

Medicinal drug use in Slovenia

JURIJ FÜRST, JURE PEKLAR and VITA SAMALUK

Health Insurance Institute of Slovenia, Medicinal Products Department, Miklosiceva 24, 1507 Ljubljana

Corresponding author: jurij.furst@zzzs.si

ABSTRACT

Background: Overprescribing of some psychoactive drugs can lead to tolerance, dependence and abuse. The purpose of the article is to show the use of antipsychotics, anxiolytics and hypnotics/sedatives in Slovenia, to correlate it to some foreign countries and to point at some interesting findings.

Methods: We have searched the Institute for Public Health and Health Insurance Institute Prescription Database for all prescriptions of antipsychotics, anxiolytics and hypnotics/sedatives prescribed for ambulatory use in Slovenia in last 5 years. Data are shown in defined daily doses (DDDs) per 1000 inhabitants per day.

Results: The use of antipsychotics has increased mostly on account of new, atypical preparations. They represent more than a half of antipsychotic consumption. The intramuscular depo preparations represent 21 % of antipsychotics. Use of anxiolytics has decreased for 14 % in 2001–5, but the use of hypnotics/sedatives has increased for 13 %. There are significant regional differences in the use of all groups of drugs. The highest difference in regional use of anxiolytics is 100 % and in use of hypnotics/sedatives 60%. The regional differences in the use for diazepam 10 mg and bromazepam 6 mg, which can point to potential abuse, are even higher. Potentially excessive prescribing to the elder patients is shown by the high number of different drugs prescribed to them and with the number of patients with drugs for dementia and benzodiazepines prescribed at the same time. The comparison to four Scandinavian countries shows favourably low use of hypnotics and higher use of anxiolytics in Slovenia, but overall use of both groups is lower in Slovenia.

Conclusions: Slovenian total use of anxiolytics and hypnotics is lower as in Scandinavian countries. Anyway, it would be reasonable and, regarding high regional differences possible, to decrease it.

Key words: drug use, antipsychotics, anxiolytics, benzodiazepines, hypnotics and sedatives, Slovenia

INTRODUCTION

Slovenia has the social insurance scheme, similar to the Bismarck type. The provider of compulsory health insurance is Health Insurance Institute of Slovenia, which conducts its business as a public institute. Almost 70% of the population of 2 million are voluntary health insured. A voluntary co-insured person does not co-pay for drugs and health-care services. There is no extra payment (participation) for prescriptions. For interchangeable drugs with the price higher than the reference level, one co-pays the difference. The health care benefits arising from the compulsory health insurance fund is quite comprehensive. Consumption of drugs and their structure is comparable to other EU countries and new drugs are reimbursed without significant delay (1).

Some psychoactive drugs, especially benzodiazepine anxiolytics and hypnotics can lead to tolerance and dependence with a risk of abuse (2, 3). Prescribing to elderly can increase the risk for hip fracture and has effects on cognitive function. That's why they are not recommended to the elderly and should be carefully prescribed (4–6).

PURPOSE

The purpose of our work is to show the use of psychiatric drugs, especially anxiolytics (ATC N05B) and hypnotics/sedatives (ATC N05C) in Slovenia and to point on some patterns of prescribing and possibilities of abuse of benzodiazepines.

METHODS

We have searched the Institute for Public Health and Health Insurance Institute Prescription Database for all prescriptions of antipsychotics, anxiolytics and hypnotics/sedatives prescribed for ambulatory use in Slovenia in 2001–5. Data are shown in defined daily doses (DDDs) per 1000 inhabitants per day. That methodology enables drug use comparisons among regions and countries (7). The use of diazepam 10 mg and bromazepam 6 mg is shown as a marker for the non-therapeutic use of psychoactive drugs (8). For international comparisons publicly available consumption data of Scandinavian countries are available (9–12).

