CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July - August

BRAND NAME
Tymlos®

GENERIC NAME
Abaloparatide

MANUFACTURER
Radius Health

DATE OF APPROVAL
April 28, 2017

PRODUCT LAUNCH DATE
May 1, 2017

REVIEW TYPE

☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Reviews for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
Tymlos (abaloparatide) was approved by the U.S. Food and Drug Administration for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

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OFF-LABEL USES
Not applicable

CLINICAL EFFICACY [1, 2, 3, 4, 5]

The safety and efficacy of abaloparatide was investigated in an international, multicenter, randomized, double-blind, placebo-controlled phase 3 trial in postmenopausal women with osteoporosis aged 49 to 86 years who were randomized to receive 80 mcg of Tymlos (N= 824) or placebo (N=821), given subcutaneously once daily for 18 months. The efficacy study was extended to an open-label study in which patients no longer received Tymlos or placebo but remained in their original randomized groups and received alendronate 70mg weekly, with calcium and vitamin D supplements for 6 months.

The primary efficacy end point was the percentage of participants with one or more incidents of new vertebral fracture comparing abaloparatide and placebo. The key secondary end points included percent change in bone mineral density (BMD) at the total hip, femoral neck, and lumbar spine at 18 months and incident of nonvertebral fractures, both of which were compared between abaloparatide and placebo.

Tymlos resulted in a significant reduction in the incidence of new vertebral fractures compared to placebo at 18 months (0.6% TYMLOS compared to 4.2% placebo, $p < 0.0001$). In the extension study, the incidence of new vertebral fractures at 25 months was 0.6% in patients treated with Tymlos followed by alendronate, compared to 4.4% in patients treated with placebo followed by alendronate ($p < 0.0001$).

CONTRAINDICATIONS
Not applicable

BLACK BOX WARNINGS
Tymlos has a black box warning for potential risk of osteosarcoma. The drug should not be prescribed for patients who are at increased baseline risk for osteosarcoma. Risk factors include, prior external beam or implant radiation therapy involving the skeleton, Paget's disease of bone or unexplained elevations of alkaline phosphatase and pediatric and young adult patients with open epiphyses.

DRUG INTERACTIONS
Not applicable

ADVERSE REACTIONS

Orthostatic Hypotension, hypercalcemia, hypercalciuria, dizziness, nausea, headache, palpitations

DOSAGE AND ADMINISTRATION
80 mcg subcutaneously once daily

PRODUCT AVAILABILITY
Injection: 3120 mcg/1.56 mL in a single-patient-use prefilled pen (to deliver 30 doses of 80 mcg/dose).

THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Forteo (teriparatide)	20 mcg/day subcutaneously	
alendronate (Fosamax®)	PMO treatment: 10 mg PO QD or 70 mg PO once weekly Male osteoporosis treatment: 10 mg PO QD or 70 mg PO once weekly GIO treatment: 5 mg PO QD or 10mg PO QD (in postmenopausal women not receiving estrogen)	10 mg/day or 70 mg/week
Fosamax Plus D (alendronate/cholecalciferol) *	PMO and male osteoporosis treatment: 70 mg alendronate/2,800 units cholecalciferol or 70 mg alendronate/5,600 units cholecalciferol PO once weekly	70 mg alendronate/5,600 units cholecalciferol/week
risedronate (Actonel®)*	PMO treatment: 5 mg PO QD or 35 mg PO once weekly or 150 mg PO once monthly Male osteoporosis treatment: 35 mg PO once weekly GIO treatment: 5 mg PO QD	5 mg/day 35 mg/week 150 mg/month
ibandronate (Boniva®)*	PMO treatment (tablets): 150 mg PO once monthly PMO treatment (injection): 3 mg IV	PO: 150 mg/month

	every 3 months over 15 to 30 seconds	IV: 3 mg per dose

Utilization Management Recommendation

- There is significant potential for inappropriate use and utilization management should be considered for the following reason(s):
    - To ensure appropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcomes.
        - Treatment guidelines from the North American Menopause Society recommend bisphosphantes as first line treatment for reduction in risk of vertebral and non-vertebral fracture, including hip fracture, in postmenopausal women.

i) Recommended utilization management tool(s): (check all that apply)
(1) ☒ Prior authorization
(2) ☐ Quantity limits
(3) ☐ Provider newsletter
(4) ☐ Hard block (plan exclusion)
(5) ☐ Messaging
(6) ☐ Electronic step therapy
(7) ☐ Clinical Program

Product Comparison

- CPAC score: 52 vs. Forteo – Equal therapeutic outcomes anticipated.
- It would be clinically appropriate to provide equal access to Tymlos and Forteo or to require a trial of one before the other.
- It would be clinically appropriate to require a trial of bisphosphanates (e.g., alendronate, ibandronate, risedronate, Reclast) prior to a PTH analog.

[1] Tymlos Prescribing Information. Waltham, MA: Radius Health. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208743lbl.pdf

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[2] Miller PD, Hattersley G, Riis BJ et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis. JAMA 2016: 316 (7):722-733.
[3] Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.
[4] Tymlos Drug Monograph. Clinical Pharmacology. Accessed May 2017. http://www.clinicalpharmacology-ip.com/.
[5] National Osteoporosis Foundation Clinician's Guide to Prevention and Treatment of Osteoporosis. Available at: https://my.nof.org/bone-source/education/clinicians-guide-to-the-prevention-and-treatment-of-osteoporosis. Accessed May 15, 2017.