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Compliance with alendronate 10 treatment in elderly women with postmenopausal osteoporosis

Stopień przestrzegania zaleceń przewlekłej terapii alendronianem 10 przez pacjentów leczonych z powodu osteoporozy

Ewa Sewerynek[1, 3], Katarzyna Dąbrowska[1, 3], Elżbieta Skowrońska-Jóźwiak[2, 3], Arkadiusz Zygmunt[2, 3], Andrzej Lewiński[2, 3]

[1]Department of Endocrine Disorders and Bone Metabolism, Chair of General Endocrinology
[2]Department and Chair of Endocrinology and Metabolic Diseases, Medical University, Lodz
[3]Memorial Mother's Hospital at Lodz

Abstract

Introduction: It has been shown that more than 50% of people with a chronic disease, including osteoporosis, discontinue treatment during its first year. This problem increases with the time of observation.
The aim of this study was to assess alendronate compliance over a period of 6 or 18 months in clinical practice of postmenopausal osteoporosis.
Material and methods: Using a retrospective study of clinical histories (357) obtained in our Outpatient Clinic, as well as telephone interviews with patients, the compliance with alendronate therapy in postmenopausal patients was assessed.
Results: After 1.5 years on observation 20.4% of patients, and after 0.5 years 8.5% of patients, discontinued their treatment as a result of intolerance (especially side effects on the gastrointestinal tract) (47.8%), health problems unrelated to osteoporosis (8.7%), inconvenience of the daily regimen (13.1%), costs (4.3%), and improvement of clinical condition (26.1%). It is worth mentioning that in both periods of observation (1.5 and 0.5 years) almost the same percentage of patient discontinued visits at our Outpatient Clinic (15.6% and 14.4%, respectively). Telephone interviews with patients who stopped attending the Outpatient Clinic at the Regional Centre of Menopause and Osteoporosis revealed that more than 50% of them discontinued the treatment.
Conclusions: Not all patients treated with alendronate are compliant. Osteoporosis is a chronic disease, which needs long clinical observation and constant adherence to medication. Effective communication between doctor and patient, and follow-up visits that are more frequent would greatly improve the adherence to osteoporosis treatment modalities. Compliant patients achieved increases in bone mass density with simultaneous fracture risk reduction. **(Pol J Endocrinol 2009; 60 (2): 76–81)**

Key words: *osteoporosis, compliance, alendronate 10, reasons for discontinuation*

Streszczenie

Wstęp: Wykazano, że ponad 50% pacjentów leczonych z powodu chorób przewlekłych, w tym osteoporozy, przerywa terapię w ciągu pierwszego roku jej stosowania. Problem ten narasta z czasem trwania obserwacji.
Celem pracy była ocena stopnia przestrzegania zaleceń terapii przewlekłej przez pacjentki leczone z powodu osteoporozy.
Materiał i metody: Ocenie poddano 357 losowo wybranych historii chorób osób, które pierwszy raz były konsultowane w Regionalnym Ośrodku Osteoporozy i Menopauzy w łodzi w roku 2003 i 2004. Analizą objęto pacjentów leczonych preparatem alendronian 10. Wzięto pod uwagę czas trwania obserwacji, zakres kontynuacji, przyczynę przerwania stosowanego leczenia.
Wyniki: W okresie 18 miesięcznej obserwacji leczenie przerwało 20,4% pacjentów, natomiast w okresie obserwacji 6 miesięcznej 8,5%. Przyczyny przerwania terapii alendronianem 10 były następujące: brak tolerancji ze strony przewodu pokarmowego (47,8%), współistniejące choroby (8,7%), uciążliwość przyjmowania leku w terapii codziennej (13,1%), cena leku (4,3%) oraz poprawa kliniczna (26,1%). Zarówno w jednym, jak i drugim okresie obserwacji stwierdzono porównywalną grupę pacjentów, którzy nie zgłosili się ponownie na konsultacje lub z którymi nie ma kontaktu od co najmniej pół roku do roku (odpowiednio: 15,6% dla obserwacji 1½ rocznej; 14,4% dla obserwacji ½ rocznej). Po weryfikacji telefonicznej stwierdzono, że ponad połowa pacjentów nie zgłaszających się nie kontynuuje zalecono leczenia.
Wnioski: Nie wszyscy pacjenci leczeni z powodu osteoporozy kontynuują zalecone leczenie. Im dłużej trwa leczenie tym większy jest odsetek pacjentów przerywających terapię. Choroba przewlekła wymaga wypracowania zasad współpracy pomiędzy prowadzącym lekarzem a pacjentem, której celem jest lepsze przestrzeganie zaleconych zasad postępowania terapeutycznego co może odnieść wymierny skutek w postaci poprawy stanu klinicznego. **(Endokrynol Pol 2009; 60 (2): 76–81)**