RESULTS

Psychiatric drugs are economically the second most important drug group after cardiovascular drugs. They represent 11,2 % of ambulatory pharmaceutical expenditures. Their use has increased in 2001–05 by 24 %. There is a rapid growth of the use of new antipsychotics (+35 %) and antidepressants (+90 %). The share of depo antipsychotics is 21 %. The use of lithium is very low and is decreasing. The use of anxiolytics is in decline (–14 %) and the use of hypnotics/sedatives is slowly increasing (+13 %). The use of drugs for treatment of Alzheimer's disease – acetyl cholinesterase inhibitors has grown for 349 %; they represent already 8 % of expenditures for psychiatric drugs.

The most prescribed anxiolytics are alprazolam, diazepam, bromazepam and lorazepam. The region with the highest prescribing has twice higher consumption than the region with the lowest prescribing (fig. 1). The use of anxiolytics is higher in elderly and in women (fig. 2). In comparison to Sweden Slovenian use is higher and the difference grows with age (9). Fig. 3 and 4 present regional prescribing of diazepam 10 mg and bromazepam 6 mg in 2002–4. We have analyzed other dosages where the differences are less pronounced. The use of other dosages and other benzodiazepines is comparable to regional patterns in fig. 1.

Fig. 1: The use of anxiolytics in Slovenian Health Insurance regions in DDDs per 1000 inhabitants per day in 2002–2004. Horizontal lines show Slovenian average. CE Celje; KK Krško; KP Koper; KR Kranj; LJ Ljubljana; MB Maribor; MS Murska Sobota; NG Nova Gorica; NM Novo mesto; RA Ravne na Koroškem.

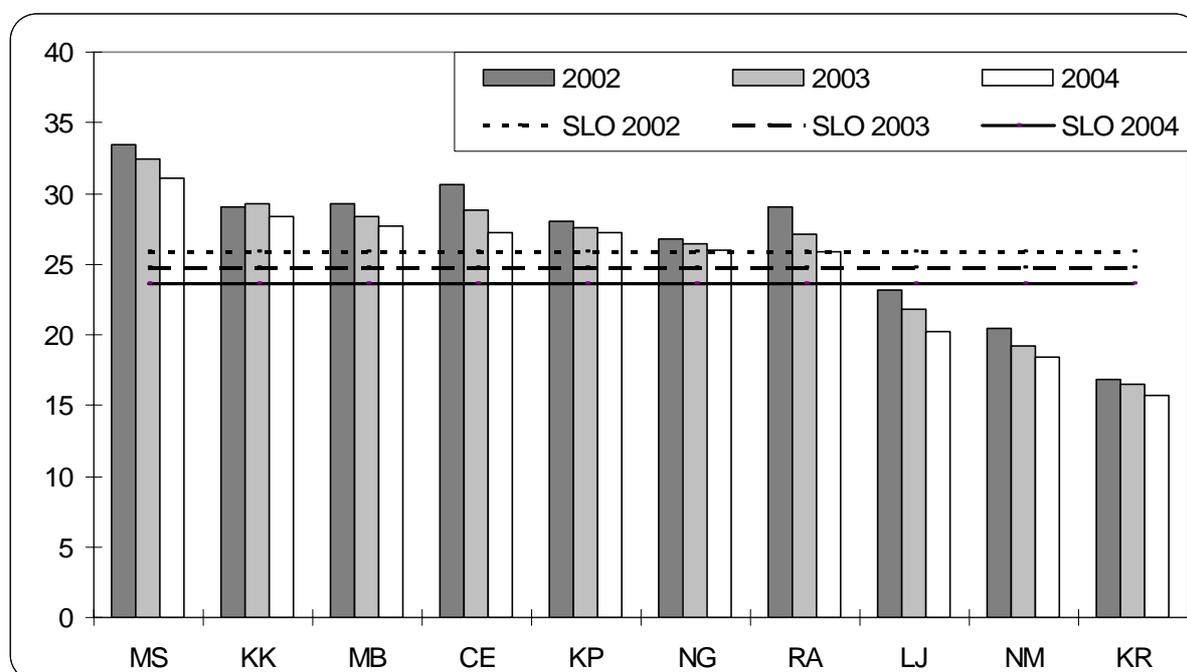


Fig. 2: The use of anxiolytics in Slovenia and in Sweden according to age and gender in DDDs per 1000 inhabitants per day in 2002. (SLO Slovenia; S Sweden)

