Analysis of the Italian generic medicines retail market: recommendations to increase the use of generic medicines

Pieter Dylst[a*], Arnold Vulto[b], Steven Simoens[a]

[a]: KU Leuven Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium

Herestraat 49, O&N 2, P.O. Box 521

3000 Leuven

Belgium

pieter.dylst@pharm.kuleuven.be; steven.simoens@pharm.kuleuven.be

[b]: Hospital Pharmacy, Erasmus University Medical Centre

Gravendijkwal 230

3015 CE Rotterdam

The Netherlands

a.vulto@erasmusmc.nl

***Corresponding author:**
Pieter Dylst
KU Leuven Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium
Herestraat 49, O&N 2, P.O. Box 521
3000 Leuven
Belgium
Pieter.dylst@pharm.kuleuven.be
Tel.: +32 16 37 72 06
Fax: +32 16 32 34 68

ABSTRACT

Italy is amongst the European countries with the lowest uptake of generic medicines. This paper provides a perspective on the Italian generic medicines retail market and how the current policy environment may affect the long-term sustainability. Fast market entrance of generic medicines in Italy is hindered by several factors: the existence of Complementary Protection Certificates in the past, the large market for copies and multiple cases of patent linkage. Prices of generic medicines in Italy are low compared to other European countries. Whereas in the past the Italian government introduced mandatory price cuts on generic medicines to contain pharmaceutical expenditures, pharmaceutical companies are currently forced to paybacks in case of overspending. As these paybacks are calculated per pharmaceutical company on their level of expenditures during last year, these paybacks are disproportionally penalizing small and fast growing companies, to which most generic companies belong to. The Italian government has already implemented different policies to increase the use of generic medicines. However, these policies seem to be insufficient to effectively increase the prescribing, dispensing or asking for generic medicines in Italy. The current market environment surrounding generic medicines in Italy (i.e. low prices, low volumes) threatens the long-term sustainability of the Italian generic medicines market. Recommendations to increase the sustainability of the Italian generic medicines retail market round off this perspective paper.

KEY ISSUES

- The use of generic medicines in Italy is low compared to other European countries.
- This paper aims to provide a perspective on the Italian generic medicines retail market and how the current policy environment may affect the long-term sustainability.
- The current regulatory framework in Italy does not support the development of a generic medicines market.
- Patent linkage has been a long-standing barrier for uptake of generic medicines in Italy and still remains a problem.
- The current payback system for pharmaceutical companies in case of overspending of the pharmaceutical retail budget disproportionally targets generic medicines companies.
- The concentration on the prices of generic medicines in combination with the limited diffusion of generic medicines in Italy may threaten the long-term sustainability.
- There is a lack of effective demand-side policies in Italy targeted at physicians, pharmacists and patients.
- The Italian government must take action to ensure the long-term sustainability of the Italian generic medicines retail market. Recommendations to increase the use of generic medicines are suggested at the end of this perspective paper.

INTRODUCTION

The Italian health care system is a regionally based, tax-funded National Health Service (NHS) which provides uniform and comprehensive health care for the entire population free of charge at point of service [1-3]. Organization of health care is split up into three tiers: the Central government at national level; 21 regional governments at regional level; and 195 local health units ("*Aziende Sanitarie Locali")* and 147 independent hospitals and university hospitals at local level [1;2;4]. The NHS is financed by national and regional taxes (97%) and patient co-payments. The health care budget is annually established at national level by the Budget Law (*"Legge Finanziaria"*), after which the available budget is allocated among the regions, mostly on an age-adjusted capitation basis [1].

A shifting of powers from the federal level to the 21 regions over the last decade has also affected the pharmaceutical sector. The Central government, by means of the Italian Medicines Agency (AIFA), remains in charge of regulating the market and monitoring the consumption of pharmaceuticals. Their responsibilities include marketing authorization, pricing, reimbursement and pharmacovigilance of all pharmaceuticals. Regional health care authorities have to work within the legislative framework as defined by the Central government. Their responsibilities include the promoting of efficiency and quality in their region as well as the controlling of pharmaceutical expenditures. Additional policies related to pharmaceuticals can be implemented autonomously by local health care authorities. Actual health services to the population are provided by local health units and hospitals, under the supervision of the regional health care authorities [1;2;4;5].