Słowa kluczowe: *przestrzeganie zaleceń lekarskich, osteoporoza, alendronian 10, przyczyny przerwania terapii*

Ewa Sewerynek M.D. Ph.D., Department of Endocrine Disorders and Bone Metabolism, Medical University of Lodz, Żeligowskiego 7/9, 90–752 Lodz, tel./fax: +48 42 63 93 127, tel. mobil: 601 95 27 47, e-mail: ewa.sewerynek@wp.pl

Introduction

Osteoporosis is a major public health problem in many countries, including Poland [1]. Currently, the available treatment options increase bone mineral density (BMD) and decrease fracture risk [2–7]. In order to obtain benefit from their medication, patients should maintain optimal compliance and persist with their osteoporosis therapy [8, 9]. The definitions of these three words: compliance, persistence and adherence, are present in many papers [10–13]. The term adherence is used to imply both compliance (medication intake regularity) and persistence (medical therapy duration).

It has been shown that more than 50% of people with chronic disease, including osteoporosis, discontinue treatment during its first year [14]. This problem increases with the time of observation. It has been observed that 13% of women who were prescribed oral daily alendronate did not even start the treatment, and 20% of patients discontinued the therapy during the first 4 months [15, 16]. This problem does not depend on the form of treatment [11].

Longitudinal, retrospective analyses in large databases illustrate that adherence to osteoporosis therapies is poor. Boguzzi and colleagues [17] presented the results of a study involving a cohort of 10,566 women, showing that adherence during one year was higher with two bisphosphonates: alendronate (60.7%) and risedronate (58.4%), and lower with raloxifene (53.9%). Persistence, however, was poor for all the agents (alendronate 23%, risedronate 19.4%, and raloxifene 16.2%). A somewhat higher range for persistence at 12 months has been presented in other papers [18]. In three examined countries, the compliance was as follows: 32% in the United States, 40% in the United Kingdom, and 44% in France. Women on daily alendronate persisted with treatment for 185 days in the United States, 208 days in the United Kingdom, and 155 days in France [18]. The persistence curves for osteoporosis medications showed a rapid decrease within the first 3 months of therapy [15–17]. Similarly, a retrospective study of postmenopausal women who used alendronate, calcitonin, HRT, raloxifene, or risedronate showed compliance below 66% during a 60-day period [19]. Adherence to medication recommendations in osteoporosis is very important because it has been shown that compliance below 66% with drug treatment results in suboptimal improvement in bone mineral density [20].

The aim of the present study was an assessment of alendronate compliance (administered daily) during the treatment of osteoporosis within the period of 6 and 18 months in the clinical practice of patients from the Outpatient Clinic at the Regional Centre of Menopause and Osteoporosis in Łódź.

Material and methods

Three hundred and fifty-seven (357) randomly selected case records of persons who were for the first time consulted at the Regional Centre of Menopause and Osteoporosis during the years 2003 and 2004 were submitted for evaluation. The analysis comprised patients treated with an agent from the bisphosphonate group (alendronate 10, administered once daily). The follow up period, the scope of continuation, and the cause of treatment withdrawal were taken into account.

