TYMLOS®
(abaloparatide) injection

FOR YOUR POSTMENOPAUSAL PATIENTS AT HIGH RISK FOR OSTEOPOROTIC FRACTURE[1]

BE AN OSTEOPOROSIS FIRST RESPONDER

1. **ASK**
   ABOUT FRACTURES
2. **DIAGNOSE**
   POSTMENOPAUSAL OSTEOPOROSIS
3. **TREAT**
   WITH TYMLOS

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF OSTEOSARCOMA

- **Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma (a malignant bone tumor) in male and female rats. The effect was observed at systemic exposures to abaloparatide ranging from 4 to 28 times the exposure in humans receiving the 80 mcg dose. It is unknown if TYMLOS will cause osteosarcoma in humans.**
- **The use of TYMLOS is not recommended in patients at increased risk of osteosarcoma including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, open epiphyses, bone metastases or skeletal malignancies, hereditary disorders predisposing to osteosarcoma, or prior external beam or implant radiation therapy involving the skeleton.**
- **Cumulative use of TYMLOS and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.**

Limitations of Use

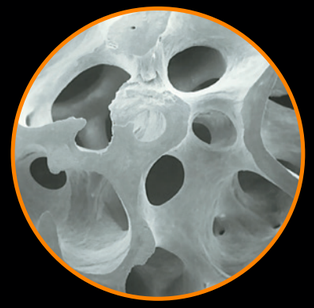
Because of the unknown relevance of the rodent osteosarcoma findings to humans, cumulative use of TYMLOS and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.

Please see accompanying Full Prescribing Information, including Boxed Warning, inside back pocket.

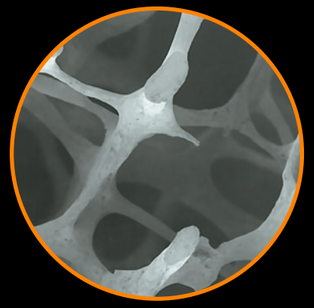
For postmenopausal women,

Osteoporotic fractures are more common than you may think[2]

Osteoporosis is characterized by **low bone mass** and **microarchitectural deterioration**, leading to increased bone fragility and fracture risk[3]



HEALTHY BONE



OSTEOPOROTIC BONE

The annual incidence of osteoporotic fracture in US women aged 50 years and older was higher than that of stroke, myocardial infarction (MI), and breast cancer combined[2,4,5]*

~3X MORE FREQUENT THAN STROKE in women of all ages[4]*

~4X MORE FREQUENT THAN MI in women older than 35 years[4]*

~5X MORE FREQUENT THAN ESTIMATED NEW CASES OF BREAST CANCER in women of all ages[5]*

! In 2005, the annual incidence of osteoporotic fractures in US women aged 50 years and older was 1,455,843[2]

*Incidence of stroke=425,000; incidence of MI=310,000; estimated new cases of breast cancer=266,120.[4,5]

IMPORTANT SAFETY INFORMATION (cont'd)

Orthostatic Hypotension: Orthostatic hypotension may occur with TYMLOS, typically within 4 hours of injection. Associated symptoms may include dizziness, palpitations, tachycardia or nausea, and may resolve by having the patient lie down. For the first several doses, TYMLOS should be administered where the patient can sit or lie down if necessary.

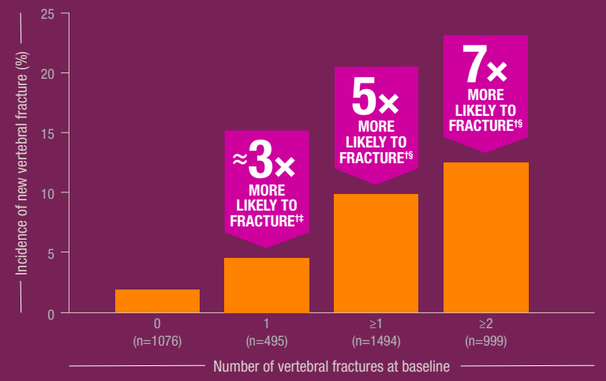
Hypercalcemia: TYMLOS may cause hypercalcemia. TYMLOS is not recommended in patients with pre-existing hypercalcemia or in patients who have an underlying hypercalcemic disorder, such as primary hyperparathyroidism, because of the possibility of exacerbating hypercalcemia.

