ÖBIG

Pharmaceutical Pricing and Reimbursement Information

ITALY

October 2007

Commissioned by
European Commission, Health and Consumer Protection Directorate-General
and
Austrian Ministry of Health, Family and Youth

Pharmaceutical Pricing and Reimbursement Information

ITALY

Pharma Profile

Final version, October 2007

PPRI Participant(s)
Italian Medicines Agency (AIFA): Pietro Folino Gallo, Simona Montilla

PPRI Pharma Profile - Authors
Italian Medicines Agency (AIFA): Nello Martini, Pietro Folino Gallo, Simona Montilla

PPRI Pharma Profile - Editorial team
WHO Regional Office for Europe: Trine Lyager Thomson (editor-in-chief), Nicole Satterley (copy-editing)
Gesundheit Österreich GmbH / Geschäftsbereich ÖBIG: Sabine Vogler, Christine Leopold (country editors)

Executive Summary

Background

At the end of 2005 Italy had a population of 58.8 Mio. inhabitants and is therefore densely populated (195 inhabitants per km^2). The percentage of elderly people has begun to increase steadily since 1985 and it is now at 20%, due to a decrease in fertility and an increase in life expectancy.

The leading causes of death are diseases of the circulatory system, neoplasms and diseases of the respiratory system. Causes of death have a different distribution by age: road accidents are the first cause in the age group (10-34 years) and breast cancer is the first cause of death in females 35-69 years old, but this is replaced by coronary heart disease and cerebrovascular disease in older age groups.

Italy's economy is the world's 8th largest, with a gross domestic product (GDP) of € 1,417 billion in 2005. The economy's overall structure consists of a small and shrinking primary sector accounting for approximately 3% of total value added, and a large service sector contributing more than two thirds. Large differences in economic development exist across geographical areas.

Government spending is still close to 50% of gross domestic product (GDP) and government debt still exceeds 100% of gross domestic product (GDP). The economy grew at an average annual rate of 1.9% in the period 1995-2000 and 0.9% in the period 2001-2004.

The Italian public sector is organised into four tiers: the central Government, 21 Regions, 103 provinces and more than 8,000 municipalities. Each level has a legislative/representative body (Parliament, Council), an executive body and a professional bureaucracy.

Between 2001 and 2005, the Regions accumulated deficits of nearly € 20 billion (51% in the Regions of Lazio and Campania). Since 1978 Italy has had a tax-funded National Health Service (*Servizio Sanitario Nazionale*, NHS) – based on the Beveridge model – covering the entire population, providing uniform and comprehensive care and delivering the majority of care free of charge. The Italian National Health Service (NHS) is organised into three tiers: the central Government, 21 regional governments (henceforth referred to as "Regions") and the Local Health Units (*Aziende Sanitarie Locali*, ASL) and Independent Hospitals (*Aziende Ospedaliere*, AO) (mainly tertiary level of care).

At the time of writing health care is a matter of shared jurisdiction between the central Government and the Regions. Within each Region, each Local Health Unit (ASL) is responsible for the health of the entire population within that given area.

The Italian National Health Service (NHS) is financed by national and regional taxes (97%) and patient co-payments. The central Government defines the economic and financial programme with a proposal for the next year's national budget and for the next three calendar years. The programme is then discussed, amended and approved by Parliament within December and becomes the annual Budget Law ("*Legge Finanziaria"*), which also establishes the amount to be spent by the Government on health care. This amount is then allocated among the Regions, mostly on an age-adjusted capitation basis. The funds assigned to the Regions are intended to

cover the provision of the so-called Essential Care Levels (LEA) which define a minimum of health care services provided by the State.

Private expenses are a significant share of total health expenditure (THE). Only 15% of Italians have private health insurance; most private outlays are consequently out-of-pocket payments (OPP).

Primary care is provided by general practitioners (GP), on average one per every 1,000 inhabitants. Each Italian resident must enrol with a general practitioner (GP) of her/his choice and can freely change subject to availability. General practitioners (GP) are also responsible for referring patients to the secondary and tertiary care levels and are thus expected to act as gatekeepers to the health system, although they lack both the powers and the incentives to effectively do so. General practitioners (GP) are not National Health Service (NHS) employees, but rather independent contracted doctors, and are paid according to the (unadjusted) number of patients on their lists. There are also some incentives for grouping together, to use computerised systems and to provide epidemiological data.

