Generic vs brand originator alendronate: analysis of persistence and compliance in five Local Healthcare Units in the Lombardy Region of Italy

Giorgio L. Colombo¹
Carlo Maurizio Montecucco²

¹ Department of Drug Sciences, University of Pavia, Pavia, Italy
² Division of Rheumatology, IRCCS Policlinico S. Matteo, University of Pavia, Pavia, Italy

Address for correspondence:
Giorgio L. Colombo, MSc
University of Pavia
Department of Drug Sciences
Viale Taramelli 12
27100 Pavia, Italy
Phone: +39 0382 987370
Fax: +39 0382 529095
E-mail: giorgio.colombo@unipv.it

Summary

Introduction. The appearance of off-patent generic drugs in the world pharmaceutical market is a highly interesting fact from the socio-economic point of view. However, the scientific documentation supporting the potential clinical and economic benefits of a growing use of off-patient alendronate in clinical practice seems to be limited in Italy as yet.

Patients and methods. Comparing differences in persistence and compliance between off-patient alendronate and off-patient brand alendronate originator (Fosamax®) in clinical practice. The retrospective analysis was carried out by using the databases of five Local Healthcare Units (ASL - Aziende Sanitarie Locali) in the Lombardy Region, in Italy.

Results. The selected sample of 5 ASLs included 20,711 patients; the average age was 73 years, with no difference between the two groups. After 34 months of observation, the persistence and compliance were no statistically different between off-patient generic alendronate vs off-patient brand alendronate. Data on days in persistence varied between 316 (Brand) vs 362 (Generic). Patients’ compliance varied in average between 0.70 (Brand) and 0.72 for generic group.

Conclusions. Off-patent generic drugs appear to be a therapy option of choice in Italy as well, both for the National Health Service and for citizens. Off-patient generic drugs can bring about an increased efficiency in health systems and increase the percentage of population benefitting from a medical care plan.

KEY WORDS: alendronate; cost analysis; persistence; compliance; generic drug.

Original article

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Introduction

Off-patent generic drugs were introduced in therapy many years ago and now encompass over 50 to 70% of prescriptions in the most advanced European countries from the healthcare point of view, they are still regarded with a sort of skepticism in Italy, both by specialists and general practitioners, and by the public (1, 2). Almost half of drug consumption in Italy and about 37% of expenditure is composed of off-patent drugs, although most prescriptions still focus on branded products, while in other European countries generic (unbranded) drugs are preferred (3). Among off-patent drugs, generic (unbranded) drugs are still a relatively minor market in Italy (about 15% as for quantities and 7% as for expenditure), in comparison with other European countries (4). In Italy, however, there is only a scarce scientific documentation on the health and social costs and on the outcomes in clinical practice after substituting the treatment with generic drugs, inducing a certain mistrust in physicians and patients towards the capacities of off-patient generic (unbranded) drugs (5, 6). However, the presence of a relevant market share of off-patient generic (unbranded) drugs is a necessary condition for price competition to unfold in the branch and for companies to start competing on prices, when patents expire, with strong reductions and simultaneous benefits for the public health system (7). In Italy, Local Healthcare Units (ASL, Aziende Sanitarie Locali) have equipped with tools to control expenditure, based on administrative databases (Banca Dati Assistito - BDA) recording and monitoring consumptions and reimbursements to patients by our National Health Service - NHS (Servizio Sanitario Nazionale, SSN) (8). These sources and their integration are a powerful tool supporting conventional methods used in epidemiological studies.

Patients and methods

The objectives of this study were to compare differences in persistence and compliance between off-patient generic alendronate (ATC - M05BA04) and off-patient brand alendronate (Fosamax®) in real clinical practice. The retrospective analysis was developed by using the administrative databases of five Aziende Sanitarie Locali (ASL, Local Healthcare Unit) (Lecco, Bergamo, Pavia, Milan, and Milano2) in the Lombardy Region, in Italy (9). All patients received at least one delivered prescription of alendronate (generic or brand) between January 2008 and December 2008. The date of first drug delivery is considered as the index date. Patients were observed for a period of 34 months starting from the index date (including index date). We excluded patients who have a delivered prescription of systemic corticosteroid in the two months prior to the index date in order to not consider patients with corticosteroid induced osteoporosis. We also exclude patients that have only one prescription of the studied drugs (sporadic patients) and patients who have received a
prescription of both generic and branded off-label drugs in the observed period. In order to consider only new patients we applied a 12 months wash-out in which patients didn’t have a delivered prescription of the studied drugs. Persistence is calculated as a continuous variable, in terms of number of therapy days for which the therapy is available, without interruption (9). The total number of therapy days was analyzed by means of the Defined Daily Dose (DDD) (10). An interval, called “maximum allowed gaps” (GAP) of 60 days were defined. This interval represents the maximum time intervals between two deliveries, in order to consider therapy interruptions. Compliance to therapy was calculated by means of the Medical Possession Ratio (MPR). MPR was defined as the ratio between the number of packs in the period of persistence multiplied by the number of DDDs per pack, divided by the total days until change of therapy (i.e., persistence) (10).