For postmenopausal women,

An osteoporotic fracture is a sentinel event[6]

The first 12 months after a fracture are a critical intervention period in which patients are at heightened risk for subsequent fracture[7]

Incidence of new vertebral fracture in first year of study[7]*



*A study of postmenopausal women with osteoporosis (n=2725) assigned to the placebo groups in 4 large clinical trials conducted between 1993 and 1998 to determine incidence of new vertebral fractures.

†In the year following a vertebral fracture versus those without fracture.[7]

‡P=0.002.[7]

§P<0.001.[7]

Incidence is based on Kaplan-Meier estimates of the survival function.[7]

Studies have shown an increased risk for subsequent hip fracture after other nonvertebral fracture[8]:

6X MORE LIKELY WITHIN 1 YEAR OF A PROXIMAL HUMERUS FRACTURE for women aged 65 years and older; the significance did not continue beyond 1 year[8‖]

2X MORE LIKELY WITH HISTORY OF WRIST FRACTURE for women aged 50 to 65 years versus those without a history of wrist fracture[9¶]

! If your postmenopausal patient has experienced an osteoporotic fracture, intervene early with treatment to help reduce the risk of vertebral and nonvertebral fractures

‖A prospective multicenter cohort of 8049 white women aged 65 years and older from the Study of Osteoporotic Fractures was followed for a mean of 9.8 years to evaluate the relationship between proximal humerus fractures and hip fractures.[8]

¶An analysis of postmenopausal women (N=158,940) aged ≥50 years from the National Osteoporosis Risk Assessment (NORA) prospective study who provided history of wrist fracture to determine future fracture risk.[9]

IMPORTANT SAFETY INFORMATION (cont'd)

Hypercalciuria and Urolithiasis: TYMLOS may cause hypercalciuria. It is unknown whether TYMLOS may exacerbate urolithiasis in patients with active or a history of urolithiasis. If active urolithiasis or pre-existing hypercalciuria is suspected, measurement of urinary calcium excretion should be considered.

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Many postmenopausal women at increased risk of fracture were not evaluated and treated[10]*

FEWER THAN 1 IN 5 WOMEN
who had primary care encounters in the 6 months after a hip fracture
WERE ASSESSED OR DIAGNOSED WITH OSTEOPOROSIS[10]*

BONE STRENGTH: a measure of quality and BMD[3]

BMD AS ASSESSED BY DXA
DOES NOT MEASURE OVERALL BONE STRENGTH OR QUALITY
but is most commonly used to diagnose osteoporosis[3,11]

IN A STUDY OF POSTMENOPAUSAL WOMEN
who reported new osteoporotic fractures at 1 year,
82% had peripheral T-scores that were not in the osteoporotic range[12†]

Osteoporosis can be diagnosed in clinical practice based on presence and/or history of fragility fractures[13,14†§]

BMD=bone mineral density; DXA=dual energy x-ray absorptiometry.

*An observational study of trends in utilization of osteoporosis-related health services within 6 and 12 months following hip fracture among a treatment-naive cohort of privately insured women aged 50 years and older (N=8349), with no prior osteoporosis diagnoses.[10]

†The longitudinal, observational NORA study of 149,524 white postmenopausal women aged 50 years and older examined reported fractures in the year following BMD measurement.[12]

†A fracture that occurs with minimal trauma, such as a fall from standing height or less.[15]

§Fragility fractures of the spine or hip, regardless of BMD; fragility fractures of the proximal humerus, pelvis, or possibly distal forearm with osteopenia or low bone mass (T-score between -1 and -2.5).[14]

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: The most common adverse reactions (incidence ≥2%) are hypercalciuria, dizziness, nausea, headache, palpitations, fatigue, upper abdominal pain and vertigo.