Italy is the third largest pharmaceutical market in Europe with a total expenditure of around €24.87bn [6]. In 2012, total health expenditure accounted for 9.2% of the GDP and 15.7% of this expenditure was spent on pharmaceuticals [7]. Pharmaceutical expenditure has been decreasing over the last decade, and this trend has only intensified considerably in response to the worldwide financial and economic crisis, which has hit Italy drastically. For instance, pharmaceutical expenditure in Italy decreased by around 9% over the period 2010-2011, while the European decline was only around 2.6% on average [7;8].

Italy has traditionally been one of the countries with the lowest uptake of generic medicines in Europe, as shown in Figure 1 [7]. In 2013, generic medicines represented 18% of the total pharmaceutical market by volume and 9,52% by value [Personal communication Assogenerici]. Due to the regionalization of

health care, generic market shares by volume vary considerably among the regions, as highlighted in Figure 2 [9]. With the off-patent market in Italy accounting for 65.66% of the total pharmaceutical market and generic medicines only accounting for 26.96% of this market, the potential for generic medicines in Italy is still substantial [9].

[Insert Figure 1 and 2 about here]

The aims of this report are to provide a perspective on the Italian generic medicines retail market. Barriers to the development of a more mature and sustainable generic medicines market are identified. The article rounds off with recommendations which could increase the use of generic medicines in Italy.

METHODOLOGY

LITERATURE REVIEW

A literature review has been carried out to explore the current situation of the Italian generic medicines market in October 2013. The following databases were searched: Pubmed and Embase. The search strategy was developed using combinations of different MeSH terms relevant to the subject. The following search terms were used: Italy; drugs, generic; health policy; cost control; cost containment; drug costs; drug legislation: economics, pharmaceutical; pharmacy administration; reimbursement mechanism; pharmaceutical services and legislation & jurisprudence.

Studies could be published in English, French, Italian or Dutch. Additional articles were found by a review of the reference lists of identified articles and articles known to the authors. The publication date was restricted to January 1997 until October 2013, as there was no definition of generic medicines before this date.

INTERVIEWS

To get a better understanding of the more specific dynamics of the Italian generic medicines market, which cannot be found in the literature, interviews have been with managers of generic medicine companies in Italy. Additionally, their opinion was asked on the most important barriers limiting the use of generic medicines and suggestions which could increase the use of generic medicines.

RESULTS

MARKET ACCESS

The term 'generic medicine' was only introduced into Italian legislation by the 1995 Budget Law, which defined a generic medicine as "*a product no longer protected by a patent or Supplementary Protection Certificate, with the same ingredients, bio-equivalence, form and indication as the originator, marketed under the INN either with or without the manufacturer's name*" [10]. Since 2003, this definition has been extended to all off-patent products, including those marketed before the patent has expired (i.e. copies) [11].

Patent protection was only introduced in 1978, which was rather late compared to other European countries [11]. Complementary Protection Certificates, which allowed for an extension of the original patent protection of up to 18 years to compensate for the time between the filing of the patent and the granting of the marketing authorization, were introduced by the Italian government in 1991 [10]. The introduction of these Complementary Protection Certificates was just before the European Commission enforced the European Supplementary Protection Certificate in 1993, which harmonised patent protection in the European Union. However, a large number of marketed active ingredients in Italy profited from this national Complementary Protection Certificate, as around 400 active ingredients obtained one between 19 October 1991 and 2 January 1993 [10]. As a result, many active ingredients in Italy profited from longer patent protection periods compared to other European countries, as shown in Table 1 [1]. To align with other European countries, Complementary Protection Certificates in Italy are being reduced by 6 months every 2 years since 2004 [12]. At this moment, the problem has almost disappeared, as around 99% of the older Italian Complementary Protection Certificates have already expired.

[Insert table 1 about here]

The late introduction of patent protection, the existence of Complementary Protection Certificates, and more recently also the spread of 'co-marketing' strategies (i.e. the same active ingredient marketed by different companies through different brands under the originator license) have created an important market for copies in Italy (i.e. branded products equivalent to originator medicines launched before parent expiry) [11]. Although copies legally fall within the definition of a generic medicine since 2003, their presence constitutes a barrier to market entrance of true generic medicines. Therefore, it is

important to distinguish between 'copies', 'branded generics' and 'pure generics' (i.e. company branded: international non-proprietary name (INN) + company name) [11].

According to the Pharmaceutical Sector Inquiry in 2009, the average time for a generic medicine to obtain a marketing authorisation in Italy was approximately 6.5 months, which was somewhat below the EU average of 7 months [13;14].

