







Diagnosis and treatment of osteoporosis: 2026 recommendations of the Polish Society for Rheumatology

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Abstract

This publication presents the official recommendations of the Polish Society for Rheumatology for the diagnosis and treatment of osteoporosis. A panel of 6 experienced rheumatologists developed the document using an evidence-informed consensus process incorporating current evidence, clinical experience and the Polish healthcare context. Unanimous agreement was reached on all recommendations. The diagnostic section outlines the diagnostic criteria for osteoporosis in different patient groups and defines, for the first time, the role of radiofrequency echographic multi-spectrometry in clinical practice. The therapeutic section provides guidance on the optimal use of anti-osteoporotic drugs, including sequential therapy, and highlights the benefits of initiating treatment with an anabolic agent in patients at very high fracture risk. The document also addresses prevention of glucocorticoid-induced osteoporosis, osteoporosis in premenopausal women, and diagnosis and treatment in the paediatric population. These recommendations are intended to support early diagnosis and effective management of osteoporosis in Poland.

Key words: osteoporosis, bone density, osteoporotic fractures, clinical practice guideline.

Introduction

Demographic changes across Europe are leading to an increase in the incidence of osteoporosis, and the medical and socio-economic consequences of osteoporotic fractures are substantial [1]. This underlines the importance of measures supporting the early detection and effective treatment of osteoporosis. These recommendations constitute the official position of the Polish Society for Rheumatology (*Polskie Towarzystwo Reumatologiczne – PTR*) and update its 2015 position statement, revised in 2017 [2]. The authors did not intend to impose restrictions on clinical practice but rather to define the current standard of care. Adherence to these recommendations is not mandatory, and

individual diagnostic and therapeutic decisions remain the responsibility of the treating physician. Such decisions require consideration of a broader context, including organisational, ethical and legal aspects, as well as patients' clinical condition, social circumstances, preferences and expectations. These recommendations are intended for all physicians involved in the care of patients with diagnosed or suspected osteoporosis.

Methods

These recommendations were developed as an evidence-informed consensus statement. The consensus panel comprised 6 rheumatologists who were PTR experts: 5 with many years of clinical experience in the dia-

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gnosis and treatment of osteoporosis in adults, and 1 paediatric rheumatologist with many years of clinical experience in the diagnosis and treatment of osteoporosis in children and adolescents. The experts were selected on the basis of their clinical experience and areas of expertise. The authors represented 4 rheumatology centres in Poland. The first stage involved identifying the clinical questions, which then informed the titles and structure of the subsequent sections of the recommendations. This was followed by a review of the English-language literature published up to the end of 2025, identified through searches of MEDLINE (via PubMed) and the Cochrane Library. This process was repeated separately for each section. As the authors aimed to develop a practical clinical position statement rather than to conduct reimbursement analyses, formal evidence-grading systems were not applied. Each source was assessed individually for methodological quality, currency and clinical relevance. When formulating the recommendations, priority was given to evidence from meta-analyses, systematic reviews and randomised clinical trials. Recommendations from other scientific societies, particularly international ones, were also reviewed, taking into account their implications for clinical practice. At the final stage, following repeated discussion and revision of the document, unanimous agreement was reached on all recommendations. This methodology ensured that current evidence, the authors' clinical experience, and the context of the Polish healthcare system were all taken into account.

Diagnosis of osteoporosis and assessment of fracture risk

Definition of osteoporosis

Osteoporosis is a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, resulting in increased bone fragility and fracture risk [3].

Role of bone densitometry in the diagnosis and monitoring of osteoporosis

Bone mineral density (BMD) is one of the strongest predictors of fracture risk, underpinning the role of bone densitometry in the diagnosis and monitoring of osteoporosis [4]. Bone densitometry is recommended in any clinical situation where the result could influence clinical management and thereby reduce fracture risk. Examples include women aged ≥ 65 years, men aged ≥ 70 years, adults with risk factors for low bone mass or bone loss (e.g. prior low-energy fracture, low body weight, diseases, or medications), and all patients receiving or being considered for anti-osteoporosis treatment [5].

Methods of bone densitometry

The gold standard for bone densitometry is dual-energy X-ray absorptiometry (DXA) [5].

A newer bone densitometry method is radiofrequency echographic multi-spectrometry (REMS). This method enables assessment of BMD at the hip and lumbar spine through automated analysis of ultrasound echoes backscattered from bone. As with DXA, REMS results are expressed in g/cm^2 and interpreted using the standard densitometric parameters (T -score and Z -score), and hip T -score values are calculated using the same NHANES III (National Health and Nutrition Examination Survey III) reference database [6]. The REMS device was cleared by the US Food and Drug Administration (FDA) in 2018 [7]. According to FDA documents, BMD measurements obtained by DXA and REMS show high correlation ($r = 0.94$ at the spine and $r = 0.93$ at the hip) and comparable precision, supporting the use of REMS in the diagnosis of osteoporosis, monitoring of BMD changes, and assessment of fracture risk [7, 8]. In 2019, the usefulness of REMS was favourably evaluated by a working group of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). The ESCEO paper presented numerous arguments in support of introducing REMS into clinical practice [9]. Also in 2019, an analysis of the clinical significance of REMS densitometry by members of the PTR Metabolic Bone Diseases Section was published [6]. Finally, in 2020, the results of a prospective study were published confirming the ability of REMS to predict low-energy fractures. The study followed 1,370 women aged 30–90 years over a 5-year period [10]. The REMS method allows reliable assessment of hip and lumbar spine BMD in women and men aged 30–90 years [8, 11]. It also has several unique features, including the portability of the equipment, the absence of ionising radiation, and the automatic exclusion of measurements affected by artefacts or technical errors [6, 12–16]. These features of REMS may improve access to bone densitometry and increase the detection of osteoporosis in Poland.

In view of the available evidence and the Polish healthcare context, REMS may be used in the diagnosis and monitoring of osteoporosis as an alternative to DXA in women and men aged 30–90 years. Given their different physical principles and the practical implications of these differences, the 2 densitometric methods may be regarded as complementary.

Densitometric criterion for the diagnosis of osteoporosis

In postmenopausal women and in men aged ≥ 50 years, osteoporosis may be diagnosed on the basis of the bone

densitometry result alone. In this population, the densitometric criterion for the diagnosis of osteoporosis is a *T*-score of ≤ -2.5 at the lumbar spine or femoral neck or total hip. This criterion may also be applied to women during the menopausal transition [5]. The menopausal transition is the period preceding menopause in which menstrual cycles become irregular and there is a persistent difference of 7 days or more in the length of consecutive cycles [17].

In women before menopause (or before the menopausal transition) and in men under 50 years of age, the primary parameter for the interpretation of BMD is the *Z*-score. A *Z*-score of ≤ -2.0 is interpreted as “BMD below the expected range for age and sex”, whereas a *Z*-score of > -2.0 is interpreted as “BMD within the expected range for age and sex”. In women before menopause (or before the menopausal transition) and in men under 50 years of age, osteoporosis cannot be diagnosed on the basis of the bone densitometry result alone, and the presence of an osteoporotic fracture is required. Therefore, there is no diagnostic criterion for osteoporosis based on the *Z*-score [5].

In adults, BMD measurement at both central sites, namely the hip and the lumbar spine, is recommended. Measurement of BMD at the 33% radius (also referred to as the one-third radius) is technically possible only with DXA and is used mainly in patients with hyperparathyroidism. A second indication for measurement at the 33% radius is the inability to obtain a reliable assessment of BMD at the hip and/or spine [5]. Examples of such situations include osteophytes, vertebral fractures, kidney stones, soft tissue calcifications, postoperative artefacts, and marked obesity [18–20]. Adapting this recommendation to current technical capabilities, measurement of BMD at the 33% radius is fully justified when a reliable bone densitometry result at the hip or lumbar spine cannot be obtained with either DXA or REMS.

