inhibitor therapy for breast cancer are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials. The most common adverse reactions leading to discontinuation of Prolia in patients with postmenopausal osteoporosis are back pain and constipation.

OVERDOSE There is no experience with overdosage with Prolia.

Abbreviated Prescribing Information Version: HKPROPI01
Please read the full prescribing information prior to administration and full prescribing information is available on request.

For medical inquiries or to report adverse events/product complaint, please contact 800 961 142 or email medinfo.JAPAC@amgen.com

EVENITY® (Romosozumab) Abbreviated Prescribing Information
EVENITY® Solution for Injection in Prefilled Syringe 105 mg/1.17 ml

INDICATIONS EVENITY is indicated in treatment of severe osteoporosis in postmenopausal women at high risk of fracture.

DOSAGE AND ADMINISTRATION The recommended dose is 210 mg romosozumab (administered as two subcutaneous injections of 105 mg each) once monthly for 12 months. Patients should be adequately supplemented with calcium and vitamin D before and during treatment. Following completion of romosozumab therapy, transition to antiresorptive therapy is recommended in order to extend the benefit achieved with romosozumab beyond 12 months. *Missed doses:* If the romosozumab dose is missed, administer as soon as it can be feasible. Thereafter, the next romosozumab dose should not be given earlier than one month after the last dose. *Elderly:* No dose adjustment is necessary in elderly patients. *Renal impairment:* No dose adjustment is required in patients with renal impairment. Serum calcium should be monitored in patients with severe renal impairment or receiving dialysis. *Hepatic impairment:* No clinical trials have been conducted to evaluate the effect of hepatic impairment. *Paediatric population:* The safety and efficacy of romosozumab in paediatric patients (age <18 years) have not yet been established. No data are available. Method of administration: Subcutaneous use. To administer the 210 mg dose, 2 subcutaneous injections of romosozumab should be given into the abdomen, thigh, or upper arm. The second injection should be given immediately after the first one but at a different injection site. Administration should be performed by an individual who has been trained in injection techniques.

CONTRAINDICATIONS Hypersensitivity to the active substance(s) or to any of the excipients. Hypocalcaemia. History of myocardial infarction or stroke.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE Myocardial infarction and stroke: In randomised controlled studies, an increase in serious cardiovascular events (myocardial infarction and stroke) has been observed in romosozumab treated patients compared to controls. When determining whether to use romosozumab for an individual patient, consideration should be given to her fracture risk over the next year and her cardiovascular risk based on risk factors (e.g. established cardiovascular disease, hypertension, hyperlipidaemia, diabetes mellitus, smoking, severe renal impairment, age). Romosozumab should only be used if the prescriber and patient agree that the benefit outweighs the risk. If a patient experiences a myocardial infarction or stroke during therapy, treatment with romosozumab should be discontinued. Hypocalcaemia: Transient hypocalcaemia has been observed in patients receiving romosozumab. Hypocalcaemia should be corrected prior to initiating therapy with romosozumab and patients should be monitored for signs and symptoms of hypocalcaemia. If any patient presents with suspected symptoms of hypocalcaemia during treatment, calcium levels should be measured. Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 ml/min/1.73 m^2) or receiving dialysis are at greater risk of developing hypocalcaemia and the safety data for these patients is limited. Calcium levels should be monitored in these patients. Hypersensitivity: Clinically significant hypersensitivity reactions, including angioedema, erythema multiforme, and urticaria occurred in the romosozumab group in clinical trials. If an anaphylactic or other clinically significant allergic reaction occurs, appropriate therapy should be initiated and use of romosozumab should be discontinued. Osteonecrosis of the jaw: Osteonecrosis of the jaw (ONJ), has been reported rarely in patients receiving romosozumab. All patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling or non-healing of sores or discharge during treatment with romosozumab. Patients who are suspected of having or who develop ONJ while on romosozumab should receive care by a dentist or an oral surgeon with expertise in ONJ. Discontinuation of romosozumab therapy should be considered until the condition resolves and contributing risk factors are mitigated where possible. Atypical femoral fractures: Atypical low-energy or low trauma fracture of the femoral shaft, which can occur spontaneously, has been reported rarely in patients receiving romosozumab. Any patient who presents with new or unusual thigh, hip, or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patient presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of romosozumab therapy should be considered, based on an individual benefit-risk assessment. Sodium content: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially sodium-free.

INTERACTIONS No drug interaction studies have been performed with romosozumab. No pharmacokinetic drug interactions are expected with romosozumab.

PREGNANCY AND LACTATION Pregnancy: Romosozumab is not indicated for use in women of child-bearing potential or in pregnant women. There are no data from the use of romosozumab in pregnant women. A risk for malformations of developing digits in the human foetus is low following romosozumab exposure due to the timing of digit formation in the first trimester in humans, a period when placental transfer of immunoglobulins is limited. Breast-feeding: Romosozumab is not indicated for use in breast-feeding women. No data are available on excretion of romosozumab in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. Fertility: No data are available on the effect of romosozumab on human fertility. Animal studies in female and male rats did not show any effects on fertility endpoints.

ADVERSE REACTIONS The most common adverse reactions were nasopharyngitis (13.6%) and arthralgia (12.4%). Hypersensitivity-related reactions occurred in 6.7% of patients treated with romosozumab. Hypocalcaemia was reported uncommonly (0.4% of patients treated with romosozumab). In randomised controlled studies, an increase in serious cardiovascular events (myocardial infarction and stroke) has been observed in romosozumab treated patients compared to controls. Adverse reactions are presented in order of decreasing seriousness by System Organ Class: *Infections and infestations:* Nasopharyngitis, Sinusitis; *Immune system disorders:* Hypersensitivity, Rash, Dermatitis, Urticaria, Angioedema, Erythema multiforme; *Metabolism and nutrition disorders:* Hypocalcaemia; *Nervous system disorders:* Headache, Stroke; *Eye disorders:* Cataract; *Cardiac disorders:* Myocardial infarction; *Musculoskeletal and connective tissue disorders:* Arthralgia, Neck pain, Muscle spasms; *General disorders and administration site conditions:* Injection site reactions

OVERDOSE There is no experience with overdose in clinical trials.

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HK-AMG-166
HK-04617-EVE-2020-Aug
Date of Approval: Oct 2020