Patent linkage (i.e. the practice of linking the patent status of the originator medicine to decisions on marketing authorizations of generic medicines) has been a long-standing problem in Italy. Following a revision of their industrial-property code in 2010, a generic applicant could only start the registration procedure 1 year before the expiration of any protection on the active substance (i.e. patent and Complementary or Supplementary Protection Certificate). As this was not conform to Directive 2001/83/EC, the European Commission finally issued a formal call on 26 January 2012 for Italy to comply with the EU rules on the marketing authorization of generic medicines [15-17]. Within days, the Italian government changed this code to fully comply with the European Directive [18]. However, the adoption of Italy's newly-passed "*Balduzzi Decree*" in November 2012 introduced another form of patent linkage. Following Article 11 of this Decree, medicines, which are 'equivalent' to reference medicines still protected by patents or Supplementary Protection Certificates, cannot be classified as reimbursable by the Italian NHS [18].

PRICING

Prices for reimbursable medicines ('class A') are determined through negotiation between the manufacturer and AIFA while free pricing is applied for non-reimbursable medicines ('class C', usually OTC products) [14]. If generic medicines wish to be listed in the same patient co-payment class, their prices have to be at least 20% lower than those of their comparable originator products [1;2;14;19]. However, this percentage of 20% is only theoretical, as the actual price of a generic medicine is the result of negotiations between the manufacturer and AIFA and usually ends up around 60% lower on average [20].

Since 1 July 2013, a new, voluntary system for pricing and reimbursement of generic medicines has been introduced in Italy. In this system, the price of the first generic medicine will be automatically determined based on two criteria: the price of the originator medicine at time of application; and the level of pharmaceutical expenditure of that medicine in the three years prior to the expiry of the patent.

Different tiers of pharmaceutical expenditure have been identified, with corresponding discount percentages (see Table 2). A generic medicine will be granted automatic pricing and reimbursement approval if the requested price is below this discounted maximum price. This fast track is available for companies alongside the classic negotiation with AIFA [21].

[Insert Table 2 about here]

In general, prices of medicines in Italy are amongst the lowest in Europe due to pricing and reimbursement regulation to control costs [14]. The price level of generic medicines in Italy is also low compared to other European countries [22;23]. A recent study by IMS, which compared the average price level of generic medicines between France, Germany, Italy, Spain and United Kingdom demonstrated that average prices of generic medicines in Italy were the lowest of the studies countries [24]. Price differences between generic and originator medicines vary substantially, depending on the active substance, ranging from 0% to 65% [22;23].

In order to control the pharmaceutical budget, a budget ceiling for expenditures of both retail (11.35%) and hospital budget (3.5%) as part of total of public health expenditures has been agreed by the Italian government. In case of overspending, the private sector and the regions are asked to cover the deficit, respectively [25] . Initially, prices of medicines were automatically reduced in case of overspending of the retail budget. In 2005, for instance, a 4.4% price cut was agreed on the public prices of all reimbursed medicines, including, for the first time in Italy, generic medicines [26-28]. Since then, generic medicines have been the subject of several mandatory price cuts imposed by authorities (i.e. 12% in 2009, 12.5% in 2010 and 14% in 2011) [12;25] [Personal communication EGA]. More recently, pharmaceutical companies have been faced with paybacks (i.e. companies have to pay back a share of their revenues) to cover the deficit in the retail budget. These paybacks are calculated per pharmaceutical company on their level of expenditures during last year [28]. In this way, small and fast growing companies (e.g. generic companies) are disproportionally targeted. For instance, generic medicines companies' payback in 2010 represented 21.4% of total payback of all pharmaceutical companies, while their market share by value was only around 8.4% [Personal communication EGA].

REFERENCE PRICING

A reference pricing system has been implemented by Italian authorities in September 2001 for reimbursable off-patent pharmaceuticals. The Italian system groups pharmaceuticals with the same

active substance, route of administration, pharmaceutical formulation, unit dosage and number of units in one reference group. Initially, the reference price was calculated as the average price (weighted by volume sales) of all equivalent medicines whose price did not exceed that of the most expensive generic medicine [2;6;25;29;30]. This reference price was modified rapidly and since December 2001, the reference price is calculated as the lowest price among equivalent products available in the regional distribution network [1;11;29]. The difference between the reference price and the actual price of the medicine is then to be paid by the patient, so-called co-payment [1;5;11]. A monthly revision of the reference groups and reference prices is provided for in the legislation [1;6]. In response to the introduction of reference pricing in Italy, originator medicines reduced their prices drastically but only after several months [11;29].