In lumbar spine densitometry, vertebrae L1–L4 are routinely assessed in the posteroanterior (PA) projection. Only those vertebrae whose assessment is unreliable because of structural changes or other artefacts should be excluded from analysis, and BMD must be measured in at least 2 vertebrae for the result to be of diagnostic value [5].

Low bone mass

The term “osteopenia” has been replaced by “low bone mass” and should not be used. Low bone mass is defined by a *T*-score lower than -1.0 and higher than -2.5 . This applies only to postmenopausal women and to men over 50 years of age. Low bone mass is not considered a disease, but an epidemiological category [4, 5].

Discrepancies between densitometry results obtained at different regions of interest or by different densitometry methods

If densitometry results obtained at different regions of interest (ROIs) – i.e. vertebrae L1–L4, the femoral neck, or the total hip – classify the patient into different diagnostic categories, clinical decisions should be based on the lower result. Similarly, if DXA and REMS densitometry results are discrepant, clinical decisions should be based on the lower result, and the method used to obtain it should be preferred for follow-up measurements. These recommendations are based on the observation that artefacts affecting densitometry results usually lead to overestimation of BMD. Artefacts leading to underestimation of BMD are very rare and, in clinical practice, are limited to the consequences of surgical procedures [18–20]. In addition, although osteoporosis is a systemic skeletal disease, the dynamics of BMD changes in different skeletal regions may differ substantially, leading to discrepancies between densitometry results obtained at individual ROIs at a given time point [21, 22].

Quality and comparability of bone densitometry results

Bone densitometry, regardless of the method used, should be performed in certified centres. The Polish Society for Rheumatology organises DXA and REMS courses, and participants who pass the examination receive a certificate valid for a limited period.

Bone densitometry by DXA should be performed and interpreted in accordance with the current Official Positions of the International Society for Clinical Densitometry (ISCD). Whenever possible, the ISCD Official Positions should also be taken into account in the performance and interpretation of REMS densitometry. This view is based on the fundamental similarities between the 2 methods and on the lack of recommendations specific to REMS densitometry.

Follow-up bone mineral density testing

Serial BMD measurements allow monitoring of disease course and response to treatment. Response to treatment may be reflected in increased or stable BMD values. A significant decrease in BMD during osteoporosis treatment requires assessment of patient adherence, identification of new risk factors, and evaluation of treatment efficacy. The frequency of follow-up BMD testing should be tailored to the individual clinical situation. Testing should be performed when the result could influence treatment decisions. Follow-up BMD testing is recommended 12 months after the initiation or modification

of osteoporosis treatment, with progressively longer intervals thereafter, usually up to 2 years, if the therapeutic effect is maintained over the long term [23]. Conditions associated with accelerated BMD loss, such as treatment with glucocorticosteroids (GCs), may justify more frequent BMD testing, usually every 6 months [24]. The follow-up DXA report should include the least significant change (LSC), which allows comparison of serial BMD measurements. For results to be comparable, BMD measurements must be performed on the same device [5].

Clinical criterion for the diagnosis of osteoporosis

In patients with a documented osteoporotic fracture, osteoporosis may be diagnosed and treatment initiated without meeting the densitometric criterion. In such cases, densitometry has no diagnostic role, but it may be useful for monitoring changes in BMD and response to treatment. Most low-energy fractures occur in patients with BMD > -2.5, highlighting the importance of bone microarchitecture [25–27].

A low-energy fracture results from a force that would not cause a fracture in healthy bone, such as a fall from standing height or a spontaneous fracture [28]. An osteo-

porotic fracture is a low-energy fracture that cannot be explained by a cause other than osteoporosis. This means that the diagnosis of osteoporosis on the basis of the clinical criterion requires exclusion of other possible causes of low-energy fractures. Low-energy fractures unrelated to osteoporosis include pathological fractures resulting from local bone lesions, such as malignancy or infection [29]. The most common sites of osteoporotic fracture are the spine, hip, proximal humerus, and distal radius. These are referred to as major osteoporotic fractures. It should be emphasised, however, that osteoporosis, as a systemic skeletal disease, may cause fractures at various sites, and the decision to classify a particular fracture as osteoporotic should be made by the physician on the basis of a comprehensive clinical assessment [4, 30–32]. The diagnostic criteria for osteoporosis are summarised in Figure 1.

Osteoporosis in rheumatic diseases

In patients with rheumatic diseases, the general principles for the diagnosis and monitoring of osteoporosis apply. Fracture risk assessment should take into account additional individual factors related to the pathophysiology, clinical manifestations, disease activity, and

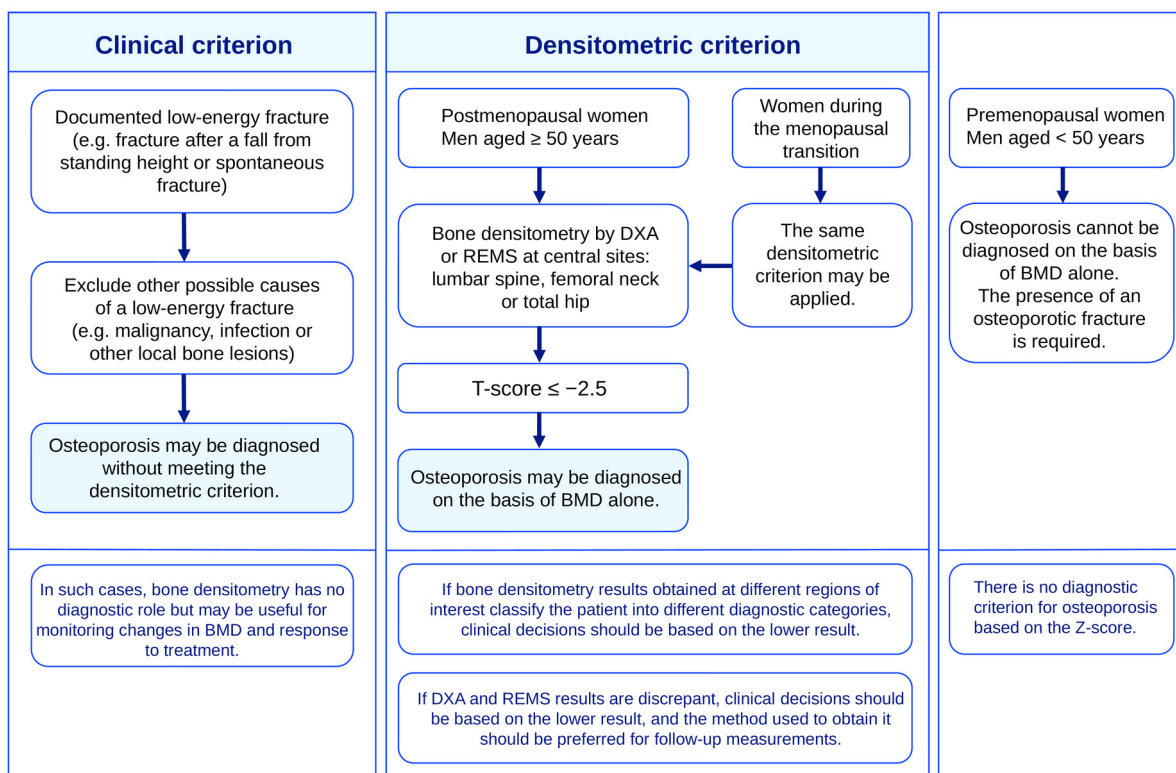


Fig. 1. Diagnostic criteria for osteoporosis.

BMD – bone mineral density, DXA – dual-energy X-ray absorptiometry, REMS – radiofrequency echographic multi-spectrometry.

treatment of the underlying disease. Chronic inflammatory diseases and GC therapy may increase fracture risk independently of classical risk factors, including BMD. To date, no tool has been developed for reliable fracture risk assessment in rheumatic diseases, and the risk calculated using standard algorithms may be underestimated [33–39].