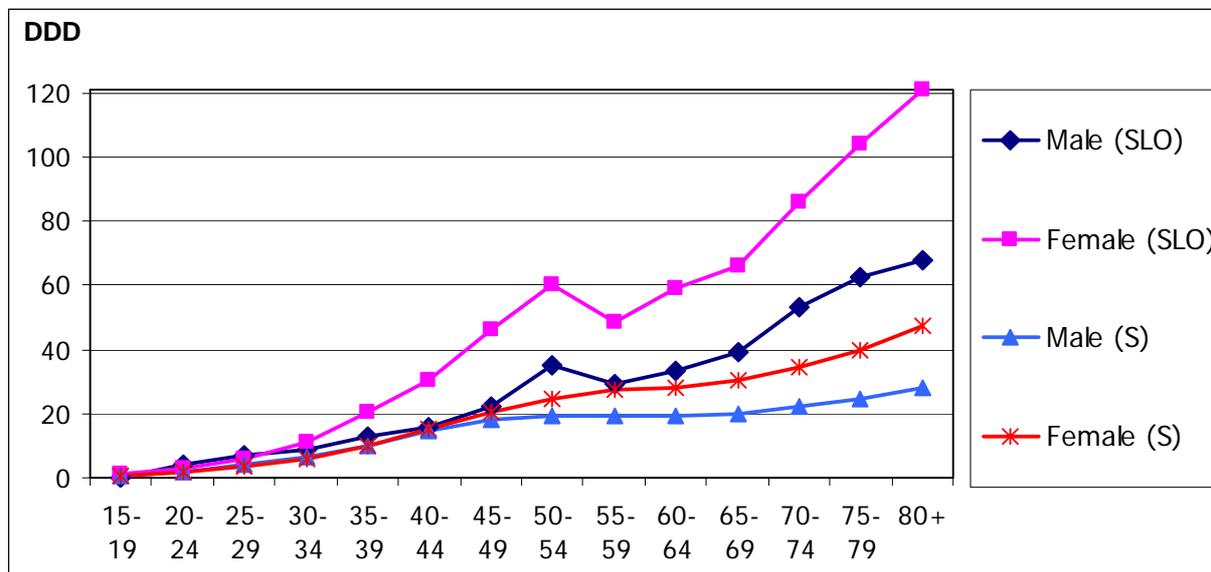


Fig. 3: The use of diazepam 10 mg in Slovenian Health Insurance regions in DDDs per 1000 inhabitants per day in 2002–2004. Horizontal lines show Slovenian average. CE Celje; KK Krško; KP Koper; KR Kranj; LJ Ljubljana; MB Maribor; MS Murska Sobota; NG Nova Gorica; NM Novo mesto; RA Ravne na Koroškem.