In contrast to other reference pricing systems in Europe, the Italian reference pricing system applies to equivalent medicines with the same unit dosage and number of units. Reimbursement limits may consequently differ significantly between different pack sizes of the same active ingredient, depending on the different competitive pressure and subsequent pricing strategies of manufacturers [29]. In addition, reference prices may also slightly differ between the regions, as reference prices are based on the local supply in the regional distribution network [29].

Re-allocation of demand, a well-known consequence of reference pricing systems based on active substance in the literature [31], has been a problem in the Italian market. As a consequence of tough price competition in the off-patent market, large pharmaceutical companies may redirect their promotional efforts towards more profitable “me-too medicines”, which are not included in the reference pricing system [11;31]. A good example of this was the case of ranitidine, one of the main off-patent products. Originator and co-marketed copies kept their prices high compared with the prices of the generic versions. This resulted in a decrease of their market shares but this eroded volume did not go to the generic versions only. A clear rise in the sales of medicines with the same therapeutic indications still under patent (i.e. proton pump inhibitors) was observed [11;31]. Estimates of the Ministry of Health pointed out that these practices increased overall public pharmaceutical expenditure by 3.1% in 2003 [11]. A recent study confirmed the decrease of the medicine prices after the introduction of the reference pricing system and demonstrated a positive correlation between the number of generic products and the extent of the decrease. However, in contrast to earlier studies, this

study did not observe an increased re-allocation of demand in response to the introduction of the reference pricing system [25].

To increase the awareness of the reference pricing system, a 'Transparency List' has been established to inform health care professionals since 2001. This 'Transparency List', which is published on a monthly basis, reports all reimbursable off-patent drugs and their reference prices, grouped by active ingredients, route of administration, pharmaceutical form, unit dosage and number of units [2;5;29].

PHYSICIANS

Italian physicians generally have a negative attitude towards generic medicines [32;33]. Several tools, such as prescribing guidelines, the 'Transparency List', etc., have been developed at national level to assist physicians to prescribe generic medicines. It is, however, up to the regional authorities to oversee the enforcement of these tools. In addition, no budgetary restrictions are applied to physicians at national level [1].

Many regions and/or local health units have adopted policies to increase the prescribing of cost-effective medicines (i.e. generic medicine or cheapest equivalent), such as monitoring prescribing activities of general practitioners, providing feedback to physicians' prescribing behavior, etc [1;20]. Campania, for instance, has introduced minimum levels of generic prescription in five therapeutic categories which account for most reimbursement costs in that region [Personal communication EGA]. However, due to the decentralization of pharmaceutical policy, generic medicine policies can differ substantially from region to region.

Physicians can freely choose to prescribe by brand name, the name of the generic product or INN [1]. General practitioners are, however, obliged by law to inform patients on the existence of cheaper alternatives in case of a prescription of off-patent medicines [26]. Since 2012, it is even obliged by law to indicate on the prescription that a brand-name drug can be substituted if a generic alternative exists. Physicians opposed heavily this new policy and the Italian Federation of General Practitioners even recommended against the use of prescribing software which supported this policy [32]. Since 2012, physicians are obliged to prescribe by INN for patients treated for the first time for a chronic disease, or being treated for a new episode of a chronic pathology [6] [Personal communication EGA & Assogenerici]. However, physicians retain the liberty to write the name of a brand-name medicine or a generic

medicine with a company name on a prescription, in addition to the INN. In this case, pharmacists are obliged to dispense the lowest priced medicine with this INN, irrespective of the name the physician indicated on the prescription, unless the patient is prepared to pay the difference between the reference price and the price of the prescribed medicine.

PHARMACISTS

In Italy, margins for reimbursable originator medicines and biosimilars differ from the margins for reimbursable generic medicines. For reimbursable originator medicines and biosimilars, the wholesale margin consists of 3% of the pharmacy retail price net while the pharmacy margin is 30.35% of this pharmacy retail price net. For reimbursable generic medicines, the wholesale margin consists of 3% of the pharmacy retail price net while the pharmacy margin can vary from 30.35% to 38.35%, as community pharmacies and wholesalers should divide an extra margin of 8% according to market forces in case of purchase of pure generics. In case of direct purchase from the industry, the margin for generic medicines consists of 41.35% [34;35]. A deadline of 1 January 2015 has been set by the Italian government to reform the remuneration of pharmacists, with the aim of introducing a fee-for-service remuneration [Personal communication Assogenerici

Pharmacists in Italy have been obliged to apply a statutory discount/rebate on pharmacist margins for medicines reimbursed by the NHS since 1997 (see Table 3) [1]. Since 2003, pharmacist margins for generic medicines priced at or below the reference price level are exempted from this statutory discount/rebate [30]. Due to this statutory discount/rebate which pharmacies have to grant the NHS, pharmacies say that their margin system is 'regressive'. Nonetheless, the current remuneration system in Italy offers very little support for the delivery of low-priced medicines [11].