Vertebral fracture assessment by dual-energy X-ray absorptiometry

Widespread use of vertebral fracture assessment (VFA) is recommended for the detection and monitoring of vertebral fractures. This technique enables automated identification of fractures of the vertebral bodies from T4 to L4 using a DXA densitometer. Fracture severity is assessed using the Genant visual semi-quantitative method. The VFA examination may complement or provide an alternative to standard radiological imaging (plain radiography or computed tomography) and should be performed in conjunction with DXA densitometry in patients at high risk of fracture [5].

Fracture Risk Assessment Tool calculator

The Fracture Risk Assessment Tool (FRAX) calculator is an algorithm for estimating the 10-year probability of a major osteoporotic fracture and hip fracture on the basis of clinical fracture risk factors and demographic data. Femoral neck BMD is an optional input that enhances fracture risk prediction [4]. The FRAX calculator was developed for patients aged 40–90 years who have not received anti-osteoporosis treatment. It is a simple and accessible tool, particularly useful in primary care. The FRAX algorithm does not take lumbar spine BMD into account, nor does it capture the severity of individual fracture risk factors, including the number of prior fractures, the exact dose and duration of GC therapy, or the number of cigarettes smoked. It also does not take into account certain important fracture risk factors, such as type 2 diabetes, chronic kidney disease, or risk of falls [40–42].

In some countries, clinical decisions are based on fracture probability calculated using FRAX, and intervention thresholds reflect the financial capacity of the country's healthcare system. For example, treatment is recommended when the probability of a major osteoporotic fracture is $\geq 20\%$ or the probability of hip fracture is $\geq 3\%$. These thresholds are derived from cost-effectiveness analyses conducted in the USA, and their extrapolation to other populations is controversial. Equally controversial is the arbitrary setting of intervention thresholds without a comprehensive epidemiological and economic assessment in the country in question. In a more appropriate approach, the FRAX intervention

threshold increases with age, but the authors consider this too difficult to implement in the Polish healthcare system at present [4].

The FRAX algorithm with BMD is a valuable adjunctive tool, but because of its important limitations it should not be the sole or definitive basis for clinical decisions.

Very high fracture risk

With the availability of anabolic agents and the need to individualise osteoporosis treatment, a category of very high fracture risk has been introduced. Examples of criteria used to identify patients at very high fracture risk include a recent osteoporotic fracture (within the last 2 years), a history of at least 2 osteoporotic fractures (including vertebral fractures), a prior osteoporotic fracture at a specific site (spine, hip or pelvis), very low BMD (T -score ≤ -3.0 or ≤ -3.5), and a low-energy fracture during osteoporosis treatment or during GC therapy. Various combinations of risk factors have also been proposed, including T -score with an osteoporotic fracture, T -score with clinical fracture risk factors, and, in some countries, the FRAX score [43–45]. The diversity of criteria reflects the absence of a uniform definition of very high fracture risk. In Poland, fracture risk should be assessed individually by the physician on the basis of a comprehensive clinical evaluation, including the densitometry result.

Trabecular bone score

Trabecular bone score (TBS) is an adjunctive tool for the quantitative assessment of bone microarchitecture derived from lumbar-spine DXA images. When interpreted in conjunction with BMD and other fracture risk factors, TBS may support clinical decision-making [46, 47].

Bone turnover markers

In clinical studies, 2 laboratory bone turnover markers have been designated as reference markers: serum procollagen type I *N*-terminal propeptide (s-PINP) as a marker of bone formation and serum C-terminal telopeptide of type I collagen (s-CTX) as a marker of bone resorption [48]. However, commercially available assays for s-PINP and s-CTX differ substantially in analytical method, measuring range, repeatability and reproducibility, which in practice precludes comparability of results. Interpretation of these results should also take into account age, sex, ethnicity, physical activity, comorbidities, medications, the circadian rhythm of the markers, and sample storage conditions, all of which would require extensive reference data [48–51].

In view of the need to standardise or harmonise laboratory assays, as well as to establish reference intervals

and decision thresholds for different clinical settings, the routine use of bone turnover markers is not currently recommended.

Key points:

- In postmenopausal women and in men aged ≥ 50 years, osteoporosis may be diagnosed on the basis of the bone densitometry result alone. The diagnostic criterion is a *T*-score of ≤ -2.5 at the lumbar spine, femoral neck or total hip. This criterion may also be applied to women during the menopausal transition.
- In women before menopause (or before the menopausal transition) and in men under 50 years of age, osteoporosis cannot be diagnosed on the basis of the bone densitometry result alone, and the presence of an osteoporotic fracture is required.
- An osteoporotic fracture is a low-energy fracture that cannot be explained by a cause other than osteoporosis. In each case, a pathological fracture resulting from local bone lesions (e.g. malignancy or infection) should be excluded.
- In patients with a documented osteoporotic fracture, osteoporosis may be diagnosed without meeting the densitometric criterion. In such cases, densitometry has no diagnostic role but may be useful for monitoring treatment.
- The gold standard for bone densitometry is DXA.
- In view of the available evidence and the Polish context, REMS densitometry may be used in the diagnosis and monitoring of osteoporosis as an alternative to DXA in women and men aged 30–90 years.
- Bone densitometry by DXA should be performed and interpreted in accordance with the current ISCD Official Positions. Whenever possible, the ISCD Official Positions should also be taken into account in the performance and interpretation of REMS densitometry.
- In adults, measurement of BMD at both central sites (the hip and the lumbar spine) is recommended.
- If DXA and REMS densitometry results are discrepant, clinical decisions should be based on the lower result, and the method used to obtain it should be preferred for follow-up measurements.
- If densitometry results obtained at different ROIs classify the patient into different diagnostic categories, clinical decisions should be based on the lower result.
- Follow-up bone densitometry is recommended 12 months after initiation or modification of osteoporosis treatment, with progressively longer intervals thereafter if a sustained therapeutic effect is maintained. Conditions associated with accelerated BMD loss, such as GC therapy, may justify more frequent densitometry.
- Widespread use of VFA is recommended for the detection and monitoring of vertebral fractures. In patients

at high fracture risk, VFA should be performed in conjunction with DXA densitometry.

- Fracture risk assessment in rheumatic diseases should take into account not only classical risk factors but also additional individual factors related to the pathophysiology, clinical manifestations, disease activity and treatment of the underlying disease.
- The FRAX algorithm with BMD is a valuable adjunctive tool. However, because of its important limitations, it should not be the sole or definitive basis for clinical decisions.

Treatment of osteoporosis

Treatment goal

The primary goal of osteoporosis treatment is the prevention of fractures. The occurrence of a low-energy fracture during treatment does not necessarily indicate treatment failure, and each case requires detailed clinical assessment. History taking should include evaluation of patient adherence, new comorbidities or medications, and other factors that may increase fracture risk. Follow-up bone densitometry should be considered in all cases [52]. If osteoporosis treatment has been ongoing for less than 12 months, it should not be considered ineffective [53].

Prevention of falls

In the treatment and education of patients with osteoporosis, efforts should be made to eliminate risk factors for falls, such as the effects of diseases or medications on balance and reaction time, uncorrected visual or hearing impairment, inappropriate footwear, and environmental hazards (slippery floors, physical obstacles, lack of handrails, insufficient lighting, etc.) [54–57].

Exercise

Regular, well-designed exercise stimulates bone formation and is an integral part of osteoporosis treatment. Weight-bearing aerobic exercises and resistance training are the most effective. By improving muscle strength, coordination and balance, physical activity plays a key role in the prevention of falls. Exercises for patients with osteoporosis should be varied and individually tailored [56–61]. In Poland, physiotherapists are responsible for selecting exercises and for providing patients with instructions on how to perform the exercises correctly.