Statistical analysis

All variables were analysed through descriptive statistics: mean, standard deviation (SD), median, maximum and minimum values for continuous variables, frequency distribution for categorical variables. The patients’ demographic profile for each therapeutic area was expressed in terms of gender (number and percentage), and age classes (number and percentage) at index date. Prescriptions were stratified by therapeutic area, molecule, and number of packs (total number of packs, number of patients, average number of packs per patient, and average number of DDDs per patient). The differences were considered statistically significant when p-value <0.05; the statistical test was the Wilcoxon. In accordance with the Italian privacy law (code concerning the protection of personal data, 30 June 2003, n.196) (11), the analysis was entirely carried out within the single ASL, which supplied aggregate data following the requested outputs.

Results

Characteristics of the patients

The selected sample of 5 ASLs included 20,711 patients; the mean age was 73 years, with no difference between the two groups; the largest group in terms of percentages included patients aged 60 to 80 years. Alendronate generic group represents 7,917 patients (38.2% vs 61.8% of brand group). Figure 1 shows the characteristics of the patients enrolled. No statistically significant differences are found in two groups of studied patients, both as to the considered age groups and as to gender.

The number of days in which the patients were persistent varied in average between 316 and 362 in the two groups. It is interesting to notice (Table 1) that patients have a better persistence with generic drugs (about 46 days), but this difference is not statistically significant. Patients’ compliance varied in average between 0.70 and 0.72 for generic group (Table 2), but also in this case, the difference was not significant. This result means that, in our sample, 70% of patients were adherent to therapy with alendronate, during persistence period.

Discussion

We analyzed two groups of patients treated with alendronate (generic vs brand originator) with the purpose to assess any differences in compliance and persistence. Data on outcomes in real clinical practice in the two groups of patients was superimposable from the statistical point of view, although there were no differences in terms of average age at enrolment (9). Data on adherence and persistence appear to be similar in the two groups (off-patent generic vs off-patent branded alendronate); it is then necessary to add the potential resource saving for patients deriving by the larger use of off-patent generic drugs, including the co-payment of the costs of thera-

Figure 1 - Characteristics of the patients enrolled.
Py by patients. Through the mechanism of the reference price, the price difference between off-patent branded drugs and off-patent generic drugs in Italy is completely charged on patients; in 2012, AIFA data (3) estimated a cost for citizens of about 1 billion euros a year due to the larger use of off-patent branded drugs than off-patent generic drugs. However, this extra expenditure by the citizens due to the higher number of prescriptions of off-patent branded drugs instead of generics may not be a neutral phenomenon in the patients’ clinical history. Studies conducted in the United States show quite clearly that the co-payment of drugs by the patients (called “ticket” in Italy) can contribute to a sub-optimal adherence to pharmacological therapies, up to their interruptions. In their work (12,13) analyzed adherence to therapy as a function of co-payment by patients. According to Ellis (12) if the co-payment share is fixed or equal to zero after two years of treatment, more than 70% of patients remain under treatment with statins, whereas monthly co-payments over 20 USD (about 14.60 EUR) reduce adherence to therapy to less than 30% of the patients originally treated with statins. The same applies to oral blood glucose lowering drugs, with which an increase of about 10 or 20 USD (about 7.30 or 14.60 EUR) in co-payment reduces the quantity of drugs taken daily by patients in a statistically significant way (14). Together with these important observations, we need however to consider some limitations of this study. First of all, the clinical variables considered may not be complete to define the comparison sample: e.g., no consideration was given to familiarity, the patients’ clinical history, and lifestyle elements that may influence the comparison (9). Furthermore, observational studies carried out using administrative databases have some limitations. The collected data directly come from invoicing by pharmacies; they give therefore a real estimate of prescribed and dispensed drugs, but not of the actual use of the drugs by patients. Off-patent generic drugs have a high social value, because they represent the main sustainable access to therapies for the most critical diseases in all socio-economic sectors, in the face of constantly increasing healthcare expenditure. In spite of these limitations, the study shows that the Italian NHS would benefit from relevant incremental resources, which could be destined to reimbursement or use, for example, of innovative therapies, if Italy got in line with the mean levels of generics use in advanced European countries.

Conflicts of interest

The statistical analysis was developed by C. Ripellino and F. Heiman, (CSD Medical Research) and supported by DOC.
Generici, Milan, Italy. The Authors are employees of independent research organizations and maintained independent scientific control over the study, including data analysis and interpretation of final results. The Authors report no conflicts of interest that are directly relevant to the content of this study.

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