[Insert table 3 about here]

As of 1 January 2005, off-patent medicines (branded or unbranded medicines) included in the 'Transparency List' and with a price correspondent to the reference price are exempted from the discount/rebate for the NHS. This was meant to financially stimulate pharmacists to promote the use of generic and less expensive equivalent medicines [1;11]. Since 2009, any negotiation between pharmacies and generic manufacturers (not originators) is forbidden. Discounts to pharmacies are thus limited to the additional 8% margin which they can earn by purchasing the generic medicines directly from the manufacturer [12;20].

Generic substitution is allowed for pharmacists since 2001. Pharmacists are obliged to propose substitution to the patient in case of a prescription of a medicine priced above the reference price. In case of substitution, pharmacists are allowed to substitute the prescribed medicine with the cheapest available equivalent medicine with patients' agreement. Physicians can also prevent substitution by indicating 'non-substitutable' on the prescription form [11;20;25]. Generic substitution is not practiced that often, as out of the total amount of medicines prescribed as "brand", 35% are dispensed as generic medicines and 65% remain "brand". The most common reason for this is the frequent use of the non-substitutable clause [Personal communication Assogenerici].

PATIENTS

With the introduction of the reference pricing system in 2001, a co-payment was introduced whereby patients have to cover the difference between the price of a more expensive pharmaceutical and the reference price. Prescription fees (named 'tickets'), where patients had to pay a fixed amount per prescription and/or pack, were abolished by the national authorities at the beginning of 2001. As of 2002, many regional authorities have reintroduced these tickets in order to contain their pharmaceutical expenditures within the planned ceiling of 11.35% of total health expenditures [1;5].

Italian patients reportedly have a general preference for originator medicines over generic medicine due to concerns on product quality and safety [37]. Additionally, the term *"generico"* in Italian is associated with 'copy' or 'false', which does not support the confidence in generic medicines. An information campaign on generic medicines for physicians, patients, and pharmacists was launched in May 2001 by the Ministry of Health in collaboration with the consumers' association "*Altroconsumo"*. This campaign aimed to inform all on the technical and economic characteristics of generic medicines and on the functioning of the reference pricing system [1;2]. In 2007, AIFA conducted pro-generic pharmaceutical media campaigns, targeted at patients [1].

DISCUSSION

Uptake of generic medicines in Italy is limited compared to other European countries [7]. The regulatory framework in Italy does not support the development of the generic medicines market: patent linkage; concentration on prices of generic medicines; a payback system which disproportionally targets generic medicines companies; and a lack of effective demand-side policies

targeted at physicians, pharmacists and patients have all contributed to the slow growth of the Italian generic medicines market.

Patent linkage has been a long-standing barrier for uptake of generic medicines in Italy. Only back in 2012, the Italian government had to alter their industrial property code to comply with the EU rules on marketing authorisation of generic medicines, as Directive 2001/83/EC explicitly states that the patent status of originator medicines may not influence decisions on marketing authorisation, pricing and reimbursement of generic medicines [15;38]. However, the introduction of the *"Balduzzi Decree"* in November 2012 once again introduced a form of patent linkage, as medicines cannot be classified as reimbursable if the reference medicine is still protected by patents of Supplementary Protection Certificates [16-18]. Article 11 of this decree is subsequently not only in opposition with the European Directive, it also constitutes a missed opportunity for savings. Without reimbursement, patients are unlikely to choose for the generic medicine instead of the reimbursed originator medicine, with a higher cost for the third-party payer.

To control increasing pharmaceutical expenditures, a budget ceiling on both hospital and retail expenditures has been implemented by the Italian government [25]. In the past, prices of medicines were automatically reduced in case of overspending of the retail budget. As a result, generic medicines faced with several mandatory price cuts over the last years [26-28]. The Italian government focused on the prices of generic medicines , while they were generally amongst the lowest in Europe [22;23]. However, previous research has demonstrated that the price level of generic medicines is associated with their market share [39]. As the business model of the generic medicines industry is based on the supply of high volume at low prices, these low price levels of generic medicines in Italy might endanger the sustainability of the generic medicines industry if they are not accompanied with appropriate measures to increase the volume of generic medicines.