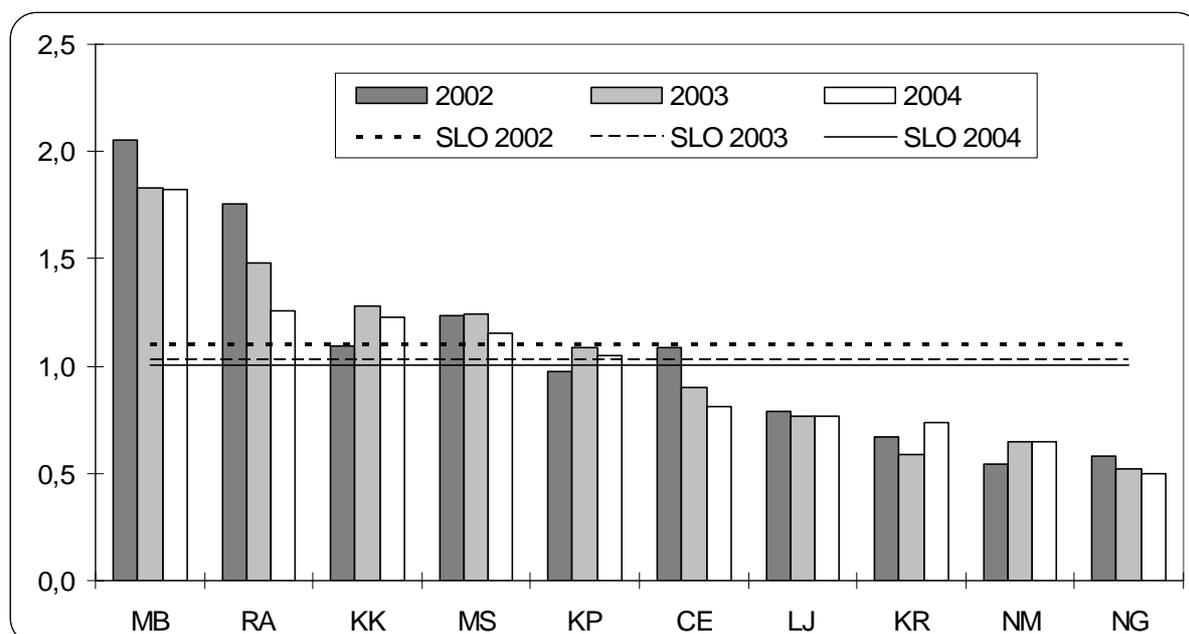
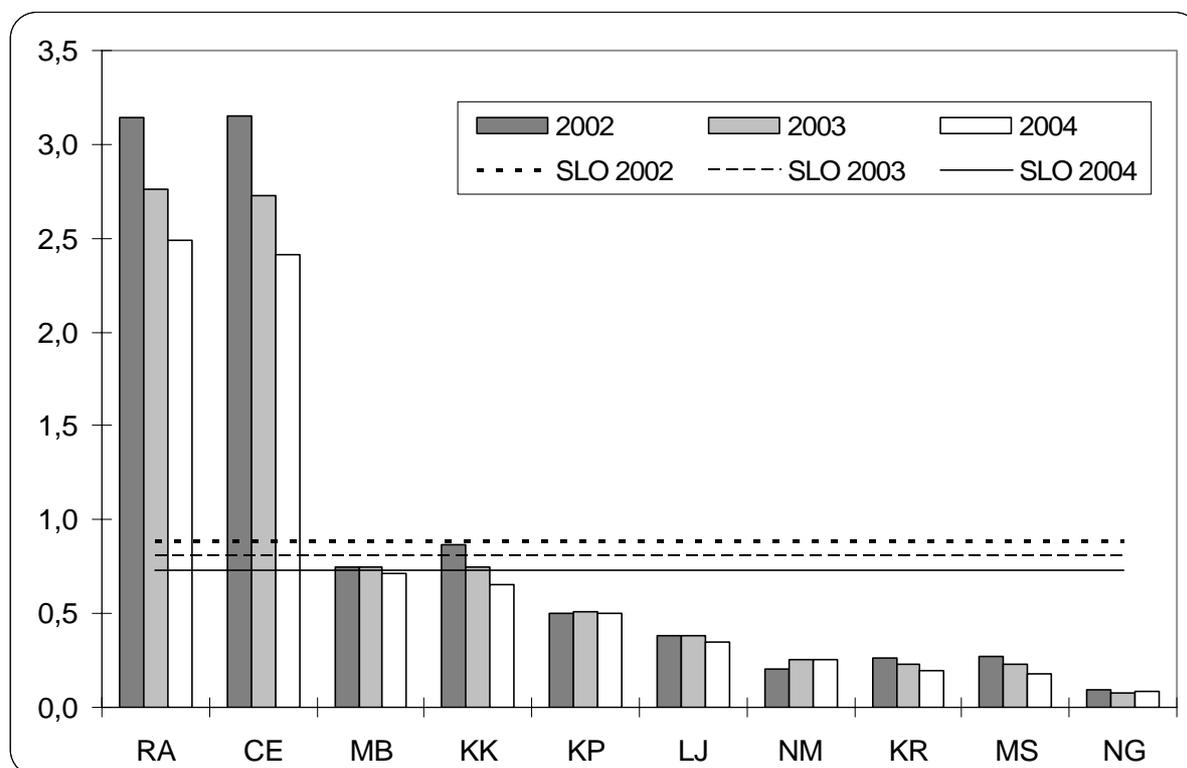