In-patient care is provided by a network of public and private hospitals. Public hospitals can either be run by Local Health Units (ASL) or set up as Independent Hospitals (AO). Private hospitals can be profit-making or non-profit-making.

Access to hospital care is free of charge and hospitalisation can occur on a planned basis (i.e. elective surgery or other planned care) or through the emergency department (i.e. myocardial infarction, road accidents, etc).

Pharmaceutical system

The main actors in the pharmaceutical system in Italy are: the Italian Medicines Agency (*Agenzia Italiana del Farmaco*, AIFA); the Ministry of Health; the Ministry of Economics; the Regions; and the Italian Institute of Public Health (*Istituto Superiore di Sanità*, ISS).

The Italian Medicines Agency (AIFA) was created on July 2004 by Law No. 326/2003. The Italian Medicines Agency (AIFA) is responsible for all matters regarding the chain of pharmaceuticals for human use, including: market authorisation, pharmacovigilance, and the pricing and reimbursement of all pharmaceuticals. The Italian Medicines Agency (AIFA) operates autonomously under the direction and vigilance of the Ministry of Health and the Ministry of Economics, cooperating with the Regions, and has juristic personality and organisational, patrimonial, financial and administrative authority. The Italian Medicines Agency (AIFA) has a fairly complex structure. The Management Board consists of the President and four members; the Executive Director, and the Board of Auditors, consisting of a president and two members. The basic organisational structure involves five technical-scientific departments, Administration, a Personel and Legal Affairs Department, and the Press and Communication Office.

The main source of funding for public pharmaceutical expenditure (PE) is general taxation, at both national and regional levels. In 2005 the total pharmaceutical expenditure (PE) amounted to € 25,440 Mio. (+78% as compared to 1995 and -0.1% compared to 2004), accounting for approximately 20.3% of the (total) health expenditure (THE) (OECD) that year. The proportion of public pharmaceutical expenditure (PE) as a share of total health expenditure (THE) rose from 8.1% in 1995 to 10.2% in 2005, whereas the share of private pharmaceutical expenditure (PE) decreased from 13.0% to 10.1% (OECD).

Public pharmaceutical expenditure (PE) has grown faster than public health expenditure (HE) and gross domestic product (GDP). From 1995 to 2004 gross domestic product (GDP), public health expenditure (HE) and public pharmaceutical expenditure (PE) increased (current values) by + 51%, +81% and +135%, respectively.

According to data from the Italian National Observatory for Pharmaceutical Use (*Osservatorio Nazionale sull'Impiego dei Medicinali*, OsMed), public pharmaceutical expenditure (PE) accounts for approximately 75% of pharmaceutical expenditure (PE) in the country. Expenditure in general practice prescribing increased from 1995 to 2005 from € 6,087 to € 13,408 Mio. (+120%); the same figures for private expenditure were from € 3,785 Mio. to € 6,046 Mio. (+60%).

In 2005 the pharmaceutical sales at ex-factory level amounted to € 11,642 Mio, which was an increase of 22.4% compared to the year 2000. Prescription-only medicine(s) (POM) represent the higher share of the market and have increased considerably in recent years, along with hospital-only medicine(s) (HOM).

The share of generics in terms of value was at 4.5% of total pharmaceutical sales in 2005. Parallel imports amount to very few in Italy, with only three market authorisations for these obtained in 2002.

There are 229 pharmaceutical companies based in Italy, represented by the manufacturers' association "Farmindustria". In 2005 there were 61 companies specialising in generics and these were members of the "AssoGenerici" association. The industry employed 74,000 people in 2005 and 70,770 in 2004, with a percentage increase of 4.6 % since 2000. There are 246 wholesalers in Italy.

In Italy only registered pharmacists are allowed to dispense pharmaceuticals. Dispensing of any pharmaceutical to the public may take place in community pharmacies (private or public), in some hospital pharmacies, and since July 2006 in devoted areas in large-scale retail outlets (supermarkets). These operate under the supervision of a pharmacist and can sell only a restricted number of over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (*Senza Obbligo di Prescrizione*, SOP). In 2006 there were 17,524 community pharmacies, 16,112 of which were private (92%) and there were fewer than 300 devoted areas in supermarkets in August 2006.