Diet

In patients with osteoporosis or at high risk of fracture, the diet should provide an adequate intake of protein

and calcium. A healthy dietary pattern is recommended, including vegetables, fruit, whole grains, poultry, fish, nuts, legumes and low-fat dairy products, while limiting processed foods [62–65].

Vitamin D and calcium

Vitamin D plays an important role in the regulation of calcium-phosphate homeostasis and bone remodelling. In patients with osteoporosis, vitamin D and calcium deficiencies are risk factors for accelerated BMD loss. In addition, vitamin D affects skeletal muscle metabolism and regeneration [66]. In a meta-analysis including more than 61,000 individuals, daily supplementation with ≥ 700 IU of vitamin D significantly reduced the risk of falls, and this effect was greater when calcium was co-administered [67].

It is estimated that vitamin D deficiency affects two-thirds of the Polish population [68]. Calcifediol (25(OH)D) is the best marker of vitamin D status [66]. The optimal serum 25(OH)D concentration is 30–50 ng/ml, and values below 20 ng/ml indicate vitamin D deficiency [69].

Oral cholecalciferol (vitamin D₃) is recommended for the prevention and treatment of vitamin D deficiency [70]. In adults, the vitamin D supplementation dose is 800–2,000 IU daily. Higher doses of 2,000–4,000 IU daily are recommended in obesity, malabsorption syndromes, or in people with dark skin [69]. This wide dose range reflects individual variation in response to vitamin D supplementation, although for most healthy individuals a daily dose of 1,000 IU is sufficient [71].

For more rapid correction of vitamin D deficiency, loading doses of 6,000–10,000 IU daily may be used during the first 4–12 weeks, followed by supplementation at the recommended doses [69]. Where very rapid correction of vitamin D deficiency is required, higher loading doses may be considered, up to 60,000 IU daily for 7 consecutive days, but this requires specialist supervision and monitoring of serum calcium concentrations [72].

Intermittent dosing of vitamin D, for example once weekly or once monthly, is as safe and effective as daily dosing. This applies both to supplementation and to loading doses [69]. When intermittent dosing is used, it is recommended that the daily dose should not exceed 60,000 IU, which is considered safe [72, 73].

To monitor treatment effectiveness, serum 25(OH)D may be remeasured 6–12 weeks after starting supplementation [69].

In patients with osteoporosis, the target 25(OH)D concentration should be achieved promptly before starting antiresorptive or anabolic therapy. In this population, vitamin D is recommended in combination with calcium supplementation, particularly when dietary calcium intake is insufficient, that is, below approximately 1,000 mg

daily [4, 74, 75]. In most clinical trials, anti-osteoporosis treatment was used in combination with calcium supplementation [69].

The use of vitamin K in combination with vitamin D is not recommended in the treatment of osteoporosis. The available data do not demonstrate clear clinical benefit of vitamin K supplementation in either the treatment or prevention of osteoporosis [76].

Key points:

- In patients with osteoporosis, an optimal serum 25(OH)D concentration of 30–50 ng/ml should be ensured.
- In the treatment of osteoporosis, vitamin D is recommended in combination with calcium supplementation.
- Anti-osteoporosis treatment should be preceded by rapid correction of vitamin D and calcium deficiencies.
- The use of loading and/or intermittent doses of cholecalciferol is safe and may be helpful in achieving optimal vitamin D status.

Pharmacotherapy

Anti-osteoporosis drugs exert antiresorptive, anabolic (bone-forming), or dual (anabolic-antiresorptive) effects. The main pharmacological treatment options are summarised in Table I.

Sequential and combination therapy

Sequential therapy is the use of different anti-osteoporosis drugs in sequence to optimise the efficacy and safety of long-term treatment. The use of antiresorptive drugs after treatment with agents whose therapeutic effects are rapidly reversible upon discontinuation (e.g. denosumab, romosozumab or teriparatide) prevents predictable BMD loss and is referred to as consolidation therapy. Initiating sequential therapy with an osteoanabolic agent, followed by consolidation with an antiresorptive drug, leads to the greatest BMD gains and the greatest and most sustained reduction in fracture risk. Conversely, prior antiresorptive treatment reduces the efficacy of anabolic agents. Consistent with these data, in patients at very high fracture risk, sequential therapy should be initiated with an osteoanabolic agent, followed by consolidation with an antiresorptive drug [43–45].

Conclusive evidence on the safety and efficacy of combination therapy with different anti-osteoporosis drugs is still lacking [77]. Therefore, combination therapy is not currently recommended – its use should be limited to rare, well-justified cases, based on the available evidence, and reserved for specialist centres.

Table 1. Pharmacological treatment of osteoporosis

Drug	Dose	Mechanism of action	Indications	Fracture-risk reduction [†]			Treatment duration	Consolidation therapy
				Vertebral	Non-vertebral	Hip		
Alendronate	70 mg orally once weekly	Antiresorptive	– Treatment of osteoporosis in women and men, including GIOP	Yes	Yes	Yes	Data on the safety and efficacy of oral bisphosphonate treatment for >10 years or >6 years are limited*	N/A
Risedronate	35 mg orally once weekly	Antiresorptive	– Prevention of osteoporosis in patients at increased fracture risk, including prevention of GIOP	Yes	Yes	Yes		N/A
Zoledronate	5 mg intravenously every 12 months	Antiresorptive	– Treatment of osteoporosis in postmenopausal women	Yes	Yes	Yes		N/A
Ibandronate	150 mg orally once monthly or 3 mg intravenously every 3 months	Antiresorptive	– Treatment of osteoporosis in postmenopausal women	Yes	No [‡]	No		N/A
Denosumab	60 mg subcutaneously every 6 months	Antiresorptive	– Treatment of osteoporosis in postmenopausal women at increased fracture risk and in men at increased fracture risk	Yes	Yes	Yes	Data on the safety and efficacy of treatment for >10 years are limited*	– Bisphosphonate treatment should be initiated 6 months after the last denosumab injection and continued for at least 1 year
Romosozumab	210 mg subcutaneously once monthly as 2 injections of 105 mg each	Anabolic-antiresorptive	– Treatment and prevention of GIOP in adults at increased fracture risk	Yes	Yes	Yes		– Zoledronate or alendronate is recommended
Romozosumab	210 mg subcutaneously once monthly as 2 injections of 105 mg each	Anabolic-antiresorptive	– Treatment of severe osteoporosis in postmenopausal women at high fracture risk	Yes	Yes	Yes	Treatment lasts 12 months	– Antiresorptive treatment should be initiated 1 month after the last dose of romosozumab and continued for at least 1 year
Teriparatide	20 µg subcutaneously daily	Anabolic	– Recommended as initial osteoporosis treatment in postmenopausal women at very high fracture risk	Yes	Yes	No [§]	Maximum total duration of treatment is 24 months	– Most evidence is available for denosumab, alendronate and zoledronate
Teriparatide	20 µg subcutaneously daily	Anabolic	– Treatment of osteoporosis in postmenopausal women at increased fracture risk	Yes	Yes	No [§]	Maximum total duration of treatment is 24 months	– Antiresorptive treatment should be initiated immediately after stopping teriparatide and continued for at least 1 year
Raloxifene	60 mg orally once daily	Antiresorptive	– Treatment of GIOP in women and men at increased fracture risk	Yes	No	No	Data on the safety and efficacy of treatment are limited to 8 years	– The efficacy of bisphosphonates and denosumab has been demonstrated
Raloxifene	60 mg orally once daily	Antiresorptive	– Recommended as initial osteoporosis treatment in patients at very high fracture risk	Yes	No	No	Data on the safety and efficacy of treatment are limited to 8 years	– The efficacy of bisphosphonates and denosumab has been demonstrated

*Decisions about longer continuation of therapy should be made on an individual basis and jointly with patients.

[†]Fracture-risk reduction demonstrated for vertebral, non-vertebral or hip fractures in postmenopausal women treated for osteoporosis.