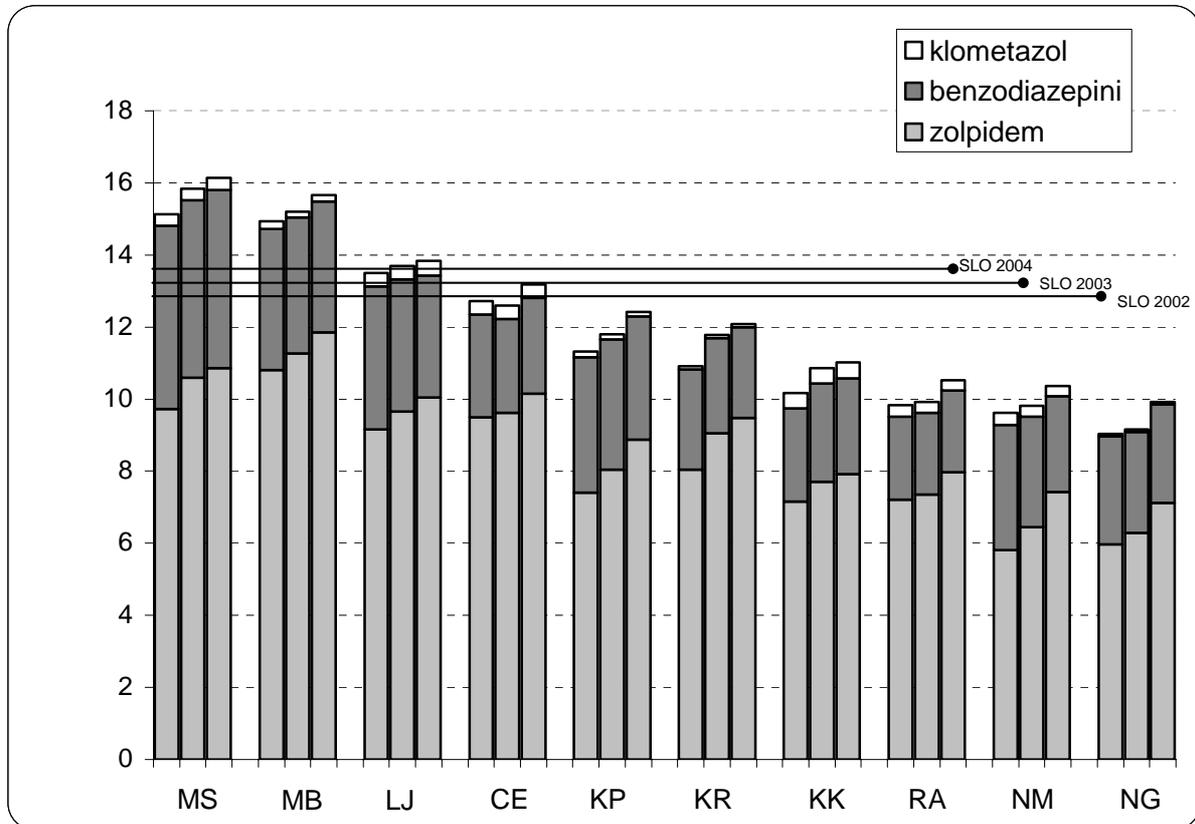