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Treat postmenopausal osteoporosis before it gets worse

Osteoporosis treatments can be broadly grouped into 2 classes[14,16]:

ANABOLIC AGENTS
increase osteoblasts[16,17]

[Help build new bone]

ANTIRESORPTIVE AGENTS
decrease osteoclasts[17,18]

[Help slow bone loss]

RECEIVING PRIMARY CARE WAS THE STRONGEST AND MOST CONSISTENT PREDICTOR
of which patients used recommended osteoporosis-related services after a fracture[10]*

You are on the front line of postmenopausal osteoporosis and play a critical role in your patients' treatment decision

*An observational study of trends in utilization of osteoporosis-related health services within 6 and 12 months following hip fracture among a treatment-naive cohort of privately insured women aged 50 years and older (N=8349), with no prior osteoporosis diagnoses.[10]

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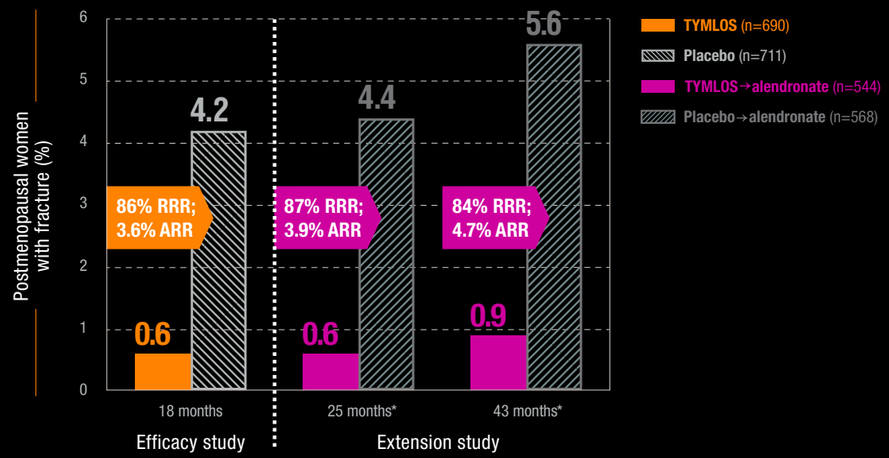
Extended efficacy results with TYMLOS, an anabolic[1,19]

New vertebral fracture risk reduction achieved with TYMLOS was extended with alendronate[1]

Incidence of new vertebral fractures[1,20]



ARR=absolute risk reduction; RRR=relative risk reduction.
Primary endpoint.[1]
P<0.0001 at all time points.[1,21]
*TYMLOS or placebo for 18 months, followed by 1 month of no treatment, then up to 24 months of alendronate.[22]

The primary and secondary efficacy endpoints for the extension study were at 25 months. The 43-month data are exploratory endpoints.[21]

Efficacy study design: A randomized, multicenter, double-blind, placebo- and active-controlled clinical study in postmenopausal women with osteoporosis aged 49 to 86 years (mean age 69 years) who were randomized to receive TYMLOS 80 mcg (n=824) or placebo (n=821) subcutaneously once daily for 18 months.[1,23]

Extension study design: Enrolled patients who had received 18 months of TYMLOS (n=558) or placebo (n=581), followed by 1 month of no treatment. Patients were maintained within their original treatment group and transitioned to receive up to 24 additional months of open-label alendronate.[1,20,21]

IMPORTANT SAFETY INFORMATION (cont'd)

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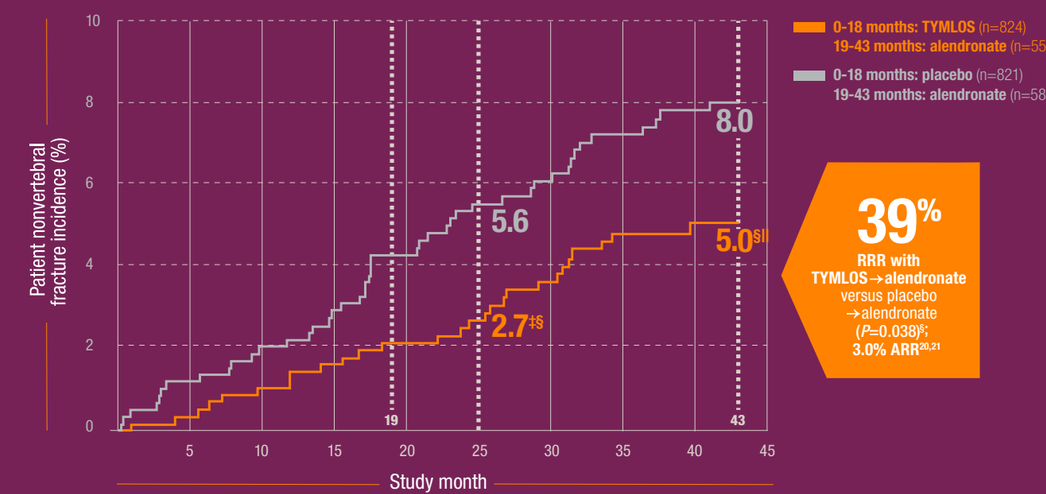
TREAT WITH TYMLOS