Results

The reasons for the patient's first visit at the Osteoporosis Outpatient Clinic — own experience: 1. A patient untreated before (in our material, following randomly selected case records in 2003 — 69%; in 2004 — 77%): suspected diagnosis of osteoporosis in radiological studies of bones, identified bone fracture, prompting the diagnosis of osteoporosis, abnormal bone density results in screening tests. 2. A patient treated before (in our material, on the basis of randomly selected case records 2003 — 31%; 2004 — 23%): other examinations performed before: forearm, spine DXA, or sonographic imaging, which prompted the onset of treatment, a change of osteoporosis therapy centre due to the observed lack of improvement, patient's referral to a specialist unit following the failed attempt of osteoporosis treatment by glucocorticosteroids.

Following our own observations, patients who attend the clinic for the first time are prompted by: a conscious intention to have BMD evaluated, especially in the case of post-menopausal patients who are referred for secondary osteoporosis diagnostics or BMD prior to steroid therapy administration.

According to the evaluated case records, it was found that, out of the group of patients attending the clinic for the first time, approximately 62% required continuation of previously administered therapy. The remaining patients required verification of the earlier diagnosis, obtained from X-ray picture or peripheral densitometry.

It appears from the analysis that during the 1.5-year observation period of the patients treated with alendronate 10, the therapy was discontinued by 20.4% of the patients (Table I), while during a 6-month observation period, 8.5% of the patients discontinued treatment (Table II).

While evaluating the reasons for treatment discontinuation, it was determined that, most often, it resulted from poor gastric tolerance of the agent (47.8%), followed by concomitant diseases (8.7%), inconveniences associated with drug intake by daily dose regimen

Table I. *Based on the records of 137 patients admitted for the first time in 2003, anti-resorptive treatment was applied in 72 cases, where alendronate was administered in 64 in doses of 10 mg/d.*

Tabela I. *Analiza dokumentacji medycznej 137 pacjentów hospitalizowanych po raz pierwszy w 2003 roku wykazała, że leki przeciwresorpcyjne zalecono u 72 osób, przy czym 64 osoby otrzymały alendronian w dawce 10 mg/d*

Administered treatment	Number of subjects	Compliance	
Alendronate 10	64	Yes	41 (64%)
		No	13 (20.4%)
		Lost contact for the last year	10 (15.6%)

Table II. *Based on the records of 204 patients admitted for the first time in 2004, anti-resorptive treatment was applied in 125 cases, where alendronate was administered in 118 in doses of 10 mg/d.*

Tabela II. *Analiza dokumentacji medycznej 204 pacjentów hospitalizowanych po raz pierwszy w 2004 roku wykazała, że leki przeciwresorpcyjne zalecono u 125 osób, przy czym 118 osób otrzymało alendronian w dawce 10 mg/d.*

Administered treatment	Number of subjects	Compliance	
Alendronate 10	118	Yes	91 (77.1%)
		No	10 (8.5%)
		Lost contact for the last year	17 (14.4%)

(13.1%), drug costs (4.3%), and clinical improvement rate (26.1%) (Table III).

It should be underlined that after both the first and the second observation periods, a comparative group of patients was found, who did not turn up for follow up visits or with whom all contact had been lost for at least half a year (15.6% for the 18-month observation and 14.4% for the 6-month observation, respectively). Following telephone verification, it turned out that more than half of the non-attending patients discontinued the recommended treatment (Tables I and II).

It appears from our observations that 63% of the patients during the follow up period used one agent, while 37% of the subjects were treated with several combined medications, which was associated with intolerance to the drug, inconvenience of daily drug intake, or with financial aspects (Table IV).

