

## Health Technology Briefing December 2021

### Abaloparatide for treating osteoporosis in males aged 40 to 85 years

Company/Developer

Radius Health Inc

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 24215

NICE ID: 10667

UKPS ID: N/A

#### Licensing and Market Availability Plans

In phase III clinical development.

#### Summary

Abaloparatide is in clinical development for the treatment of males with osteoporosis, including osteoporosis associated with hypogonadism. Osteoporosis is a condition that causes weakening of the bones, which can result in increased risk of fractures or breaks. Although osteoporosis predominately affects postmenopausal women, approximately 20-25% of men over the age of 50 years will experience osteoporotic fractures in their lifetime. In many cases the cause of osteoporosis in men is unknown, however, decreases in testosterone (a male hormone), which helps keep the bones healthy, may be a contributor. Hypogonadism is a condition which leads to a decrease of testosterone levels and is associated with an increased risk of osteoporosis.

Abaloparatide is similar to, and can act in place of, part of the human parathyroid hormone. It stimulates bone formation by acting on osteoblasts (bone-forming cells). Abaloparatide is administered by a subcutaneous (SC) (under the skin) injection once daily. If licenced, abaloparatide would offer an additional treatment option for males with osteoporosis. It is able to more quickly and consistently increase bone mineral density than current treatment options and also does not require refrigeration.

## Proposed Indication

Treatment of adult male patients aged 40 to 85 years with primary osteoporosis or osteoporosis associated with hypogonadism.<sup>1</sup>

## Technology

### Description

Abaloparatide (Tymlos, BA058) is a proprietary peptide analogue of human parathyroid hormone-related protein (PTHrP). PTHrP is critical for promoting new bone formation, with a distinct role from parathyroid hormone, or PTH, which primarily regulates calcium homeostasis and bone resorption. In target cells, abaloparatide acts as an agonist on PTH type 1 receptor (PTH1R) and activates both G protein-mediated cAMP signalling and  $\beta$ -arrestin-mediated ERK-1/2 signalling pathways with similar potency.<sup>2</sup>

Abaloparatide is currently in clinical development for adult male patients (aged 40-85 years) with osteoporosis, including osteoporosis associated with hypogonadism. In the phase III clinical trial (NCT03512262, ATOM) patients receive one SC injection of 80 $\mu$ g abaloparatide per day over 12 months.<sup>1</sup>

### Key Innovation

Abaloparatide is an anabolic agent, which is used to treat osteoporosis by promoting new bone formation.<sup>3</sup> According to the recently updated clinical practice guidelines from the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO), for patients at high risk of fracture, starting treatment with an anabolic agent seems most appropriate to promptly reduce the fracture risk.<sup>4</sup>

Currently in the UK, teriparatide is only one approved anabolic agent for the treatment of osteoporosis in men with increased risk of bone fracture.<sup>5</sup> If approved, abaloparatide will provide an alternative anabolic agent for the treatment of osteoporosis in men with an increased risk of bone fracture.<sup>3</sup> Abaloparatide increases bone mineral density more quickly and more consistently than teriparatide, particularly at sites enriched in cortical bone including the hip.<sup>6,7</sup> Unlike teriparatide, abaloparatide does not require refrigeration and it can be administered via an injector pen on a monthly basis, making it more convenient for patients.<sup>8</sup>

### Regulatory & Development Status

Abaloparatide is not currently licenced for any indication in the UK/EU.

Abaloparatide is currently in phase II/III clinical development for the treatment of post-menopausal women with osteoporosis; pelvic fracture healing; lumbar disc degeneration amongst others.<sup>9</sup>

## Patient Group

### Disease Area and Clinical Need

Osteoporosis is a condition that weakens bones, which makes them more fragile and likely to fracture and/or break. This results in common injuries, such as a fractured or broken wrist, hip, or vertebrae. A broken bone is often the first sign of osteoporosis, and it is not usually painful until that point. Although a broken bone is often the first sign of osteoporosis, some older people develop the characteristic stooped

(bent forward) posture. It happens when the bones in the spine have broken, making it difficult to support the weight of the body.<sup>10</sup>

Osteoporosis and associated bone fractures can significantly affect the health-related quality of life (HRQOL) of men.<sup>11</sup> 20-25% of men over 50 years old will have a fragility fracture during their lifetime, which contributes to dependency, morbidity and higher mortality in the first year.<sup>12,13</sup> Additionally, almost one-third of hip fractures occur in men. Whilst the rate of bone loss is slower in men, the mortality risk is twice as high after a hip fracture compared to women.<sup>14,15</sup> In a 2013 International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA) report reviewing the management, epidemiology and burden of osteoporosis in the European Union, it was estimated that in 2010, 5.5 million men had osteoporosis and almost 1.2 million had suffered fragility fractures.<sup>16</sup>

