



FINANCIAL AVAILABILITY OF IN-HOME MEDICAL TREATMENT OF PATIENTS WITH ALZHEIMER'S DISEASE

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SUMMARY

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder and presents a great burden for the person, family and society as a whole. Since 2012, in Bulgaria, AD is accepted as a disorder of a great socio-economic significance and the drugs for home treatment are included in the reimbursement list of the National Health Insurance Fund (NHIF).

Objective: To trace the access to treatment of Alzheimer's in-home patients, as a result of generic substitution on the base of share distribution of the original and generic products.

Methods: We collected data for the sales of pharmaceutical products (PP's), containing donepezil hydrochloride and memantine hydrochloride from a distributor for the Northeast region of Bulgaria (Varna) in the period 2014-2015. An analysis of the percentage share distribution of the original and generic products was conducted.

Results: According to our results original product Aricept accounts for only 4%, while the market share for its generics is 96%. In this group the share to be paid from NHIF is 25%, the remaining 75% from the cost is paid by the patients. The original product Axura occupies 8% market share, the generics- 92%. In this group the share to be paid from NHIF is 50% for generics, while Axura was removed from the Positive reimbursement list. We comment the significant differences in the sale shares in several directions.

Conclusion: The reduction of expenses, with the use of generics, would help more patients to receive an optimal treatment and the savings could be redirected for other costly treatments.

Key words: Alzheimer's disease, cholinesterase inhibitors, memantine, financial costs, generics

Introduction:

Alzheimer's disease (AD) is the most common cause of dementia among people aged 65 and older and accounts for 60%-70% of all cases [1]. In Bulgaria they are about 60 000 [2]. AD is a progressive neurodegenerative disorder and presents a great burden for the person, family and society as a whole. The underlying causes of Alzheimer's dementia (AD) remain unclear, but it most likely results from a combination of genetic and environmental factors, meaning the

disease requires a genetic predisposition that interacts with the environment to result in illness. Imbalanced brain chemistry, specifically in the neurotransmitters dopamine and glutamate may also play a role in the development of AD. As the world's population ages the number of people with AD is rising dramatically. Additional risks are female gender, history of head trauma, a low level of education [1].

People suffering from dementia exhibit two main types of symptoms: cognitive and neuropsychiatric. The decline in cognition involves one or more cognitive domains (learning and memory, language, executive function, complex attention, perceptual-motor, social cognition) [3].

Behavioural and Psychic Symptoms of dementia (BPSD) include hallucinations, delusions and different types of agitated behaviours [4, 5].

The treatment of AD addresses [6]:

- Cognitive enhancers (cholinesterase inhibitor therapy; NMDA-receptor antagonists) to improve, temporally stabilize or slow the rate of cognitive decline
- Disease-modifying factors to reduce progression (antioxidants, selegiline, ginkgo biloba, etc.)
- Psychotropic agents to treat BPSD [7, 8]
- Treatment of non-psychiatric comorbidity [9,10]
- Working with caregivers –education, emotional and social support, etc.

Neurotransmitter enhancement therapy with cholinesterase inhibitors (ChE-Is) improve cholinergic function in AD by inhibiting the destruction of intrasynaptic acetylcholine by acetyl-cholinesterase, thus increase cholinergic synaptic transmission by inhibiting acetylcholinesterase in the synaptic cleft. They still represent the mainstay of symptomatic treatment in AD. Three medications belonging to this class are currently widely available and are approved for the symptomatic treatment of AD for mild to moderate dementia: donepezil, rivastigmine, and galantamine. Several randomised, controlled trials (RCTs) of ChE-Is in AD have demonstrated variable rates of improvement, ranging between 18 and 48 per cent [11]. The authors discuss that their beneficial effects, demonstrated through meta-analyses, are modest in terms of cognitive and global measures of response. A number of adverse effects associated with ChE-Is are not benign and may limit their use in individual patients. Another point of discussion concerns costs [12]. In a review Birks (2015) discussed the results of 10 randomized, dou-

ble blind, placebo controlled trials. They demonstrate that treatment for 6 months, with donepezil, galantamine or rivastigmine at the recommended dose for people with mild, moderate or severe dementia due to Alzheimer's disease, produced improvements in cognitive function. Benefits of treatment were also seen on measures of activities of daily living and behaviour. None of these treatment effects are large [13].