Pricing

In Italy prices of pharmaceuticals reimbursed by the National Health Service (NHS) are regulated at the central level and are the same across the whole country. Prices of non-reimbursed pharmaceuticals are freely established, with some limitations, by pharmaceutical companies. Prices of over-the-counter (OTC) pharmaceuticals may be rebated/discounted by pharmacists, thus the actual price may differ from the official maximum price.

In January 2004, the old system based on the Average European Prices (AEP) was withdrawn and a new price setting system was introduced based on a negotiation procedure applicable to all reimbursable pharmaceuticals, whatever the procedure of market authorisation.

The negotiation procedure with manufacturers is managed by the Italian Medicines Agency (AIFA) Pricing and Reimbursement Unit (PRU), assisted by the Committee for Pricing and Reimbursement (*Comitato Prezzi e Rimborso*, CPR), which is chaired by the Italian Medicines Agency (AIFA) Executive Director and composed of 12 members. Pricing and reimbursement decisions are strictly interlinked because they are the responsibility of the same body and also because both decisions are made within the same procedure. The Italian Medicines Agency (AIFA) Technical Scientific Committee (*Commissione Tecnico-Scientifica*, CTS) expresses an opinion on reimbursement classification. The process of negotiation takes place only after its reimbursement evaluation. In case of absence of an agreement about the price as a result of the negotiation, the reimbursement decision made by the Technical Scientific Committee (CTS) is amended and the pharmaceutical is classified as non-reimbursable and listed in Class C. The negotiation procedure is conducted following criteria based on: product therapeutic value; pharmacovigilance data; price in other European Union (EU) Member States; price of similar products within the same pharmacotherapeutic group; internal market forecasts number of potential patients; and therapeutic innovation. The prices are negotiated at ex-factory level and also define the pharmacy retail prices (PRP). Prices negotiated represent, in the case of hospitals, the maximum sale price for the National Health Service (NHS), but pharmaceutical companies must grant a rebate/discount to hospitals.

The margins of reimbursable pharmaceuticals for pharmaceutical companies, wholesalers and pharmacies are fixed by law at 66.5%, 6.65% and 26.7%, of the net pharmacy retail price (PRP), respectively. The fixed pharmacy mark up for products reimbursed by the National Health Service (NHS) is linear, but it has been made regressive due to a “statutory discount” granted by pharmacists to the National Health Service (NHS), calculated according to a regressive method. Since 1997 the rate of value-added tax (VAT) applied to all pharmaceuticals has been 10%.

In Italy the main price and expenditure control mechanisms used at the time of writing are dictated by the provisions of Law No. 405/2001 which introduced an expenditure ceiling for outpatient pharmaceutical care: it cannot exceed 13% of the overall health expenditure (HE) at national and regional levels and the amount of the overall pharmaceutical expenditure (PE), including pharmaceutical in-patient expenditure, cannot exceed 16% of the total health expenditure (THE). When the ceiling is exceeded, corrective measures are applied, including cuts in the positive list of reimbursable pharmaceuticals (National Pharmaceutical Formulary (*Prontuario Farmaceutico Nazionale*, PFN)) and a reduction in the producers’ earning margin on the price of pharmaceuticals.

Reimbursement

The Italian reimbursement system covers all relevant diseases across the whole country and provides universal pharmaceutical coverage to the whole population (Italian citizens and legal residents).

The system groups pharmaceuticals into two main reimbursement categories according to a combination of relevance in terms of effectiveness and cost: Class A (fully reimbursed) and Class C (not reimbursed).

Reimbursable pharmaceuticals are included in a positive list, named the National Pharmaceutical Formulary (PFN), and are administered at the central level by the Italian Medicines Agency (AIFA). The positive list for reimbursement is updated annually, or every six months if public pharmaceutical expenditure (PE) exceeds the 13% ceiling.

A reference price system was introduced in 2001: the National Health Service (NHS) reimburses the lowest price among the prices of off-patent pharmaceuticals with equal composition of active ingredients, and with the same pharmaceutical form, the same method of administration, the same number of units and the same unit dosage.

The reimbursement system in Italy has two main types of out-of-pocket payments (OPP) by patients: prescription fees (named “ticket”) – a fixed amount per prescription and/or per pack (at regional level and only in some Regions); or a co-payment for pharmaceuticals (at regional and national levels) in the form of a payment of the difference between the price of a more expensive pharmaceutical and a cheaper product containing the same active substance (co-payment under the reference price system).