Nonvertebral fracture risk reduction achieved with TYMLOS was extended with alendronate[1]:

- **43% RRR with TYMLOS** (fracture incidence: 2.7%) vs placebo (fracture incidence: 4.7%) and **2.0% ARR** at 19 months (*P*=0.049)[1]

Cumulative incidence of nonvertebral fractures* over 43 months[1,20,21†]



Results reported in the extension study intent-to-treat (ITT) population, which included patients randomized in the efficacy study.[20]
*Nonvertebral fractures excluded those of the sternum, patella, toes, fingers, skull, and face, and those associated with high trauma.[20]
†TYMLOS or placebo for 18 months, followed by 1 month of no treatment, then up to 24 months of alendronate.[22]
‡*P*=0.017.[1]
§*P*-value based on the log-rank test.[20]
‖*P*=0.038.[20]

BMD increases achieved with TYMLOS were extended with alendronate:

- **Increases in BMD achieved with TYMLOS** at the lumbar spine, total hip, and femoral neck at 18 months were extended at 25 and 43 months with alendronate[1,20†]

The primary and secondary efficacy endpoints for the extension study were at 25 months. The 43-month data are exploratory endpoints.[21]

IMPORTANT SAFETY INFORMATION (cont'd)

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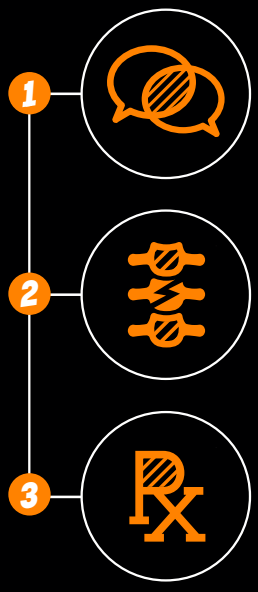
YOU ARE AT THE FOREFRONT
OF POSTMENOPAUSAL OSTEOPOROSIS TREATMENT



ASK ABOUT FRACTURES

For postmenopausal women, osteoporotic fractures are a sentinel event that can lead to subsequent fractures, especially in the first 12 months[6,7]

DIAGNOSE POSTMENOPAUSAL OSTEOPOROSIS

Osteoporosis can be diagnosed in clinical practice based on presence and/or history of fragility fractures[13,14]*

TREAT WITH TYMLOS

TYMLOS provided reductions in new vertebral and nonvertebral fractures and increases in BMD that were extended with alendronate[1,20]

If your postmenopausal patient had a recent osteoporotic fracture, don't wait to treat.

Find out how you can be a first responder in identifying and treating osteoporosis at TYMLOSfirstresponder.com

*Fragility fractures of the spine or hip, regardless of BMD; fragility fractures of the proximal humerus, pelvis, or possibly distal forearm with osteopenia or low bone mass (T-score between -1 and -2.5).[14]

INDICATIONS AND USAGE

TYMLOS is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, TYMLOS reduces the risk of vertebral fractures and nonvertebral fractures.

Limitations of Use

Because of the unknown relevance of the rodent osteosarcoma findings to humans, cumulative use of TYMLOS and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.

