EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PAEDIATRIC OSTEOPOROSIS

REGULATORY OVERVIEW

The objective of the Paediatric Regulation

- To facilitate the development and availability of medicines for children
- To ensure that medicines for children are of high quality, ethically researched and authorised appropriately
- To improve the availability of information on the use of medicines for children

- without subjecting children to unnecessary trials
- without delaying authorisation of medicines for use in adults.

OSTEOPOROSIS IN CHILDREN

- OSTEOGENESIS IMPERFECTA (OI)
- GLUCOCORTICOID INDUCED OSTEOPOROSIS (GIOP)
- IDIOPATHIC OSTEOPOROSIS

MEDICINES FOR THE TREATMENT OF OSTEOPOROSIS

- **Bisphosphonates**
- Strontium ranelate
- Selective estrogen receptor modulators
- Teraparatide
- **Denosumab**

Approved for the treatment and/or prevention of postmenopausal osteoporosis and glucocorticoid induced osteoporosis in adults

Not approved for treatment in children but at least some bisphosphonates are standard of care and extensively used in OI and in GIOP

REGULATORY CHALLENGES

- The Paediatric Regulation requires development of new medicines for children where there is **an unmet need**
- **Unmet need** could be defined as “no approved medicine available” for children suffering from a specific condition
- Although there is extensive off-label use of bisphosphonates in the paediatric population, there are no approved medicines

REGULATORY CHALLENGES

- Extensive use of bisphonates – still limited data confirming efficacy/safety
- Need for safety studies? Need for long-term FU studies?

  Safety issues: Effects on growth, physical and sexual maturation in relation to the underlying condition. Others???

  Duration of study and FU for safety/efficacy? Numbers? Age groups?

  What should be the objective for treatment in children??
  - **to prevent osteoporosis**
  - **to prevent fracture**

REGULATORY CHALLENGES

Which conditions:

- Children are treated with glucocorticoids for varying conditions: *JIA, SLE, IBD, ALL, cancer, idiopathic nephrotic syndrome, Duchenne etc,* conditions which are very different and likely to affect fracture risk very differently
- In some of those conditions, glucocorticoid treatment has become less frequent, affecting the number of patients eligible for CTs

REGULATORY CHALLENGES

Study design – placebo or active comparator? What active comparator?

Inclusion criteria: ISCD osteoporosis diagnosis: Low BMD + 2 lower limb fractures or one lower limb and ≥1 vertebral fracture? Or only low BMD??

Investigating the treatment of osteoporosis (ie fracture prevention), outcome measure should be new fracture??

REGULATORY CHALLENGES

Fracture endpoints – which fractures? All? Vertebral?

Fracture may be too infrequent, how reliable are surrogate endpoints? (BMD increase together with biochemical markers)

Can efficacy be extrapolated from adults or older children in any condition/age group??