Specific types of exemption from co-payment are applied for particular categories of people, including chronically ill patients, people with rare diseases, disabled people and pregnant women. Some Regions use criteria for exemption based on income and/or age.

Reimbursement in the in-patient sector does not differ from that in the out-patient sector. Some pharmaceuticals are classified as hospital-only medicine(s) (HOM), requiring specialist supervision, and are grouped in Class H (sub-class of Class A). These pharmaceuticals and others employed for in-patient care are fully reimbursed and the criteria for reimbursement in the hospital sector are equal to those of the out-patient sector. The main "payer" of pharmaceuticals in hospitals is the National Health Service (NHS), via the Regions.

The most relevant change in the Italian National Pharmaceutical Formulary (PFN) occurred in 2003. The aims of the reform were: definition of a sustainable price; elimination of major differences in price among analogous products; and realignment of pharmaceutical prices. The reform also put forward a methodology for setting the reference price (cut-off methodology). Pharmaceuticals have been first clustered into so-called homogeneous classes (i.e. groups of interchangeable pharmaceuticals), and within each homogeneous class a reimbursement level (cut-off) was then identified; accordingly, pharmaceutical companies were asked to adjust their price. The reimbursement price set for the whole cluster then becomes the reference price for the class. In 2005 the National Pharmaceutical Formulary (PFN) was updated again, but only with minor changes and a few cuts.

Rational use of pharmaceuticals

At national level there are no pharmaceutical budgets or prescribing budgets applied to doctors. There is no sanction system applied to general practitioners (GP). At local level, many Regions and/or Local Health Unit (ASL) monitor the prescribing activities of general practitioners (GP) in terms of expenditure, giving them a feedback in order to control and contain the public pharmaceutical expenditure (PE) within the expenditure ceiling set out in Law No. 405/2001.

The Italian Medicines Agency (AIFA) publishes Notes of Limitations (named “AIFA Notes”) to be applied in prescribing pharmaceuticals in order to increase the appropriateness of the use

of classes of pharmaceuticals proven to be effective for the treatment of specific diseases and those associated with frequent severe adverse events. These pharmaceuticals – included in the category “Class A with Notes”- are fully reimbursed by the National Health Service (NHS) for specific diseases only: if the pharmaceutical is prescribed for a disease not included in the list of Class A with AIFA Notes it will be not reimbursed.

All advertising for pharmaceuticals in Italy is subject to the requirements of the Community Medicine Code (Legislative Decree No. 219/2006). The Ministry of Health and the Italian Medicines Agency (AIFA) are respectively the competent institutions in charge of authorising, monitoring and controlling industry activities in advertising to the general public and advertising to health care professionals. Advertising of pharmaceuticals on the Internet is not allowed for over-the-counter (OTC) pharmaceuticals and prescription-only medicine(s) (POM).

Use of health economic analysis for regulatory purposes is limited in Italy. At the time of writing, health economic analyses are mainly commissioned by pharmaceutical companies and are addressed to the regulator, in order to support the pricing and reimbursement process; they are also used to influence doctors when prescribing pharmaceuticals. The inclusion of pharmacoeconomics information in the pricing and reimbursement dossier is not mandatory. At regional and local levels, health economic analyses are also developed to use decisions about the selection of better cost-effective options for specific disease management contexts. However, the frequency and the real impact of these analyses remain restricted. No legal national source of health economic analysis is currently available.

The generics market in Italy has been underdeveloped for a long time. Generics were, in fact, introduced for the first time in 1996, but the main policy measures to promote the generic pharmaceuticals market were launched first in 2000, comprising the reference pricing (RP) scheme, under which patients pay part of the cost of high-priced products; the pharmacists’ right of substitution; and a promotional and informational campaign to patients. In 2005 the share of generics was 2.5% of the total pharmaceutical market in terms of value and 4.5% in terms of volume. The consumption of the total off-patent market was 24.1% of total defined daily dose (DDD) and the correspondent expenditure was 13.1% of the net public expenditure in 2005. Furthermore, the net expenditure for unbranded generics was 3.0% in 2005.