A dysfunction of glutamatergic neurotransmission, manifested as neuronal excitotoxicity, is hypothesized to be involved in the etiology of Alzheimer's disease. Targeting the glutamatergic system, specifically NMDA receptors, offers a novel approach to treatment. Memantine is the first in a novel class of AD medications acting on the glutamatergic system by blocking NMDA receptors. Memory loss in Alzheimer's disease is due to a disturbance of message signals in the brain. Memantine hydrochloride acts on these (NMDA)-receptors improving the transmission of nerve signals and the memory. Memantine hydrochloride is used for the treatment of patients with moderate to severe Alzheimer's disease.

Treatment with the cognitive enhancers should start as the diagnosis of AD is established and should be continued in advanced phases [5].

The long duration and pervasive social impact of the disease is reflected in the breakdown of the overall cost. AD-associated costs include direct medical costs such as medications, non-medication in-home or institutional care and indirect costs such as lost productivity of both patient and members of the family.

Patients' clinical characteristics include cognitive status, functional capacity, psychotic symptoms, behavioral problems, depressive symptoms, comorbidities, and duration of illness [14].

Since 2012, in Bulgaria, AD is accepted as a disorder of a great socio-economic significance and the drugs for home treatment are included in the reimbursement list of the National Health Insurance Fund (NHIF).

Paying for care is a big concern during the course of AD. The type and level of care needed change over time. Some in-home care costs include:

- Ongoing medical treatment for Alzheimer's-related symptoms
- Treatment for other medical conditions
- Prescription drugs
- Personal care supplies
- In-home care services

According to Rice et al. (2001) opportunities exist through patient management programs targeted toward early diagnosis, effective use of medications, control of comorbidities, and patient and family support to partially offset these costs while providing quality patient care [15].

The cost of dementia could be significantly reduced. Improvements in diagnosis, treatment and care and support for people with dementia and their carers would help planning, avoidance of future admissions and improved clinical management [16]. A great deal of cost savings come from generic substitution of drugs.

The aim of our study is to trace the access to treatment of Alzheimer's in-home patients, as a result of generic substitution on the base of share distribution of the original and generic products.

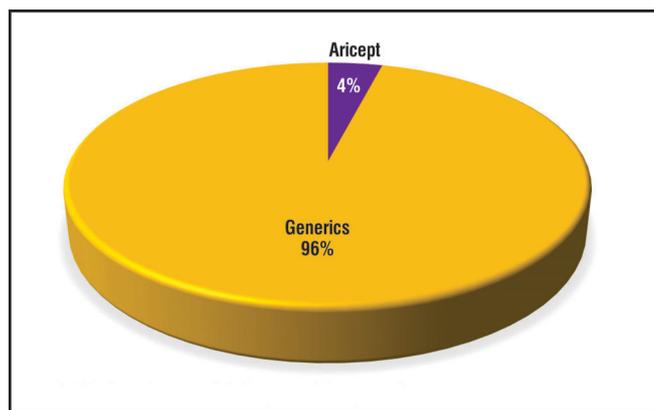
METHODS:

We collected data for the sales of pharmaceutical products (PP's), containing donepezil hydrochloride and memantine hydrochloride from a distributor for the North-east region of Bulgaria (Varna) in the period 2014-2015. An analysis of the percentage share distribution of the original and generic products was conducted. We chose to report sale rates shares because of the different distributors and the frequent updating in the prices of the PP's in the reimbursement list, which limits the accuracy of the analysis.