[‡]A reduction of non-vertebral fracture risk with ibandronate was demonstrated only in a post hoc analysis of a subgroup of women with a femoral neck T-score < -3.0.

[§]The effect on hip fracture risk could not be reliably assessed in individual clinical trials because of the low number of observed fractures; however, a meta-analysis of 23 randomised clinical trials suggests a significant reduction in this risk.

GIOP – glucocorticoid-induced osteoporosis, N/A – not applicable.

Bisphosphonates

Bisphosphonates are synthetic analogues of pyrophosphate that inhibit osteoclast activity and promote osteoclast apoptosis, thereby reducing bone resorption [78]. A unique feature of bisphosphonates is their prolonged skeletal retention, allowing the antiresorptive effect to persist long after treatment has been stopped. The half-life of bisphosphonates in bone may exceed 10 years [79].

Alendronate, risedronate and zoledronate significantly reduce the risk of vertebral and non-vertebral fractures, including hip fractures [80–83]. By contrast, ibandronate reduces vertebral fracture risk only, which limits its usefulness. A reduction of non-vertebral fracture risk with ibandronate has been demonstrated only in a post hoc analysis of a subgroup of women with a femoral neck *T*-score < -3.0 [84].

Bisphosphonates are recommended for the treatment of osteoporosis in women and men, including glucocorticosteroid-induced osteoporosis (GIOP). Evidence allowing comparison of the anti-fracture efficacy of different bisphosphonates is limited [80, 81]. Given their effect on hip fracture risk, alendronate, risedronate and zoledronate may be regarded as first-line options, whereas ibandronate may be regarded as a second-line option. It should also be noted that ibandronate is not licensed for the treatment of osteoporosis in men.

Bisphosphonates are also used in the prevention of osteoporosis in patients at increased fracture risk [4]. The main example of such an indication is the prevention of GIOP. The efficacy of alendronate, risedronate and zoledronate has been demonstrated in the prevention and treatment of GIOP [85–87]. The use of bisphosphonates may be considered for the prevention of secondary osteoporosis in rheumatic diseases, although their efficacy in this indication has been studied almost exclusively in patients receiving GCs [88, 89].

Bisphosphonates may be administered orally (alendronate – 70 mg once weekly, risedronate – 35 mg once weekly, ibandronate – 150 mg once monthly) or intravenously (zoledronate – 5 mg every 12 months, ibandronate – 3 mg every 3 months). The route of administration should be chosen on the basis of the anticipated safety and efficacy profile in the individual patient. Intravenous administration is preferred in patients with contraindications to oral treatment. Where possible, patients' preferences regarding the route and frequency of administration, as well as treatment costs, should be taken into account [4].

There is still no clear evidence on the optimal duration of bisphosphonate therapy or the criteria for restarting treatment after a break, referred to as a “drug holiday” [90]. The indications for and contraindications to continued treatment should be assessed after

5 years of oral bisphosphonate therapy or 3 years of intravenous therapy, or if a new fracture occurs. Although a drug holiday may reduce the risk of adverse events, it increases fracture risk [91]. A treatment break lasting several years increases the risk of clinical fractures by 20–40%, and vertebral fracture risk is approximately doubled [4, 92]. Risk factors for fractures during a drug holiday include low BMD at the time of drug discontinuation (hip *T*-score ≤ -2.5), prior osteoporotic fracture, older age, underweight, and poor adherence to bisphosphonate therapy. During a drug holiday, zoledronate has the most durable anti-fracture effect, particularly after 6 annual infusions [79]. A drug holiday should be considered mainly in patients who are not at high fracture risk, including those without a prior osteoporotic fracture and with a hip *T*-score > -2.5 after 5 years of effective oral bisphosphonate therapy or 3 years of intravenous therapy. During a treatment break, patients should be followed up regularly. Because no validated fracture risk assessment strategy exists for this period, an individualised approach is required. Follow-up BMD testing is recommended 12 months after treatment discontinuation, with further testing at intervals of no more than 2 years. Because evidence is lacking, decisions to restart bisphosphonate therapy or to introduce another anti-osteoporosis drug should be based on an individual assessment of risks and benefits. Factors favouring the resumption of treatment include a new osteoporotic fracture, a hip *T*-score < -2.5 accompanied by a decrease in BMD equal to or greater than the LSC, and the appearance of new fracture risk factors or worsening of existing ones [91]. Data on the safety and efficacy of oral bisphosphonate treatment for > 10 years or intravenous treatment for > 6 years are limited, and therefore decisions about longer continuation of therapy should be made on an individual basis and jointly with patients [91, 92].

The most serious adverse events associated with bisphosphonates, namely atypical femoral fracture (AFF) and osteonecrosis of the jaw (ONJ), are very rare. In 3 randomised clinical trials including more than 14,000 women treated with bisphosphonates for up to 10 years, no cases of AFF or ONJ were observed [91]. The risk of AFF increases with the duration of bisphosphonate use, but this is an increase from 2.5/10,000 person-years with 3 to < 5 years of use to 13.1/10,000 person-years with ≥ 8 years of use [93]. This risk decreases rapidly after drug discontinuation – by as much as 70% per year [94]. In a study including almost 200,000 women treated with bisphosphonates over a 10-year period, the number of osteoporotic fractures prevented by treatment substantially exceeded the number of AFFs at all time points. According to these data, in a hypothetical cohort of 10,000 White women, over 5 years of therapy,

8 AFFs occurred, while 286 hip fractures and 859 clinical fractures were prevented [93]. An even rarer adverse event associated with bisphosphonates is ONJ, and more than 90% of cases occur in patients receiving intravenous bisphosphonate treatment for bone metastases. In the treatment of osteoporosis, the doses used are 6–10 times lower, and ONJ risk at these doses ranges from 1/100,000 to 1/10,000 person-years, only slightly higher than the incidence in the general population [92, 95].

Although invasive oral surgery is a risk factor for ONJ, it does not justify routine interruption of bisphosphonate therapy in patients with osteoporosis. In patients requiring extensive oral surgery and with coexisting ONJ risk factors (e.g. diabetes, periodontal disease, GC therapy, immunodeficiency, smoking), treatment may be withheld until soft tissue healing has occurred. Necessary dental treatment should be completed before bisphosphonates are started, followed by regular dental check-ups [95]. Dental care should not substantially delay osteoporosis treatment.

Key points:

- Bisphosphonates are recommended for the treatment of osteoporosis in women and men, including GIOP.
- Bisphosphonates are also used in the prevention of osteoporosis in patients at increased fracture risk.
- Alendronate, risedronate and zoledronate reduce the risk of vertebral and non-vertebral fractures, including hip fractures.
- Ibandronate reduces vertebral fracture risk only and is not licensed for the treatment of osteoporosis in men.

Denosumab

Denosumab is a human monoclonal IgG2 antibody against receptor activator of nuclear factor- κ B ligand (RANKL). It inhibits the binding of RANKL to the receptor RANK on osteoclasts and their precursors, thereby reducing osteoclast differentiation, survival and activity and consequently inhibiting bone resorption. The anti-resorptive effect of denosumab is reversible. After denosumab discontinuation, bone turnover increases rapidly, with BMD loss and increased fracture risk, necessitating sequential therapy [96].

Denosumab significantly reduces the risk of vertebral and non-vertebral fractures, including hip fractures. It also significantly increases BMD at the hip and spine [97, 98].

Denosumab is recommended for the treatment of osteoporosis in postmenopausal women at increased fracture risk, osteoporosis in men at increased fracture risk, and for the treatment and prevention of GIOP in adults at increased fracture risk. For these indications,

denosumab is administered as a 60 mg subcutaneous injection once every 6 months. The efficacy of denosumab has been confirmed not only in patients who have not previously received any anti-osteoporosis drug, but also as sequential therapy after bisphosphonates, romosozumab or teriparatide [99]. In patients with renal impairment, denosumab may be used at the standard dose, but the higher risk of hypocalcaemia should be taken into account. Hypocalcaemia has been observed most often after the first dose of denosumab and in patients with more advanced stages of chronic kidney disease [100, 101]. In patients with rheumatoid arthritis (RA) and osteoporosis, denosumab reduced the progression of bone erosions, suggesting inhibition of bone resorption in affected joints [102]. No contraindications have been identified for the concomitant use of denosumab with biological disease-modifying antirheumatic drugs in patients with inflammatory rheumatic diseases [102–105].

