BIOSIMILARS IN BONE HEALTH TREATMENT

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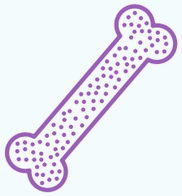
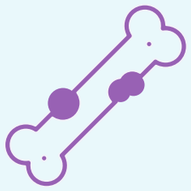
BONE HEALTH is a serious public health concern that is undertreated in both osteoporosis and metastatic bone disease.[1,2] Biosimilars can increase treatment options, and potentially lower costs through market competition.[3]

OSTEOPOROSIS:



- Osteoporosis is underdiagnosed and undertreated[1]
- Osteoporosis increases the risk of fractures, which are associated with pain, disability, and mortality[4,5]
- After a major osteoporotic fracture, the risk of a second fracture within one year is **2.7-fold higher** than among the general population[6]
- **60–85%** of females >50 years of age with osteoporosis did not receive treatment in 2018[7]

BONE METASTASIS:



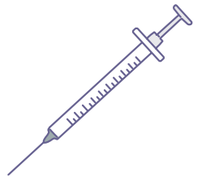
- Antiresorptive medications* are underused in patients with bone metastases[2]
- It is estimated that more than half of cancers develop bone metastases[8]
- Most (**~68%**) of patients with skeletal metastasis experience pain, and many sustain fractures,[8] leading to significant deterioration in quality of life and worsened survival[2]
- Many (**39%**) of patients with mCRPC did not receive bone health agents during follow-up[2]

*Antiresorptive drugs include bisphosphonates, denosumab, oestrogens, calcitonin, and others.

TREATMENT OPTIONS

- **Anti-resorptive medications** are the first-line treatment to reduce fractures in adults with osteoporosis,[4,9] and the first-line nonsurgical treatment of bone metastases[8]
- Treatment recommendations to reduce the risk of fractures in people with **osteoporosis*** (EU/USA):

  - Bisphosphonates or another inhibitor of bone resorption, such as denosumab, are recommended in those at high risk of fracture[4,9-12]
  - **Denosumab** is particularly recommended for those who have contraindications to, or experience adverse effects of, bisphosphonates[4,11]
  - **Denosumab** is indicated for the treatment of adults with osteoporosis who are at high risk of fracture[13,14]



  - **HRT** can be used in younger postmenopausal females (aged ≤60 years) at high risk of fractures, and with a low risk for adverse malignant and thromboembolic events[11]

- Treatment recommendations to reduce the risk of fractures in people with bone metastases (EU/USA):

  - Guidelines recommend the use of bisphosphonates or denosumab in metastatic bone disease[15,16]

*Anabolic drugs such as teriparatide and/or romosozumab, followed by a bisphosphonate, are recommended for use in postmenopausal females, and in males ≥50 years of age with osteoporosis at very high risk of fractures[4,8,11]

TREATMENT APPROVAL TIMELINES

Timeline of approvals for bone health treatments for osteoporosis and bone metastasis (USA/EU):

BISPHOSPHONATES

1990 — **First approved for bone metastasis:**
- EMA[17]

1995 — **First approved for osteoporosis:**
- EMA[17]
- FDA[18]

1996 — **First approved for bone metastasis:**
- FDA[19]

DENOSUMAB

2010
First approved for osteoporosis:
- FDA[13]
- EMA[14]

First approved for bone metastasis:
- FDA[20]

2011 — **First approved for bone metastasis:**
- EMA[21]

2024
First biosimilar approved for osteoporosis:
- FDA[22]
- EMA[23]

First biosimilar approved for bone metastasis:
- FDA[24]
- EMA[25]

*Anabolic drugs: Romosozumab was first approved by the EMA/FDA for osteoporosis in 2019.[26,27] Teriparatide was first approved for osteoporosis in 2002 by the FDA,[28] and 2003 by the EMA.[29] The first teriparatide biosimilar for osteoporosis was approved in 2017 by the EMA[30] and 2023 by the FDA.[31]

BIOSIMILARS

Reference medicine

A biosimilar is a biological medicine that is highly similar to another biological medicine already approved (the 'reference' medicine)[3,32]

Because they are made by living organisms, biologic medicines usually contain slight variations of a protein. This variability exists both between batches of a biologic medicine, and between a reference medicine and a biosimilar[3,32]

These minor differences are not clinically meaningful; for example, there may be differences in glycosylation, but the amino acid sequence of the protein remains the same in all batches.

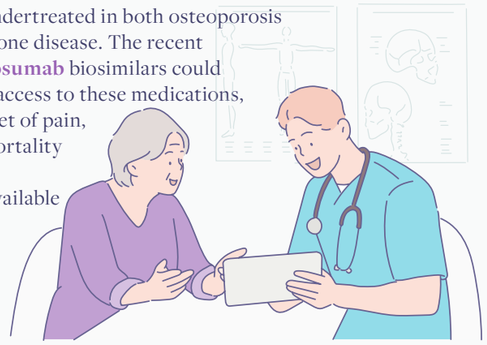
In order to be approved, biosimilars must demonstrate that they are highly similar to, and have comparable safety and efficacy to, the reference medicine[3,32]

The availability of biosimilars can provide patients with more treatment options, increase access to lifesaving medications, and potentially lower healthcare costs through market competition[3]

Biosimilar medicine

KEY LEARNINGS

Bone health is undertreated in both osteoporosis and metastatic bone disease. The recent approval of **denosumab** biosimilars could improve patient access to these medications, reducing the onset of pain, disability, and mortality associated with fractures once available on the market.



Key:
EMA: European Medicines Agency; EU: European Union; FDA: U.S. Food and Drug Administration; HRT: hormone replacement therapy; mCRPC: metastatic castration-resistant prostate cancer.

See references on next page.

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