Table III. *Causes of treatment discontinuation*

Tabela III. *Przyczyny zaprzestania leczenia*

Administered treatment	Number of subjects	Compliance	
Alendronate 10	23	Intolerance	11 (47.8%)
		BMD improvement	6 (26.1%)
		Concomitant diseases	2 (8.7%)
		Price	1 (4.3%)
		Inconvenience of intake, lack of confidence	3 (13.1%)

Table IV. *Causes of treatment changes*

Tabela IV. *Przyczyny zmiany leczenia*

Treatment continuation	N (132 subjects)	Causes
Alendronate — the same agent	83 (62.9%)	
With various agents	49 (37.1%)	Intolerance
		Inconvenience of drug intake
		Financial aspects

Discussion

Osteoporosis is a chronic disease, which needs long clinical observation and constant adherence to medication.

In the present study, alendronate compliance in the clinical practice of osteoporosis was time dependent and, overall, moderate. The analysis of clinical records has shown that 62% of patients with osteoporosis had been treated before and, after our initial consultation, the treatment was continued. In the remaining group, after our initial consultation, the treatment was stopped. The main reason for therapy discontinuation was the introduction of a new treatment before initial consultation with the patient and before central densitometry was done, according to the resolutions of the Position Development Conferences for the purpose of establishing standards and guidelines for indications, acquisition, and interpretation of bone density tests [21, 22], which is also obligatory in our country [23, 24].

The data from our study have shown that, after 18 months of observation 20.4% of patients, and after

Table V. *Studies which show the scale of therapy discontinuation with bisphosphonates, compared to our results*

Tabela V. *Częstość zaprzestania leczenia bisfosfonianami w doniesieniach z badań klinicznych w porównaniu z rezultatami uzyskanymi przez autorów*

Clinical Trials	No. of subjects	Discontinuation of therapy (in months)	
Lombas [14]	401	ALE 10	51% within 12 70% within 24
Roldan ECMO [39]	1,877	ALE 10	20% within 4
Negri ECMO [16]	2,552	ALE 70	13% within 6
Papadimitropoulos CANDOO [25]	1,196	ETI	14.5% within 6 19.1% within 12
Papadimitropoulos CANDOO [25]	477	ALE 10	29.9% within 12 35.8% within 24
Ettinger [29]	812	ALE 10	44% within 13
Ettinger [27]	211,319	ALE 10	39% within 12
Curtis [32]	101,038	Oral bisphosphonates	44% within 12 39% within 24 35% within 36
Ringe [35]	452 769	ALE 10 ALE 70	21% within 12 35% within 12
Own data	118	ALE 10	8.5% within 6 on the average (+14.4%)
	64	ALE 10	20.4% within 18 (+15.6%)

6 months 8.5% of patients, discontinued their treatment. It is worth mentioning that in both periods of observation (18 or 6 months) almost the same percentage of people stopped consultations at our Outpatient Clinic (15.6% and 14.4%, respectively). Telephone interviews with the patients who stopped attending the Outpatient Clinic revealed that more than 50% of them discontinued the treatment. The results of our paper are compared to the work of a Canadian group (Table V) [25]. The Canadian Database of Osteoporosis and Osteopaenia (CANDOO), a prospective observational database designed to capture clinical data, was searched for patients who started therapy with 1,196 initiating etidronate, 477 alendronate therapy for women and men, and 294 hormone replacement therapy for women. After 1 year, 90.3% of patients were still taking etidronate compared with 77.6% for daily alendronate and 80.1% of patients on HRT, which decreased to 44.5% after 6 years. Reginster and Lecart [26] suggest that the persistence rates in the CANDOO study may be artificially high. The study took place in a clinic where the patients initially gave signed consent and were given verbal encouragement to continue treatment. Our observations were equally encouraging, bearing in mind the fact that, contrary to the prospective CANDOO study, our data were retrospective.

The results of persistence have not been very optimistic in a number of reports. For example, medication persistence was only in 39.0% of patients, receiving daily alendronate therapy at month 12 of the study period [27]. In a questionnaire study of 219 women with osteoporosis taking daily risedronate, 1 in 4 did not comply correctly with dosing instructions, despite counselling [28]. In a subsequent paper, using a telephone interview survey, it was reported that within 13 months of observation of 812 women with osteoporosis, treated daily with alendronate, 56% of the patients were noncompliant [29].