Risk factors for developing osteoporosis include hormone disorders, a family history of osteoporosis; a body mass index (BMI) of  $\leq 19$ ; long-term use of high-dose steroid tablets; eating disorders; heavy drinking and smoking; rheumatoid arthritis; malabsorption issues; long periods of inactivity; and taking some medicines used to treat breast and prostate cancers that can affect hormone levels.<sup>17</sup>

Osteoporosis can affect men and women and is more common in older people. In most cases the cause of osteoporosis in men is unknown, however, there are links to lower testosterone production. Men with low levels of testosterone have an increased risk of developing osteoporosis, which could be related to taking certain medicines, such as steroid tablets, alcohol misuse and hypogonadism.<sup>17</sup>

Hypogonadism is when the testes produce lesser amounts of sex hormones and occurs in up to 12.3% of men.<sup>18,19</sup> Hypogonadism causes systemic bone loss, and is a significant contributor to osteoporosis. When men age there is a gradual decline in testosterone production and, in some cases, older men may develop late-onset hypogonadism.<sup>20</sup> Hypogonadism that appears later on in life, rather than presenting at birth, is called late-onset.<sup>18</sup>

Due to a particular focus on postmenopausal women, osteoporosis in men can be underestimated.<sup>21</sup> Osteoporosis in men is commonly categorised as idiopathic although there are a number of different diagnoses that can be given.<sup>21</sup> In England, 2020-21, there were 61 finished consultant episodes (FCEs) for male patients with idiopathic osteoporosis (ICD-10 code M81.5), leading to an estimated 53 day cases and 15 FCE bed days.<sup>22</sup>

In England, 2020-21, there were 3,201 FCE for osteoporosis, unspecified (ICD-10 code M81.9) in men, this resulted in an estimated 3,147 day cases and 179 FCE bed days.<sup>22</sup>

### Recommended Treatment Options

Osteoporosis treatment aims to prevent fragility fractures through a combination of lifestyle changes and pharmacological treatment. Lifestyle changes include increasing physical activity; smoking cessation; maintaining a normal BMI; reducing alcohol intake. Patients at risk of osteoporosis should ensure adequate intake of calcium and vitamin D, with supplements recommended if necessary (when there is a risk of deficiency).<sup>23</sup>

Oral bisphosphonates, alendronic acid or risedronate sodium are among the recommended first-line treatments for osteoporosis in men. Zoledronic acid or denosumab may be offered as alternatives for men who are intolerant of oral bisphosphonates or where oral bisphosphonates are unsuitable. Teriparatide or strontium ranelate are also additional alternatives.<sup>23</sup>

According to the recently update clinical practice guidelines from the European Society for Clinical an Economic Aspects of Osteoporosis (ESCEO), for patients at high risk of fracture, starting treatment with an anabolic agent seems most appropriate to promptly reduce the fracture risk.<sup>4</sup>

There is currently no NICE recommended treatment pathway for preventing fragility fractures in men with osteoporosis.<sup>24</sup>

### Clinical Trial Information

<b>Trial</b>	<b>ATOM; <a href="#">NCT03512262</a></b> ; A Randomized, Double-blind, Placebo-controlled, Phase 3 Multicenter Study to Evaluate the Safety and Efficacy of Abaloparatide-SC for the Treatment of Men With Osteoporosis <b>Phase III</b> – Active, not recruiting <b>Location(s)</b> : 2 EU countries and United States <b>Primary completion date</b> : August 2020
<b>Trial Design</b>	Randomised, quadruple-masked parallel assignment.
<b>Population</b>	N=225 (estimated); males aged 40-85 years old; primary osteoporosis or osteoporosis associated with hypogonadism.
<b>Intervention(s)</b>	80µg abaloparatide SC injection once daily.
<b>Comparator(s)</b>	Matched placebo.
<b>Outcome(s)</b>	Lumbar spine bone mineral density (BMD) [ Time Frame: 12 months ] Percent change from baseline in lumbar spine BMD  See trial record for full list of other outcomes.
<b>Results (efficacy)</b>	-
<b>Results (safety)</b>	-

### Estimated Cost

The estimated cost of abaloparatide is not known.

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal guidance. Bisphosphonates for treating osteoporosis (TA464). August 2017.
- NICE clinical guideline. Osteoporosis: assessing the risk of fragility fracture (CG146). August 2012.

#### NHS England (Policy/Commissioning) Guidance

- NHS England interim clinical commissioning policy statement: Teriparatide for osteoporosis in men (adults). NHS England Reference: 201101P. January 2021.

#### Other Guidance

- Scottish Intercollegiate Guidelines Network (SIGN). Management of osteoporosis and the prevention of fragility fractures. Clinical guideline 142. June 2020 (updated January 2021).<sup>25</sup>
- The National Osteoporosis Guideline Group (NOGG). Clinical guideline for the prevention and treatment of osteoporosis. April 2017 (updated July 2019).<sup>26</sup>
- Endocrine Society. Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline. May 2012.<sup>27</sup>

### Additional Information

Radius Health Inc did not enter information about this technology onto the UK PharmaScan database at the time of writing this technology briefing. UK PharmaScan is the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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