At this moment, pharmaceutical companies are forced to cover the amount of overspending of the retail budget by means of a payback [28]. The current payback, however, disproportionally targets small and fast growing companies (e.g. generic companies). So while already contributing to a decrease of pharmaceutical expenditures, generic medicines companies are additionally penalized for their growth.

While the Italian government concentrated on the price level of generic medicines in the past, the demand-side has been relatively left aside. The importance of demand-side policies to increase the use of generic medicines is, nevertheless, highlighted by the varying generic market shares between the regions, which are each responsible for their own pharmaceutical policy. Despite some initiatives at national level to assist physicians to prescribe generic medicines (e.g. guidelines, Transparency List), most regional governments have failed to implement or enforce effective incentives for physicians to prescribe generic medicines (e.g. prescribing budgets, prescribing targets, etc.) [1]. This lack of effective incentives, in combination with mainly negative perceptions on generic medicines amongst most physicians and the power of originator companies in Italy, make that physicians are not stimulated to prescribe generic medicines. At the level of pharmacists, the Italian government has tried to stimulate the dispensing of generic medicines by allowing generic substitution, applying discount/rebates to make pharmacists' remuneration regressive and exempting less expensive medicines from these discount/rebates [20;25]. However, pharmacists' remuneration still stimulates the dispensing of more expensive medicines and pharmacists have subsequently no incentive to dispense a generic medicine [36]. Also Italian patients have a general preference for originator medicines due to a variety of reasons: negative perceptions on generic medicines related to quality and safety caused by bad press; limited support from physicians; power of the brand; and a bad connotation of the term "*generico*" in Italy. For instance, the amount of copayments paid by patients for choosing an off-patent originator medicine instead of a generic medicine in Italy is almost equal to the entire value of the Italian generic medicines market [40].

In times of current economic and financial hardship, the Italian government is increasingly looking for ways to contain the escalating health care budget. In that respect, both the Italian government and regional authorities in Italy should introduce policies to increase the use of generic medicines, as they offer equally high-quality treatment at lower costs, resulting in substantial savings for authorities, third-party payers and patients [30]. For instance, the expiry of the patent on atorvastatin has saved the Italian NHS an estimated €293 million in the first 12 months since the medicine lost patent protection [Personal Communication EGA]. An increased use of generic medicines will be especially important in Italy, as the current environment of generic medicines (i.e. low prices, low volume) threatens the sustainability of the generic medicines industry, and by this means also future competition in the Italian

medicines market. Therefore, this article will round off with recommendations to increase the use of generic medicines, which have shown to be effective in other European countries.

RECOMMENDATIONS TO INCREASE THE USE OF GENERIC MEDICINES

1. **Abolish patent linkage**

   Patent linkage is a cause for delayed market access to generic medicines and therefore constitutes a missed opportunity for savings. As it is not conform to the European Directive, all forms of patent linkage should be abolished in Italy. Both the Ministry of Health and AIFA should not take into account the patent status of the originator medicine for their decision on marketing authorization, pricing or reimbursement of generic medicines.

2. **Exclude generic companies from payback**

   The current payback system for pharmaceutical companies in Italy penalizes small and fast-growing pharmaceutical companies (i.e. generic medicine companies). Generic medicines companies should be excluded from the payback system as their growth already contributes to a decrease of pharmaceutical expenditure.

3. **Reduce pressure on prices of generic medicines**

   Prices of generic medicines in Italy are already amongst the lowest in Europe. However, the generic medicines industry will only be able to offer low prices if they are ensured a high volume of the market. To maintain the future sustainability of the generic medicines industry in Italy, the government must shift their focus from policies to reduce the prices of generic medicines towards policies to increase the use of generic medicines.

4. **Improve physicians' training and education in drug selection**

   Physicians' training and education on generic medicines should be enhanced, as a negative perception on generic medicines is common among Italian physicians. The education should already start in medical school and continued afterwards by academic detailing programs and continuous medical education events, sponsored independent of pharmaceutical companies.

5. **Stimulate physicians to prescribe generic medicines**

   - *Prescription budgets:* Physicians should be financially stimulated to prescribe generic medicines. Prescription budgets, whereby physicians are financially penalized/rewarded for keeping their budget, might provide a stimulus for physicians to prescribe the most cost-effective (generic) medicines.