Good adherence to osteoporosis treatment is very important for its effectiveness. Among the 999 respondents — patients with osteoporosis, the effectiveness was ranked as the most important determinant of preference (79%), compared with the time on market (14%), dosing procedure (4%), and dosing frequency (3%). Incorporation of patient preferences in the medication decision-making process could enhance patient compliance and clinical outcomes [30]. This last opinion is very important because it has been shown that compliance below 66% in drug treatment results in sub-optimal improvement in bone density [20]. On the other hand, improving compliance in the actual practice may significantly decrease osteoporosis-related fracture risks (a 16% lower fracture risk during 2 years) [31]. It has been observed that the antifracture effectiveness, associated with high adherence to oral bisphosphonates, varied substantially according to age and fracture type [32]. Caro et al. [33] showed that poorly compliant patients were significantly more frequently hospitalized (53.4%), compared to compliant ones (42.6%), leading to 14% higher costs of medical services.

In our analysis, the main reason for discontinuation of alendronate treatment was intolerance (especially side effects from the gastrointestinal tract) (47.8%), health problems unrelated to osteoporosis (8.7%), inconvenience with the daily regimen (13.1%), costs (4.3%), and poor improvement of the clinical condition (26.1%). This is in agreement with the results of other authors [20, 34].

Among patients completing another study (4,231), the percentage of patients with high compliance was 80% (Raloxifene), 79% (Alendronate 10), 65% (Alendronate 70) and 76% (Risedronate). The discontinuation, due to side effects, was highest on alendronate 70 (7.0%), followed by alendronate 10 (6.4%), raloxifene (3.8%), and risedronate (3.4%). The discontinuation rate was higher for patients with a history of surgical menopause, increased age, lack of knowledge about medical prevention of osteoporosis, and thin frame as a reason for intervention [35].

Another observation, made during our study, was connected with the large number of alendronate generics in our country. During the time of our observation, 63% of the patients received the same active substance, whereas in 37% of patients, pharmaceutical generics were changed due to intolerance, inconvenience, or cost. In the group of studied patients, some of them requested that the mode of application be changed from daily to weekly, for their convenience. This is in conformity to other results [34]. They have found that the main reasons for discontinuing therapy with antiresorptive treatment were: side effects (40%), high cost of medicine (27%), ineffective treatment (17%), patient's demands (12%), changing medicines by another doctor (3%), and therapeutic success (1%). Claxton (36) suggested that the prescribed number of doses per day is inversely related to compliance. Simpler, less frequent dosing regimens resulted in better compliance across a variety of therapeutic classes. This is reflected in osteoporosis therapy. Postmenopausal women prescribed a weekly regimen of bisphosphonates had significantly greater rates of compliance than women prescribed a daily regimen did, and they persisted longer with treatment. However, compliance and persistence rates were suboptimal for both regimens [18, 37].

Osteoporosis is a chronic disease, which needs long clinical observation and constant adherence to medication recommendations. Analyzing our observations and the results of others, we suggest that the main reasons for discontinuation of treatment are not only digestive incidents but also problems with receiving prescriptions within the first 3 months of treatment, dissatisfaction with the clinical condition, and bad monitoring. In our opinion, effective communication and more frequent follow-up visits would greatly improve the adherence to osteoporosis treatment modalities. Variations in the compliance with medical treatment of osteoporosis might also depend on other factors: patient beliefs, social and economic conditions, physical predisposition, or health problems. Compliance could be improved with the patient's preference of treatment regimen. It is of utmost importance to inform patients about their diagnosis and long-term treatment plan, highlighting the role of persistence with therapy and compliance with dosing recommendations [38]. Adherence to drug administration regime improves BMD, reduces femoral neck and spine fracture risks, while also decreasing the costs of in-house therapy.

Conclusions

The obtained results demonstrate moderate incompliance to medical recommendations by patients treated for osteoporosis with alendronate 10. The critical points, decisive for treatment discontinuation, include therapy-induced adverse effects, no continuous contact with consultant, and no subjective clinical improvement.