References: 1. Tymlos™ [prescribing information]. Waltham, MA: Radius Health, Inc; 2017. **2.** Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. *J Bone Miner Res.* 2007;22(3):465-475. **3.** NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA.* 2001;285(6):785-795. **4.** Mozaffarian D, Benjamin EJ, Go AS, et al. Executive summary: heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation.* 2016;133(4):447-454. **5.** National Cancer Institute. Cancer stat facts: female breast cancer. https://seer.cancer.gov/statfacts/html/breast.html. Accessed July 9, 2018. **6.** National Coalition for Osteoporosis and Related Bone Diseases. National Action Plan for Bone Health: Recommendations From the Summit for a National Action Plan for Bone Health. http://www.oif.org/site/DocServer/BoneHealthReport.pdf. Accessed July 9, 2018. **7.** Lindsay R, Silverman SL, Cooper C, et al. Risk of new vertebral fracture in the year following a fracture. *JAMA.* 2001;285(3):320-323. **8.** Clinton J, Franta A, Polissar NL, et al. Proximal humeral fracture as a risk factor for subsequent hip fractures. *J Bone Joint Surg Am.* 2009;91(3):503-511. **9.** Barrett-Connor E, Sajjan SG, Siris ES, Miller PD, Chen Y-T, Markson LE. Wrist fracture as a predictor of future fractures in younger versus older postmenopausal women: results from the National Osteoporosis Risk Assessment (NORA). *Osteoporos Int.* 2008;19(5):607-613. **10.** Gillespie CW, Morin PE. Osteoporosis-related health services utilization following first hip fracture among a cohort of privately-insured women in the United States, 2008-2014: an observational study. *J Bone Miner Res.* 2017;32(5):1052-1061. [Erratum in: *J Bone Miner Res.* 2018;33(3):549]. **11.** Biver E, Durosier-Izart C, Chevalley T, van Rietbergen B, Rizzoli R, Ferrari S. Evaluation of radius microstructure and areal bone mineral density improves fracture prediction in postmenopausal women. *J Bone Miner Res.* 2018;33(2):328-337. **12.** Siris ES, Chen YT, Abbott TA, et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. *Arch Intern Med.* 2004;164(10):1108-1112. **13.** van den Bergh JP, van Geel TA, Geusens PP. Osteoporosis, frailty, and fracture: implications for case finding and therapy. *Nat Rev Rheumatol.* 2012;8(3):163-172. **14.** Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2016. *Endocr Pract.* 2016;22(suppl 4):1-42. **15.** Giangregorio L, Papaioannou A, Thabane L, et al. Do patients perceive a link between a fragility fracture and osteoporosis? *BMC Musculoskelet Disord.* 2008;9:38. **16.** Baron R, Hesse E. Update on bone anabolics in osteoporosis treatment: rationale, current status, and perspectives. *J Clin Endocrinol Metab.* 2012;97(2):311-325. **17.** Khan A-W, Khan A. Anabolic agents: a new chapter in the management of osteoporosis. *J Obstet Gynaecol Can.* 2006;28(2):136-141. **18.** Seeman E, Martin TJ. Co-administration of antiresorptive and anabolic agents: a missed opportunity. *J Bone Miner Res.* 2015;30(5):753-764. **19.** Moreira CA, Fitzpatrick LA, Wang Y, Recker RR. Effects of abaloparatide-SC (BA058) on bone histology and histomorphometry: the ACTIVE phase 3 trial. *Bone.* 2017;97:314-319. **20.** Bone HG, Cosman F, Miller PD, et al. ACTIVExtend: 24 months of alendronate after 18 months of abaloparatide or placebo for postmenopausal osteoporosis. *J Clin Endocrinol Metab.* doi:10.1210/jc.2018-00163. **21.** Data on file. Radius Health, Inc; Waltham, MA. **22.** Cosman F, Miller PD, Williams GC, et al. Eighteen months of treatment with subcutaneous abaloparatide followed by 6 months of treatment with alendronate in postmenopausal women with osteoporosis: results of the ACTIVExtend trial. *Mayo Clin Proc.* 2017;92(2):200-210. **23.** Miller PD, Hattersley G, Riis BJ, et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial. *JAMA.* 2016;316(7):722-733. [Erratum: *JAMA.* 2017;317(4):442].

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FIRST RESPONDER

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