Among 1,343 women with postmenopausal osteoporosis treated with denosumab in a clinical trial, BMD continued to increase over 10 years of therapy [98]. Data on the safety and efficacy of denosumab treatment for > 10 years are limited, and therefore decisions about longer continuation of therapy should be made on an individual basis and jointly with patients [106, 107].

To maintain the therapeutic effect after stopping denosumab, consolidation therapy with a bisphosphonate should be initiated. Zoledronate or alendronate is recommended for this purpose. The main factors favouring the choice of zoledronate are contraindications to oral therapy, prior vertebral fracture, high fracture risk, and denosumab treatment for > 2.5 years. Consolidation therapy should be started 6 months after the last denosumab injection and continued for at least 1 year. Further decisions should be based on an individual assessment of fracture risk, including the bone densitometry result. The rebound effect after denosumab discontinuation, characterised by rapid BMD loss and increased fracture risk, may last for up to 2 years [108].

The risk of AFF and ONJ during denosumab treatment is low [106]. In a 10-year clinical trial, the incidence rates of AFF and ONJ were 0.8/10,000 person-years and 5.2/10,000 person-years, respectively. No cases of AFF or ONJ were observed during the first 3 years of therapy [98]. In a recently published meta-analysis, no significant association was found between denosumab therapy and ONJ in patients with dental implants, although data on this issue are limited [109].

Necessary dental treatment should be completed before denosumab is started, followed by regular dental check-ups [95]. Dental care should not substantially delay osteoporosis treatment.

Key points:

- Denosumab is recommended for the treatment of osteoporosis in postmenopausal women at increased fracture risk, osteoporosis in men at increased fracture risk, and for the treatment and prevention of GIOP in adults at increased fracture risk.
- After stopping denosumab, bisphosphonate treatment should be initiated as sequential therapy.
- Denosumab biosimilars may improve access to osteoporosis treatment and increase its cost-effectiveness.

Romosozumab

Romosozumab is a humanised monoclonal IgG2 antibody directed against sclerostin. It blocks sclerostin-mediated inhibition of osteoblast proliferation and differentiation, while also reducing RANKL synthesis. This results in increased bone formation and reduced bone resorption [110].

Romosozumab significantly reduces the risk of vertebral and non-vertebral fractures, including hip fractures. It also significantly increases BMD at the hip and spine [110–113].

Romosozumab is recommended for the treatment of severe osteoporosis in postmenopausal women at high fracture risk. In the large clinical trial that confirmed its efficacy, the criterion for high fracture risk was a prior vertebral or hip fracture [112]. Although the greatest efficacy of romosozumab has been demonstrated in patients who have not previously received any anti-osteoporosis drug, its effectiveness has also been confirmed when used after teriparatide, bisphosphonates or denosumab [99, 114]. Because of its anabolic effect, romosozumab is one of the drugs recommended as initial osteoporosis treatment in postmenopausal women at very high fracture risk [43–45]. Preliminary evidence supports the efficacy of romosozumab in the treatment of osteoporosis in women with RA, including those receiving GCs [115–117].

The recommended dose of romosozumab is 210 mg, administered as 2 subcutaneous injections of 105 mg each once monthly for 12 consecutive months. Because the effect of romosozumab is reversible, antiresorptive treatment should be initiated as sequential therapy after its discontinuation. For this purpose, the largest body of evidence is available for denosumab, alendronate and zoledronate [114, 118]. Sequential therapy should be started 1 month after the last dose of romosozumab and continued for at least 1 year. Further decisions should be based on an individual assessment of fracture risk, including the bone densitometry result.

When deciding whether to start romosozumab, the patient's individual cardiovascular risk should be taken into account, and modifiable risk factors should be controlled [110].

Key points:

- Romosozumab is recommended for the treatment of severe osteoporosis in postmenopausal women at high fracture risk.
- Because of its anabolic effect, romosozumab is one of the drugs recommended as initial osteoporosis treatment in postmenopausal women at very high fracture risk.
- Romosozumab treatment lasts 12 months.
- After stopping romosozumab, antiresorptive treatment should be initiated as sequential therapy.
- When deciding whether to start romosozumab, the patient's individual cardiovascular risk should be taken into account, and modifiable risk factors should be controlled.

Teriparatide

Teriparatide is a recombinant, biologically active N-terminal fragment of human parathyroid hormone (PTH 1–34). In contrast to continuous overproduction of parathyroid hormone (hyperparathyroidism), intermittent exposure to low doses of parathyroid hormone stimulates bone formation. The anabolic effect of daily teriparatide administration results from stimulation of osteoblast activity and differentiation, with inhibition of osteoblast apoptosis. In addition, teriparatide increases renal calcium reabsorption and phosphate excretion, and promotes hydroxylation of calcifediol to calcitriol, which increases intestinal calcium absorption [119].

Teriparatide significantly reduces the risk of vertebral and non-vertebral fractures. It also significantly increases BMD at the hip and spine. The effect of teriparatide on hip fracture risk could not be reliably assessed in individual clinical trials because too few fractures were observed, but a meta-analysis of 23 randomised clinical trials suggests a significant reduction in this risk. Most evidence for the anti-fracture efficacy of teriparatide comes from studies in postmenopausal women with osteoporosis and a prior low-energy fracture, most commonly a vertebral fracture [120–122].

Teriparatide is recommended for the treatment of osteoporosis in postmenopausal women at increased fracture risk, osteoporosis in men at increased fracture risk, and for the treatment of GIOP in women and men at increased fracture risk. Although the greatest efficacy of teriparatide has been demonstrated in patients who have not previously received any anti-osteoporosis drug, its effectiveness has also been confirmed when used after bisphosphonates. Because teriparatide does not prevent BMD loss after denosumab discontinuation, this treatment sequence is not recommended [99, 123]. Because of its anabolic effect, teriparatide is one of the drugs recommended as initial osteoporosis treatment in

patients at very high fracture risk [43–45]. Preliminary evidence supports the efficacy of teriparatide in the treatment of osteoporosis in postmenopausal women with RA, including those receiving GCs [124, 125].

Teriparatide is administered subcutaneously at a dose of 20 µg daily, and the maximum total duration of treatment is 24 months. Because the effect of teriparatide is reversible, antiresorptive treatment should be initiated as sequential therapy after its discontinuation [45]. For this purpose, the efficacy of bisphosphonates and denosumab has been demonstrated [99, 123]. The effectiveness of romosozumab when used after teriparatide has recently been demonstrated, but this sequence also requires consolidation with an antiresorptive drug [126–128]. Sequential therapy should be started immediately after teriparatide discontinuation and continued for at least 1 year [129]. Further decisions should be based on an individual assessment of fracture risk, including the bone densitometry result.

Key points:

- Teriparatide is recommended for the treatment of osteoporosis in postmenopausal women at increased fracture risk, osteoporosis in men at increased fracture risk, and for the treatment of GIOP in women and men at increased fracture risk.
- Because of its anabolic effect, teriparatide is one of the drugs recommended as initial osteoporosis treatment in patients at very high fracture risk.
- The maximum total duration of teriparatide treatment is 24 months.
- After stopping teriparatide, antiresorptive treatment should be initiated as sequential therapy.
- Teriparatide biosimilars may improve access to osteoporosis treatment and increase its cost-effectiveness.

Menopausal hormone therapy

The use of oestrogens alone or in combination with a progestogen to relieve bothersome menopausal symptoms and prevent BMD loss is referred to as menopausal hormone therapy (MHT) [130].