RESULTS AND DISCUSSION:

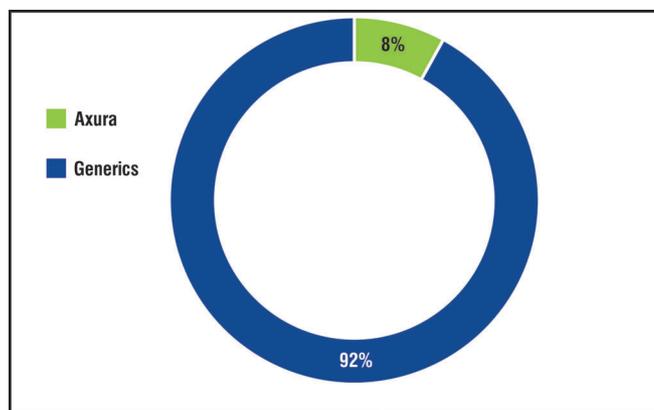
According to our results original product Aricept accounts for only 4%, while the market share for its generics is 96% (**Fig. 1**). In this group the share to be paid from NHIF is 25%, the remaining 75% from the cost is paid by the patients.

Fig. 1. Market shares of Aricept and its generics



The original product Axura occupies 8% market share, the generics- 92% (**Fig. 2**). In this group the share to be paid from NHIF is 50% for generics, while Axura was removed from the Positive reimbursement list.

Fig. 2. Market shares of Axura and its generics



We comment the significant differences of the sale shares in several directions. First, the considerable price differentials between original and generic PP's. Cheaper does not mean lower quality. Secondly, the low reimbursement rate from the NHIF. Thirdly, the removal of the original PP from the Positive reimbursement list.

Treatment tendencies of AD patients are aligned with the Rational Drug Policy, which is a part of the National Health Strategy and are prerequisites for successful access of the patients to medications, reimbursed by NHIF. The final goal is an expanded access to effective treatment and to meet the drug therapy needs of all health insured persons. The efforts are aimed at protecting the interests of patients through creating financial savings through generics and biosimilars and the generated resources to be redirected to expensive, modern and innovative therapies.

It is not possible to develop adequate drug therapy without the base of generics. Generic drugs are required to have the same active ingredient, strength, dosage form, and route of administration as the brand name product.

The stimulation of generics' production and distribution after the expiry of patent protection of the original product is a part of the Drug policy and targets a facilitated access at a lower price for the patients and the society. Availability of generics' drug treatment consists in their cost, which is between 20% and 90% lower in comparison with the original products [17].

Generic drug policy includes a number of measures to encourage physicians and pharmacists in prescribing and dispensing generic drugs as well as for patients receiving their free system for reimbursement. For countries like Bulgaria, where incomes are low, encouraging the use of generics is essential to improve patient access to treatment. Patients' preference may depend on a number of factors, including knowledge about generics and branded drugs, drugs the patient is now using or has used in the past and

financial incentives to use generic drugs [18].

Data from WHO show that the presence of generic competition for five years decreased drug prices by 3 times while in the absence of such policies drug prices remained almost unchanged [19].

We would like to give some recommendations: A consistent and coherent generic drug policy should be introduced. The automatic approval of a price, inclusion in the reimbursement list and a status of substitution for the generic drugs, as soon as they have received marketing authorization, in cases where the declared value is lower than the original product compared, to be enabled. Reimbursement should be performed according to more clear criteria among clinical adequacy and pharmacotherapeutic evaluation of one product to another and thus ensuring no replacement with pseudo-innovative products with the same characteristics and a high price on account of cheaper generic products. Physicians should be encouraged to prescribe generics and share information for successful prescription practices. Provision of information and promotion to patients to demand generic drugs.

CONCLUSION:

Neurotransmitter enhancement therapy with ChEIs and NMDA-receptor antagonists is a treatment approach for patients with mild to moderate and severe AD. Treatments slow cognitive decline, facilitate the care and delay placement of the patients in a nursing home, thus having economic benefits. The reduction of expenses, with the use of generics, would help more patients to receive an optimal treatment and the savings could be redirected for other costly treatments. The implementation of the above recommendations would lead to increased market competition between producers of original products and generics, in terms of production and distribution, and of price regulation.