Fig. 4: The use of diazepam 10 mg in Slovenian Health Insurance regions in DDDs per 1000 inhabitants per day in 2002–2004. Horizontal lines show Slovenian average. CE Celje; KK Krško; KP Koper; KR Kranj; LJ Ljubljana; MB Maribor; MS Murska Sobota; NG Nova Gorica; NM Novo mesto; RA Ravne na Koroškem.



There are three classes of hypnotics/sedatives: benzodiazepines (available in Slovenia are flurazepam, midazolam and nitrazepam), cyclopyrrolones (only zolpidem) and others with clomethiazole as the only representative in Slovenia. Zolpidem is the most prescribed (74 % of consumption), next are midazolam (10 %) and flurazepam (8 %). The share of clomethiazole use is 2 %. The regional pattern of hypnotics/sedatives' use shows less pronounced differences as with anxiolytics (fig. 5).

Fig. 5: The use of hypnotics/sedatives in Slovenian Health Insurance regions in DDDs per 1000 inhabitants per day in 2002–2004. Horizontal lines show Slovenian average. CE Celje; KK Krško; KP Koper; KR Kranj; LJ Ljubljana; MB Maribor; MS Murska Sobota; NG Nova Gorica; NM Novo mesto; RA Ravne na Koroškem.



DISCUSSION

The guidelines for prescribing of anxiolytics and hypnotics/sedatives are restrictive. The lowest effective dose for a maximum period of one month should be prescribed (13, 14). They should not be combined with other sedatives and prescribed to addiction-prone individuals. Significant regional differences point to the assumption that they could be prescribed more rationally in regions with the high consumption. Prescribing for the elderly should be especially careful. All benzodiazepines can impair cognitive function in elderly and increase the risk of falls and consecutive hip fractures (4–6). Analyses of Slovenian 2004 prescription database show that 99 % of inhabitants aged over 65 have received at least one prescription. In comparison with the age group of 40–64 they have received 2,4 times more prescriptions. 13.333 persons age 65 or more have received 10 or more drugs (active substances) in the period of 3 months. 989 persons have received even more than 15 drugs (15). 629 patients have received at least one prescription for an antidementive drug and a benzodiazepine. This combination is probably only exceptionally indicated. Extensive prescribing of benzodiazepines to Slovenian elderly in comparison to Swedish population and prescribing of to many different drugs is a cause for public concern.

Extreme regional differences in prescribing highest doses of diazepam and bromazepam can point to prescribing to the drug addicts (8). When Health Insurance Institute of Slovenia presented those results to the psychiatrists, prescribing began to decrease (fig. 3, 4).

The optimal use of anxiolytics and hypnotics is not defined. Regarding prescribing guidelines we assume that lower consumption is more rational than higher consumption. A comparison to Scandinavian countries has shown that Slovenia has comparable use of anxiolytics to Denmark and Norway but higher than Sweden and lower than Finland. On the other side it has only a fourth to a half of Scandinavian use of hypnotics/sedatives (16). We have prepared a new comparison that shows similar proportions (tab. 1). In Slovenia and in all Scandinavian countries the consumption of anxiolytics has decreased in last years. In contrast to the antibiotics where Scandinavian countries are known for their rational use that is lower than Slovenian (17), Slovenian use of hypnotics can be assessed as more rational.

Tab. 1. The use of anxiolytics and hypnotics/sedatives in DDDs per 1000 inhabitants per day in Slovenia and in Scandinavian countries in 2004. *Norwegian data include also hospital consumption.

Group/ATC	Slovenia	Denmark	Norway*	Sweden	Finland
Anxiolytics/N05B	23,3	20,1	21,0	13,0	28,3
All hypnotics/sedatives/N05C	13,0	30,9	39,1	47,9	51,6
- benzodiazepines/N05CD	3,1	11,4	8,7	7,1	19,4
- ciclopirolones/N05CF	9,6	19,5	30,3	28,0	30,9
- other/N05CM	0,3	0,0	0,1	12,8	0,5
Sum of anxiolytics and hypnotics/sedatives	36,3	51,0	60,1	60,9	79,9

Comments on consumption of other psychiatric groups of drugs are out of scope of that presentation.