In healthy postmenopausal women, MHT significantly reduces the risk of vertebral and non-vertebral fractures, including hip fractures. It also significantly increases BMD at the hip and spine. These effects have been demonstrated with 0.625 mg of conjugated equine oestrogens daily [131–133].

Menopausal hormone therapy may be used for the prevention of osteoporosis in postmenopausal women when treatment is aimed primarily at achieving extraskeletal benefits, such as control of vasomotor symptoms of menopause. When deciding whether to initiate or continue MHT, the patient's individual cardiovascular

and thromboembolic risk, as well as the risk of breast cancer and gallbladder disease, should be taken into account. Before MHT is initiated, all patients require a full gynaecological assessment, followed by regular follow-up visits. Given its safety profile, initiating MHT in women aged over 60 years or more than 10 years after menopause onset is not recommended. To date, the optimal duration of MHT has not been established, and data from randomised clinical trials are limited to 10 years. Menopausal hormone therapy should be prescribed at the lowest effective dose and for no longer than necessary [130, 133]. After MHT discontinuation, BMD loss accelerates, which should be taken into account in the treatment and monitoring of patients, although the optimal sequential therapy has not yet been established. A randomised clinical trial has demonstrated the efficacy of 12 months of treatment with alendronate in this setting [134–136].

Key points:

- Menopausal hormone therapy may be used for the prevention of osteoporosis in postmenopausal women when treatment is aimed primarily at achieving extraskeletal benefits.
- When deciding whether to use MHT, the patient's individual cardiovascular and thromboembolic risk, as well as the risk of breast cancer and gallbladder disease, should be taken into account.
- Initiating MHT in women aged over 60 years or more than 10 years after menopause onset is not recommended.
- Menopausal hormone therapy should be prescribed at the lowest effective dose and for no longer than necessary.
- After MHT discontinuation, BMD loss accelerates, which should be taken into account in the ongoing monitoring and treatment of patients.

Selective oestrogen receptor modulators

Selective oestrogen receptor modulators are non-hormonal agents that act as agonists or antagonists at oestrogen receptors, depending on the target tissue. In Europe, raloxifene and bazedoxifene are licensed for the treatment of osteoporosis. Both drugs act as partial oestrogen receptor agonists in bone, where they reduce bone resorption through effects on osteoclasts and osteoblasts [137]. Bazedoxifene is not available in Poland and will not be discussed in these recommendations.

- Raloxifene significantly reduces the risk of vertebral fractures and significantly increases BMD at the spine and hip. Clinical trials have not demonstrated an effect of raloxifene on the risk of non-vertebral fractures, including hip fractures [138–140]. A reduction in non-

vertebral fracture risk with raloxifene was suggested only by a post hoc analysis in a subgroup of women with severe vertebral fractures [141].

Raloxifene may be used for the treatment and prevention of osteoporosis in postmenopausal women when all other drugs are contraindicated.

Raloxifene is administered at a dose of 60 mg once daily. The optimal duration of raloxifene treatment has not been established, and data from randomised clinical trials are limited to 8 years [142]. Most data are from postmenopausal women aged 50–70 years [143].

Raloxifene significantly reduces the risk of invasive breast cancer, particularly oestrogen receptor-positive disease [142]. It also has a favourable effect on the lipid profile. In women receiving raloxifene, significant reductions in total cholesterol and low-density lipoprotein cholesterol, together with an increase in high-density lipoprotein cholesterol, were found [144]. A significant reduction in atherogenic lipoprotein(a) concentrations was also observed [145].

In clinical trials, raloxifene use was associated with an increased risk of venous thromboembolism, but compared with placebo, this was an increase from 1.3 to 2.2/1000 person-years [146]. Less serious but much more common adverse effects, such as hot flushes, flu syndrome, leg cramps and peripheral oedema, may lead patients to discontinue treatment [138, 139, 143]. When deciding whether to start raloxifene, the patient's individual cardiovascular and thromboembolic risk should be taken into account. In patients undergoing surgery, raloxifene should be discontinued 3 days before planned immobilisation. If immobilisation occurs unexpectedly, raloxifene should be discontinued as soon as possible. Resumption of treatment may be considered once the patient is fully mobile [143].

Key points:

- Raloxifene may be used for the treatment and prevention of osteoporosis in postmenopausal women when all other drugs are contraindicated.
- When deciding whether to start raloxifene, the patient's individual cardiovascular and thromboembolic risk should be taken into account.
- Raloxifene may be particularly beneficial in postmenopausal women without marked menopausal symptoms, with concomitant hypercholesterolaemia and/or increased breast cancer risk, if the lack of effect on non-vertebral fracture risk is acceptable.

Strontium ranelate

Strontium ranelate has been withdrawn from the market in the European Union and will not be discussed in these recommendations [147].

Calcitonin

Because of its unfavourable benefit-risk balance, calcitonin is not recommended for the treatment of osteoporosis and will not be discussed in this document [148].

Prevention of glucocorticosteroid-induced osteoporosis

Glucocorticosteroid use is the most common cause of secondary osteoporosis. Treatment with prednisone at doses of ≥ 2.5 mg daily has been shown to increase the risk of hip fractures, whereas the risk of vertebral fractures increases even at doses < 2.5 mg daily. The most rapid BMD loss occurs within the first 3–6 months of treatment. Therefore, prevention of GIOP should be considered at the initiation of GC therapy. Glucocorticoid therapy should be used at the lowest effective dose and for no longer than necessary. It is important to ensure adequate calcium intake, optimal vitamin D status, and control of other risk factors for accelerated BMD loss. In patients beginning or continuing GC therapy at a prednisone-equivalent dose of ≥ 2.5 mg daily for > 3 months, a comprehensive fracture risk assessment is recommended, including bone densitometry and either VFA or spine radiographs. Subsequent fracture risk assessments during GC therapy are recommended at least every 12 months. In patients beginning or continuing GC therapy at a prednisone-equivalent dose of ≥ 2.5 mg daily for > 3 months, the initiation of antiresorptive treatment should be considered for the prevention of GIOP. After GCs are discontinued, fracture risk should be reassessed and a decision made about whether to continue, modify or stop antiresorptive treatment. If denosumab is being discontinued, consolidation therapy with a bisphosphonate is required. After discontinuation of an anti-osteoporosis drug used for GIOP prevention, regular fracture risk assessment every 1–2 years is recommended, including bone densitometry and, ideally, VFA. The prevention and treatment of GIOP should follow the 2022 American College of Rheumatology (ACR) guideline, which summarises the clinical evidence in this area [53].

Key points:

- Glucocorticosteroid therapy should be used at the lowest effective dose and for the shortest possible duration.
- In patients beginning or continuing GC therapy at a prednisone-equivalent dose of ≥ 2.5 mg daily for > 3 months, a comprehensive fracture risk assessment is recommended, including bone densitometry and either VFA or spine radiographs.
- Subsequent fracture risk assessments during GC therapy are recommended at least every 12 months.

- In patients beginning or continuing GC therapy at a prednisone-equivalent dose of ≥ 2.5 mg daily for > 3 months, the initiation of antiresorptive treatment should be considered for the prevention of GIOP.
- The prevention and treatment of GIOP should follow the ACR guideline.