REFERENCES:

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington 2013 [[CrossRef](#)]
2. National Consensus on dementia diagnosis, treatment and care. *Bulgarian Society of Dementia*. 2015. [[Internet](#)]
3. Larson EB. Evaluation of cognitive impairment and dementia. Editors DeKosky ST, Schmader KE, Eichel AF. *Up to Date*. 2016 Apr, last updated: 2015 Oct 28. [[Internet](#)].
4. Finkel S, Burns A, Cohen G. Behavioral and Psychological symptoms of Dementia /BPSD/: A Clinical and Research Update. Overview. *Int Psychogeriatr* 2000; 12 /Suppl. 1/:13-18.
5. Cummings J. The Neuropsychiatry of Alzheimer's Disease and Related Dementias. *London: Martin Dunitz Ltd*. 2003. 309 p.
6. Ballard C, Corbett A. Management of neuropsychiatric symptoms in people with dementia. *CNS Drugs*. 2010 Sep; 24(9):729-739. [[PubMed](#)]
7. Rosenberg PB, Mielke MM, Han D, Leoutsakos JS, Lyketosos CG, Rabins PV, et al. The association of psychotropic medication use with the cognitive, functional, and neuropsychiatric trajectory of Alzheimer's disease. *Int J Geriatr Psychiatry*. 2012 Dec;27(12):1248-57. [[PubMed](#)]
8. Maust DT, Kim HM, Seyfried LS, Chiang C, Kavanagh J, Schneider LS, et al. Antipsychotics, Other Psychotropics, and the Risk of Death in Patients With Dementia Number Needed to Harm. *JAMA Psychiatry*. 2015 May; 72(5): 438-445. [[PubMed](#)]
9. Poblador-Plou B, Calderón-Larrañaga A, Marta-Moreno J, Hanco-Saavedra Sicras-Mainar A, Soljak M, et al. Comorbidity of dementia: a cross-sectional study of primary care older patients. *BMC Psychiatry*. 2014 Mar; 14:84. [[PubMed](#)]
10. Duthie A, Chew D, Soiza RL. Non-psychiatric comorbidity associated with Alzheimer's disease. *QJM*. 2011 Nov;104(11):913-20. [[PubMed](#)].
11. Lanctot KL, Herrmann N, Yau KK, Khan LR, Liu BA, LouLou MA,

et al. Efficacy and safety of cholinesterase inhibitors in Alzheimer's disease: A meta-analysis. *CMAJ*. 2003 Sep;16; 169(6):557-564.

12. Loveman E, Green C, Kirby J, Takeda A, Picot J, Payne E, et al. The clinical and cost-effectiveness of donepezil, rivastigmine, galantamine and memantine for Alzheimer's disease. *Health Technol Assess*. 2006 Jan; 10(1):iii-iv. ix-xi: 1-160. [[PubMed](#)]

13. Birks JS. Cholinesterase inhibitors for Alzheimer's disease. *Cochrane Database of Systematic Reviews*, 2015. [[CrossRef](#)]

14. Zhu W, Scarmeas N, Torgan R, Albert M, Brandt J, Blacker D, et al. Clinical features associated with costs in early AD. *Neurology*. 2006 Apr; 66(7):1021-1028. [[PubMed](#)]

15. Rice DP, Fillit HM, Max W, Knopman DS, Lloyd JR, Dutttagupta S. Prevalence, costs, and treatment of Alzheimer's disease and related dementia: a managed care perspective. *Am J Manag Care*. 2001 Aug;7(8):809-18. [[PubMed](#)]

16. Living Well With Dementia: a national dementia strategy. Guidance. 3 Feb 2009. [[Internet](#)]

17. Ess SM, Schneeweiss S, Szucs TD. European healthcare policies for controlling drug expenditure. *Pharmacoeconomics*. 2003;21(2):89-103. [[PubMed](#)]

18. ASPE ISSUE BRIEF. Expanding the Use of Generic Drugs. ASPE Staff. December 1, 2010 [[Internet](#)]

19. Fischer MA, Avorn J. Economic consequences of underuse of generic drugs: evidence from Medicaid and implications for prescription drug benefit plans. *Health Serv Res*. 2003 Aug;38(4):1051-63. [[PubMed](#)]

Please cite this article as: Arnaudova M, Todorova A, Tsvetkova A. Financial availability of in-home medical treatment of patients with Alzheimer's disease. *J of IMAB*. 2016 Jul-Sep;22(3):1238-1241.

DOI: <http://dx.doi.org/10.5272/jimab.2016223.1238>

Received: 19/05/2016; Published online: 30/07/2016



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