References

1. Jaworski M, Lorenc RS. Risk of hip fracture in Poland. Med Sci Monit 2007; 13: CR206–CR210.
2. Cranney A, Guyatt G, Griffith L et al. Meta-analyses of therapies for postmenopausal osteoporosis. IX: Summary of meta-analyses of therapies for postmenopausal osteoporosis. Endocr Rev 2002; 23: 570–578.
3. Cranney A, Tugwell P, Zytaruk N et al. Meta-analyses of therapies for postmenopausal osteoporosis. IV. Meta-analysis of raloxifene for the prevention and treatment of postmenopausal osteoporosis. Endocr Rev 2002; 23: 524–528.
4. Cranney A, Wells G, Willan A et al. Meta-analyses of therapies for postmenopausal osteoporosis. II. Meta-analysis of alendronate for the treatment of postmenopausal women. Endocr Rev 2002; 23: 508–516.
5. Cranney A, Papaioannou A, Zytaruk N et al. Parathyroid hormone for the treatment of osteoporosis: a systematic review. CMAJ 2006; 175: 52–59.
6. Papadimitropoulos E, Wells G, Shea B et al. Meta-analyses of therapies for postmenopausal osteoporosis. VIII: Meta-analysis of the efficacy of vitamin D treatment in preventing osteoporosis in postmenopausal women. Endocr Rev 2002; 23: 560–569.
7. Shea B, Wells G, Cranney A et al. Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. Endocr Rev 2002; 23: 552–559.
8. Gold DT. Medication adherence: a challenge for patients with postmenopausal osteoporosis and other chronic illnesses. J.Manag Care Pharm 2006; 12: S20–S25.
9. Gold DT, Martin BC, Frytak JR et al. A claims database analysis of persistence with alendronate therapy and fracture risk in post-menopausal women with osteoporosis. Curr Med Res Opin 2007; 23: 585-94.
10. Gold DT, Safi W, Trinh H. Patient preference and adherence: comparative US studies between two bisphosphonates, weekly risedronate and monthly ibandronate. Curr Med Res Opin 2006; 22: 2383–2391.
11. Cramer JA, Gold DT, Silverman SL et al. A systematic review of persistence and compliance with bisphosphonates for osteoporosis. Osteoporos Int 2007; 18: 1023–1031.
12. Sewerynek E. Wpływ współpracy lekarza z pacjentem na efektywność leczenia osteoporozy. Terapia 2006; 3: 43–46.
13. Sewerynek E. Czynniki wpływające na przestrzeganie zasad terapii i efektywność leczenia osteoporozy — rola współpracy lekarza z pacjentem. Medycyna po Dyplomie 2008;3 (Suppl.): 39–41.
14. Lombas C, Hakim C Zanchetta JR. Compliance with alendronate treatment in an osteoporosis clinic. J Bone Miner Res 2001; 15: S529, M406.
15. Bandeira F, Kayath M Marques-Neto J et al. Patients' clinical features and compliance associated with raloxifene or alendronate after a six-month observational Brazilian Study. J Bone Miner Res 2003; 18 (Suppl. 2): M352, S379.
16. Negri AL. Short-term compliance with alendronate 70 mg in patients with osteoporosis: The ECMO Trial. Bone 2003; 23 (Suppl): P487.
17. Bocuzzi SJ, Foltz SH Omar MA et al. Adherence and persistence associated with pharmacological treatment of osteoporosis. Osteoporosis Int 2005; 16 (Suppl. 3): S24 — P129..
18. Cramer JA, Lynch NO, Gaudin AF et al. The effect of dosing frequency on compliance and persistence with bisphosphonate therapy in postmenopausal women: a comparison of studies in the United States, the United Kingdom, and France. Clin Ther 2006; 28: 1686–1694.
19. Solomon DH, Avorn J, Katz JN et al. Compliance with osteoporosis medications. Arch Intern Med 2005; 165: 2414–249.
20. Yood RA, Emani S, Reed JI et al. Compliance with pharmacologic therapy for osteoporosis. Osteoporos Int 2003; 14: 965–968.
21. Lewiecki EM, Watts NB, McClung MR et al. Official positions of the international society for clinical densitometry. J Clin Endocrinol Metab 2004; 89: 3651–3655.
22. Lewiecki EM, Kendler DL, Kiebzak GM et al. El-Hajj FG et al. Special report on the official positions of the International Society for Clinical Densitometry. Osteoporos Int 2004; 15: 779–7784.
23. Czerwiński E, Badurski JE, Marcinkowska-Suchowierska et al. Współczesne rozumienie osteoporozy w świetle stanowiska World Health Organization (WHO) i International Osteoporosis Foundation (IOF). Ortop Traumat Rehab 2007: 4: 337–356.
24. Lorenc RS, Głuszko P Karczmarewicz E et al. Zalecenia postępowania diagnostycznego i leczniczego w osteoporozie. Obniżenie częstości złamań poprzez efektywną profilaktykę i leczenie. Terapia 2007; 9: 11–39.