Treatment of osteoporosis in premenopausal women

In premenopausal women, osteoporosis is most often secondary, resulting from chronic diseases (e.g. inflammatory rheumatic diseases, endocrine, neuromuscular, haematological, pulmonary, gastrointestinal or infectious diseases, and eating disorders) or from their treatment (e.g. GCs, antiepileptic drugs or antiretroviral drugs). In rare cases, when an osteoporotic fracture has occurred and comprehensive diagnostic assessment has not identified a cause of secondary osteoporosis, idiopathic osteoporosis is diagnosed. Decisions about the treatment of osteoporosis in premenopausal women should be made on an individual basis in specialist centres. The treatment goal and monitoring approach are the same as those in postmenopausal women. In every case, optimal treatment of the underlying diseases should be ensured and the use of osteotoxic drugs limited where possible. Non-pharmacological management includes a well-balanced diet, exercise that stimulates bone formation, and prevention of falls. Pharmacological treatment begins with vitamin D and calcium supplementation at recommended doses, taking into account age, body weight, diet and comorbidities. In women at high fracture risk, particularly after a low-energy fracture, the initiation of antiresorptive or anabolic treatment should be considered. To date, no studies have assessed the effect of anti-osteoporosis drugs on fracture risk in premenopausal women. However, effects on BMD and bone microarchitecture have been demonstrated. The largest body of evidence in this area is available for bisphosphonates (zoledronate, risedronate and alendronate), with less evidence for teriparatide [149, 150]. More recently, the efficacy of denosumab as sequential therapy after teriparatide has been demonstrated in the treatment of osteoporosis in premenopausal women [151, 152]. In addition, a significant increase in lumbar spine BMD was found in a small retrospective study assessing the efficacy of romosozumab in premenopausal women with osteoporosis and anorexia nervosa [153].

Key points:

- Secondary osteoporosis is the most common form of osteoporosis in premenopausal women.
- In every case, optimal treatment of the underlying diseases should be ensured, and the use of osteotoxic drugs should be limited where possible.

- Decisions about the treatment of osteoporosis in premenopausal women should be made on an individual basis in specialist centres.
- In the treatment of osteoporosis in premenopausal women, the largest body of evidence on efficacy and safety is available for bisphosphonates (zoledronate, risedronate and alendronate), with less evidence for teriparatide.
- Randomised clinical trials assessing the efficacy of new anti-osteoporosis drugs in premenopausal women are needed, as are studies assessing the anti-fracture efficacy of all drugs in this population.

Diagnosis and treatment of osteoporosis in the paediatric population

Because osteoporosis in children and adolescents has a highly diverse aetiology, it requires an individualised approach based on current recommendations for the specific form of the disease and the patient's age. The general principles for the diagnosis and treatment of osteoporosis in the paediatric population are presented below.

Diagnostic criteria for osteoporosis in the paediatric population

According to the ISCD Official Positions, osteoporosis is diagnosed in children and adolescents when at least one of the following criteria is met [26]:

- at least one low-energy vertebral compression fracture, after exclusion of causes other than osteoporosis, or
- a clinically significant fracture history, defined as at least 2 long bone fractures by 10 years of age or at least 3 long bone fractures by 19 years of age, together with a BMD Z-score of ≤ -2.0 .

In children and adolescents, as in young adults, osteoporosis cannot be diagnosed on the basis of the bone densitometry result alone. In the paediatric population, BMD is assessed by DXA. The recommended site for assessment of BMD and/or bone mineral content is the lumbar spine (vertebrae L1–L4) in the PA projection, and from 3 years of age, assessment of total body less head is also recommended. When interpreting bone densitometry results, bone age and/or Tanner stage should be taken into account. The referring physician is responsible for providing these data [26].

In children and adolescents, a low-energy vertebral compression fracture is sufficient to establish the diagnosis of osteoporosis after other causes have been excluded. Therefore, in the paediatric population, back pain requires careful differential diagnosis, including consideration of lateral radiography of the thoracic and lumbar spine. This examination should also be performed

in all children with suspected osteoporosis or increased fracture risk to identify asymptomatic fractures [154]. Vertebral fractures are assessed using the Genant semi-quantitative method. Vertebral fracture assessment may be used to detect vertebral compression fractures in children and adolescents, providing reliable assessment of moderate and severe fractures (Genant grades 2 and 3) at a lower radiation dose than standard radiography. After VFA, additional imaging should be considered in the following situations [26]:

- when some vertebrae could not be assessed by VFA and detection of a fracture would change clinical management,
- when VFA shows a single Genant grade 1 vertebral fracture and confirmation of this finding would change clinical management,
- when VFA shows radiological features atypical of an osteoporotic fracture, for example findings suggestive of malignancy or a congenital abnormality.

The differential diagnosis of osteoporosis in children and adolescents should begin by excluding rickets/osteomalacia. It is also necessary to distinguish traumatic fractures from low-energy fractures, which can be challenging in this patient group. The next step is a comprehensive clinical assessment aimed at identifying causes of both primary osteoporosis (e.g. osteogenesis imperfecta) and secondary osteoporosis. In children and adolescents, osteoporosis is most often secondary, resulting from chronic diseases (e.g. inflammatory rheumatic diseases, inflammatory bowel disease, neuromuscular, haematological or endocrine diseases, chronic kidney disease, malabsorption syndromes and eating disorders) or from their treatment (e.g. GCs, antiepileptic drugs or radiotherapy). A diagnosis of secondary osteoporosis does not exclude co-existing primary osteoporosis, and vice versa [154–156].

Treatment of osteoporosis in the paediatric population

The goals of osteoporosis treatment in the paediatric population include reducing the risk of subsequent fractures, promoting bone mass accrual, preventing postural deformities, and improving or maintaining physical function. The developing skeleton has a high regenerative capacity, including the ability of fractured vertebral bodies to regain their shape (reshaping). Non-pharmacological management includes a well-balanced diet, exercise that stimulates bone formation, and prevention of falls. Pharmacological treatment begins with vitamin D and calcium supplementation at recommended doses, taking into account age, body weight, diet and comorbidities. Diseases affecting bone metabolism should be treated optimally, and the use

of osteotoxic drugs, especially GCs, should be limited where possible. Decisions about the treatment of osteoporosis in children and adolescents should be made on an individual basis in specialist centres. Meeting the ISCD diagnostic criteria for osteoporosis is considered an indication for antiresorptive therapy, although no drug is licensed for the treatment of osteoporosis in children and adolescents. The largest body of evidence is available for bisphosphonates, for which safety and efficacy have been demonstrated in osteogenesis imperfecta, idiopathic juvenile osteoporosis and secondary osteoporosis. In children and adolescents, intravenous bisphosphonate therapy is preferred. This preference reflects the greatest clinical experience, the best documented efficacy and ease of treatment administration. Standardised dosing regimens have not yet been established. Examples include the following: zoledronate 0.05 mg/kg body weight every 6 months, pamidronate in children older than 3 years at a dose of 1 mg/kg body weight/day for 3 consecutive days every 4 months, and neridronate 2 mg/kg body weight every 3 months. In patients who have not sustained new fractures in the previous 12 months, stopping treatment or gradually reducing bisphosphonate doses should be considered [155–158]. Monitoring during and after osteoporosis treatment follows the general principles used in adults, while taking into account the specific features of the paediatric population and recommendations for the particular form of the disease and the patient's age.

Key points:

- The diagnosis of osteoporosis in children and adolescents requires evidence of low-energy fractures whose type and number are strictly defined.
- Bone mineral density is assessed by DXA.
- Osteoporosis in children and adolescents is most often secondary.
- In every case, optimal treatment of the underlying diseases should be ensured, and the use of osteotoxic drugs, especially GCs, should be limited.
- Meeting the diagnostic criteria for osteoporosis in the paediatric population is an indication for antiresorptive therapy.
- In the treatment of osteoporosis in children and adolescents, intravenous bisphosphonate therapy is preferred.
- In patients who have not sustained new fractures in the previous 12 months, stopping treatment or gradually reducing bisphosphonate doses should be considered.

Conclusions

These recommendations present current principles for the diagnosis and treatment of osteoporosis. The pri-

mary aim was to provide physicians and patients with a wide range of therapeutic options informed by current evidence. The document was prepared on the principle that clinical recommendations should be guided by medical evidence rather than reimbursement criteria, which may restrict treatment options for non-medical reasons. The authors hope that these PTR recommendations will contribute to early diagnosis and effective treatment of osteoporosis in Poland.

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