- *Prescription quota:* Prescription quotas, linked with or without a financial reward for achieving them, may stimulate physicians to increase their prescribing of generic medicines [41].
- *Enforcement of INN prescribing:* Prescribing by INN, in combination with a pharmacist remuneration system which makes if financially neutral or attractive to dispense cost-effective (generic) medicines, may increase the use of generic medicines. This policy shifts the power of choice of the medicine from the physician to the pharmacists, without affecting their therapeutic freedom. It is, however, important for the regional authorities to oversee the effective enforcement of these policies [41]. In addition, prescriptions by INN should not include the name of a brand-name medicine or a generic medicine with a company name in addition to the INN. This practice might stimulate patients to choose for the prescribed medicine instead of the lowest priced medicine with this INN, as that medicine is recommended by the physician.
- *Implement electronic prescribing*: Electronic prescribing with decision support tools systems have shown to increase the prescribing of cost-effective (generic) medicines. These systems could also easily integrate prescribing guidelines, enforce prescribing by INN, etc [41].
- *Reduce the use of non-substitution clause:* The use of the non-substitution clause to prevent generic substitution should be limited to real medical causes. Therefore, it will be important that physicians state the medical cause on the prescription form and that the regional authorities verify for correctness.

6. Make pharmacists' remuneration independent of prices of medicines

The current pharmacists' remuneration system in Italy financially penalizes pharmacists for dispensing cheaper, generic medicines. Therefore, the Italian government should move away from this price-dependent remuneration towards a fee-for-service payment, where pharmacists are rewarded for their knowledge and their actions with regards to pharmaceutical care (e.g. dispensing fee, counselling patients, first-issue guidance, etc.) [36].

7. Introduce substitution targets for pharmacists

Generic substitution, which is allowed in Italy since 2001, is not practiced that often at this moment. Substitution targets for pharmacists might provide an incentive for pharmacists to

increase their substitution rate, as shown by the experience in France [42]. Eventually, these substitution targets could be linked to their remuneration as an incentive to reach the targets.

8. **Improve perception of generic medicines amongst patients**

   Public information campaigns, initiated by the regulatory authorities, should increase Italian patients' perception, awareness and demand for generic medicines. These campaigns should focus on the concept of generic medicines: their quality, safety, equivalence and cost-saving potential.

9. **Provide financial stimulus for patients to accept generic substitution**

   Italian patients should be stimulated to accept generic substitution, as many still refuse to generic substitution because of preferences for the originator medicine. A delayed reimbursement for patients who refuse generic substitution could be an effective tool to increase the acceptance of generic substitution, as the experience has shown in France [43].

TABLES

Table 1: Expiration of patent protection [1]

Active ingredient	Germany	United Kingdom	Sweden	Italy
Omeprazole	04/1999	03/2002	03/2003	12/2007
Simvastatin	03/2003	04/2003	02/2003	04/2007
Amlodipine	03/2004	03/2004	n.a.	12/2007
Felodipine	12/2000	07/2002	02/2003	12/2008

n.a.: not available

Table 2: New price (before entry of generic medicine) discount levels applied to generic and biosimilar medicines [Personal communication Assogenerici]

Active ingredient	Tier 1	Tier 2	Tier 3	Tier 4	Tier 5	Tier 6	Tier 7	Tier 8
Level of public pharmaceutical expenditure (€ million)*	0 – 19,99	20 – 39,99	40 – 59,99	60 – 79,99	80 – 99,99	100 – 139,99	140 – 179,99	180 and over
Discount percentage, class A drug**	45	47.50	50	55	60	65	70	75
Discount percentage, class H drug***	30	31.70	33.30	36.70	40	43.30	46.70	50

* Pharmaceutical expenditure. For inpatient expenditure, the retail price is taken into consideration. Conversely, for hospital and direct distribution of medicines, the ex-manufacturer price is considered.

** The discount on the price for the products in class A (reimbursable medicines) is calculated on the value of the current retail price of the reference product.