CONCLUSIONS

Three considerable points in use of psychiatric drugs in Slovenia might be exposed:

- Significant regional differences in use of anxiolytics
- High use of anxiolytics especially for the elderly
- Disproportionably high use of diazepam 10 mg and bromazepam 6 mg in some regions.

References

1. European Observatory on Health Systems and Policies: Slovenia. Available on 6. 11. 2006 on:

<http://www.euro.who.int/observatory/CtryInfo/CtryInfoRes?COUNTRY=SVN&CtryInputSubmit=>

2. Charney DS, Mihic SJ, Harris RA. Hypnotics and sedatives. In: Hardman JG, Limbird LE, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 10th ed. New York: The McGraw-Hill Companies; 2001: 399–427.
3. O'Brien CP. Drug addiction and drug abuse. In: Hardman JG, Limbird LE, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 10th ed. New York: The McGraw-Hill Companies; 2001: 621–42.
4. Hanlon JT et al. Benzodiazepine use and cognitive function among community-dwelling elderly. *Clin Pharmacol Ther* 1998; 64: 684–92.
5. Rummans TA et al. Learning and memory impairment in older, detoxified, benzodiazepine-dependent patients *Mayo Clin Proc* 1993; 68: 731–7.
6. Wang PS et al. Hazardous benzodiazepine regimens in the elderly: Effects of half-life, dosage, and duration on risk of hip fracture. *Am J Psychiatry* 2001; 158: 892–8.
7. The Anatomical Therapeutic Chemical Classification system with Defined Daily Doses. ATC Index with DDDs 2005. WHO Collaborating Centre for Drug Statistics Methodology. Oslo, 2005. Also available 20. 10. 2006 on: <http://www.who.int/classifications/atcddd/en/>
8. Roin A, Leanai SA. Report of the Benzodiazepine Committee. Ministry for Health and Children. Ireland, August 2002. *Dosegljivo* 27. 5. 2005 na: <http://www.dohc.ie/publications/pdf/benzo1.pdf?direct=1>.
9. Švedska poraba zdravil. *Dosegljivo* 27. 5. 2005 na: http://www.nam.fi/english/news/salesstatistics00_available.html.
10. Norveška poraba zdravil. *Dosegljivo* 27. 5. 2005 na: <http://www.legemiddelforbruk.no/>.
11. Danska poraba zdravil. *Dosegljivo* 27. 5. 2005 na: <http://www.medstat.dk/dataviewer.php>.
12. Finska poraba zdravil. *Dosegljivo* 27. 5. 2005 na: <http://www.nam.fi/uploads/Salesstatistics.pdf>.
13. Taylor D, Paton C, Kerwin R. The South London and Maudsley NHS Trust 2003 Prescribing Guidelines. 7th ed. London: Martin Dunitz, 2003: 166–8.
14. Taylor D, Paton C, Kerwin R. The South London and Maudsley NHS Trust 2003 Prescribing Guidelines. 7th ed. London: Martin Dunitz, 2003: 158–65.
15. Samaluk V, Peklar J. Predpisovanje zdravil starostnikom s stroškovnega in strokovnega vidika. *Recept* 2005; 1: 37–8.
16. Fürst J, Kocmur M. Use of psychiatric drugs in Slovenia in comparison to Scandinavian countries. *Pharmacoepidemiology and drug safety* 2003; 12:399–403.
17. Ferech M, Coenen S, Malhotra-Kumar S, Dvorakova K, Hendricks E, Suetens C, Goosens H. European Surveillance of antimicrobial Consumption (ESAC): outpatient antibiotic use in Europe. *Journal of Antimicrobial Chemotherapy* 2006; 58: 401–7.