25. Papaioannou A, Ioannidis G, Adachi JD et al. Adherence to bisphosphonates and hormone replacement therapy in a tertiary care setting of patients in the CANDOO database. Osteoporos Int 2003; 14: 808–813.
26. Reginster JY, Lecart MP. Treatment of osteoporosis with bisphosphonates — Do compliance and persistence matter? Business Briefing: Longterm Healthcare2004: 1–9.
27. Ettinger MP, Gallagher R, MacCosbe PE. Medication persistence with weekly versus daily doses of orally administered bisphosphonates. Endocr Pract 2006; 12: 522–528.
28. Hamilton B, McCoy K, Taggart H. Tolerability and compliance with risedronate in clinical practice. Osteoporos Int 2003; 14: 259–262.
29. Ettinger B, Pressma AR Shchein J et al. Alendronate use among 812 women: prevalence of gastrointestinal complaints, non-compliance with patients instructions and discontinuation. J Managed Care Pharm 1998: 488–492.
30. Weiss TW, McHorney CA. Osteoporosis medication profile preference: results from the PREFER-US study. Health Expect 2007; 10: 211–223.
31. Caro JJ, Ishak KJ, Huybrechts KF et al. The impact of compliance with osteoporosis therapy on fracture rates in actual practice. Osteoporos Int 2004; 15: 1003–1008.
32. Curtis JR, Westfall AO, Cheng H et al. Benefit of adherence with bisphosphonates depends on age and fracture type: results from an analysis of 101,038 new bisphosphonate users. J Bone Miner Res 2008; 23: 1435–1441.
33. Caro JJ, Ishak KJ Krista F et al. Clinical and economic impact of adherence to osteoporosis medication. Osteoporos Int 2003; 14 (Suppl. 7): PL6.
34. Napiórkowska L, Franek E. Systematyczność i wytrwałość w zażywaniu leków w trakcie wieloletniego leczenia osteoporozy. Twój Magazyn Medyczny 2006; 2: 1–7.
35. Ringe JD, Christodoulakos GE, Mellstrom D et al. Patient compliance with alendronate, risedronate and raloxifene for the treatment of osteoporosis in postmenopausal women. Curr.Med Res Opin 2007; 23: 2677–2687.
36. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. Clin Ther 2001; 23: 1296–1310.
37. Cramer JA, Amonkar MM, Hebborn A et al. Compliance and persistence with bisphosphonate dosing regimens among women with postmenopausal osteoporosis. Curr Med Res Opin 2005; 21: 1453–1460.
38. Emkey RD, Ettinger M. Improving compliance and persistence with bisphosphonate therapy for osteoporosis. Am J Med 2006; 119: S18–S24.
39. Roldan EJA, Negri AL Gador SA. Shorn-term compliance to daily alendronate treatment in 1,877 patients with osteoporosis — The ECMO Study. J Bone Miner Res 2000; 15:SU 411.