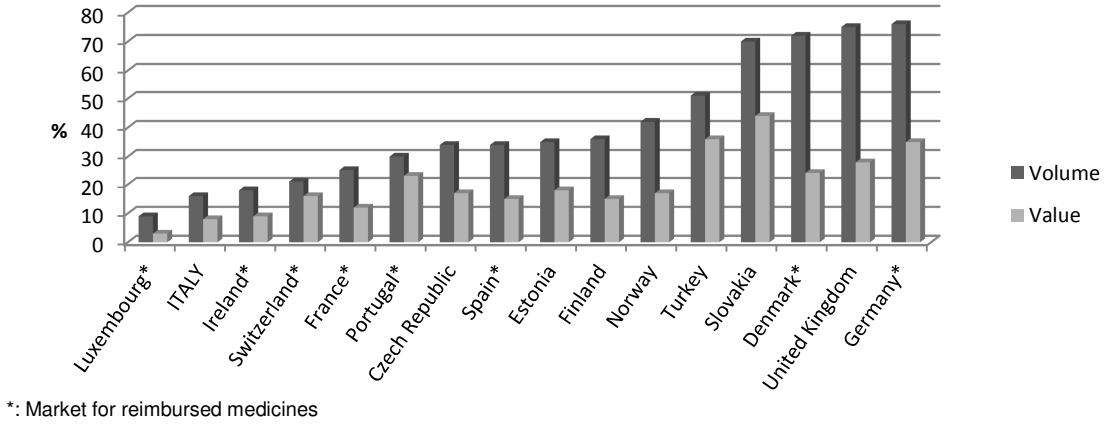
*** The percentage discount on the price for the products in class H (reimbursable, only hospital medicines) is calculated on the value of the current ex-manufacturer price of the reference product.

Table 3: Discounts paid by pharmacies in favour of NHS [1]

	Urban and rural pharmacies, non subsidized		Subsidized rural pharmacies	
Price range	**Turnover NHS > €258,228.45**	**Turnover NHS < €258,228.45**	**Turnover > €387,342.67**	**Turnover < €387,342.67**
< €25.82	3.75%+2.25%	1.5%	3.75%+2.25%	
€25.83 – €51.65	6%+2.25%	2.4%	6%+2.25%	
€51.66 – €103.28	9%+2.25%	3.6%	9%+2.25%	1.5%
€103.29 - €154.94	12.5%+2.25%	5%	12.5%+2.25%	
> €154.94	19%+2.25%	7.6%	19%+2.25%	

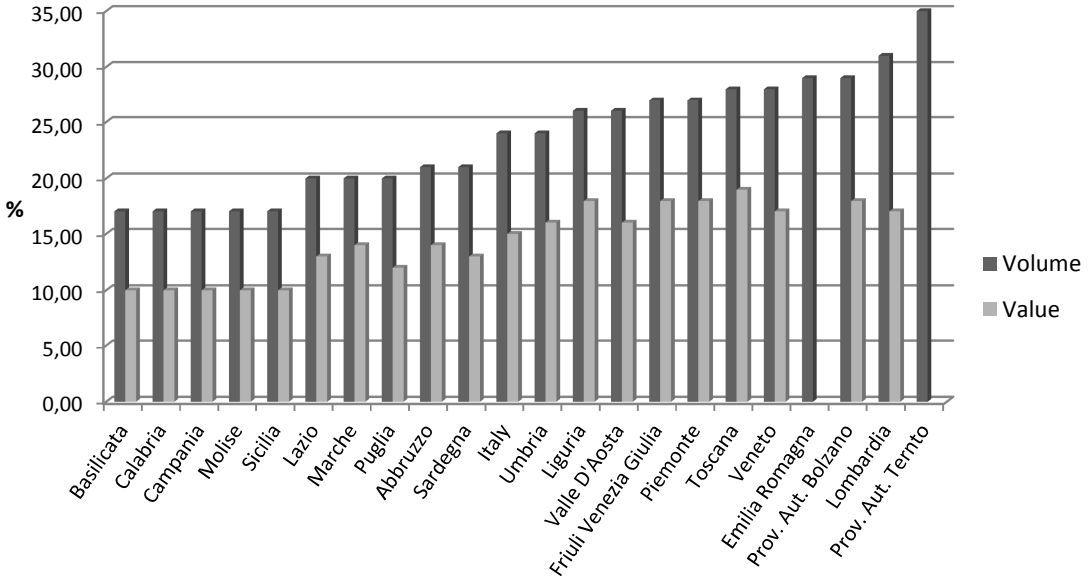
NHS: National Health Service

FIGURES



*: Market for reimbursed medicines

Figure 1: Generic market shares of the total pharmaceutical market in European countries, 2011 (or nearest year)



source: Assogenerici, 2013

Figure 2: Generic market shares of the 100% reimbursed prescription market in 21 Italian regions (January – July 2013)

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