Current challenges and future developments

The main challenge that the pharmaceutical system currently faces is the implementation of a central database named “*Tracciabilità del Farmaco*” (Traceability of Medicines), collecting and recording information about each pharmaceutical marketed in Italy. The “Traceability of Medicines” offers the opportunity to track each single pack throughout the process from the manufacturer to the individual patient, in order to gain information about the individual pharmaceutical product. It offers the possibility to gain epidemiological information on the use of pharmaceuticals both from specific hospitals and the local region, as well as their impact on health; to analyse prescribing and appropriateness of use through the availability of high-quality data.

Furthermore, in 2007 the Italian Medicines Agency (AIFA) is implementing a structural revision of the pharmaceutical pricing method and monitoring and control of public pharmaceutical expenditure (PE). The new system, not yet launched, will be based on the following principle: the expenditure ceiling will be based at national level and regional level (corresponding to a fixed

amount of the total health expenditure (THE)). In the period 2007-2009 pharmaceutical expenditure (PE) is forecast to increase by 12.8% (approximately 4% per year), compared to the total health expenditure (THE) of the year 2006. A ceiling expenditure will be defined for each active ingredient and for each manufacturer, with incentive mechanisms for innovative products; in the case of exceeding of the expenditure ceiling, the manufacturers should refund the National Health Service (NHS) through a pay-back mechanism.

Table of contents

List of tables

List of figures

List of abbreviations

ADF	Associazione Distributori Farmaceutici / Association of Pharmaceutical Distributors
AEP	Average European Price
AIC	Autorizzazione all'Immissione in Commercio / Market authorisation number
AIFA	Agenzia Italiana del Farmaco / Italian Medicines Agency
AO	Aziende Ospedaliere / Independent Hospitals
ASL	Aziende Sanitarie Locali / Local Health Units
ATC	Anatomic Therapeutic Chemical Classification
CCP	Certificato Complementare di Protezione / Complementary Protection Certificate
CIPE	Comitato Interministeriale Programmazione Economica / Interministerial Committee for Economic Planning
CPR	Commissione Prezzi e Rimborso / Committee for Pricing and Reimbursement
CRS	Commissione Ricerca e Sviluppo / Committee for Research and Development
CTS	Commissione Tecnico Scientifica / Technical Scientific Committee
CUF	Commissione Unica del Farmaco / National Medicine Evaluation Board
DDD	Defined Daily Dose
DRG	Diagnosis-Related Groups
EMEA	European Medicines Agency
EMU	Economic and Monetary Union
EU	European Union
FAD	Formazione a Distanza / E-learning programmes
GCP	Good Clinical Practice
GDP	Gross Domestic Product
GGE	General Government Expenditure
GP	General Practitioner
G.U.	Gazzetta Ufficiale della Repubblica Italiana / Official Journal of the Italian Republic
HE	Health Expenditure
HOM	Hospital-Only Medicine(s)
ICD	(WHO) International Classification of Diseases
INN	International Non-proprietary Name
ISS	Istituto Superiore di Sanità / Italian Institute of Public Health

ISTAT	Istituto Nazionale di Statistica / Italian National Institute for Statistics
LEA	Livelli essenziali di assistenza / Essential levels of care
Mio.	Million
NHS	National Health Service
NUTS	Nomenclature des unités territoriales statistiques / Nomenclature of Territorial Units for Statistics
OECD	Organisation for Economic Co-operation and Development
OPP	Out-of-Pocket Payment
OsMed	Osservatorio Nazionale sull'Impiego dei Medicinali / Italian National Observatory for Pharmaceutical Use
OTC	Over-The-Counter (pharmaceuticals)
PE	Pharmaceutical Expenditure
PFN	Prontuario Farmaceutico Nazionale / National Pharmaceutical Formulary
PHT	Prontuario della Distribuzione Diretta / Direct Distribution Formulary
PNLG	Piano Nazionale Linee Guida / National Guidelines Programme
POM	Prescription-Only Medicine(s)
PPP	Pharmacy Purchasing Price
PPPa	Purchasing Power Parity
PPRI	Pharmaceutical Pricing and Reimbursement Information project
PRP	Pharmacy Retail Price
PRU	Pricing and Reimbursement Unit of the Italian Medicines Agency (AIFA)
PTOA	Prontuario Terapeutico Ospedaliero Aziendale / Hospital Pharmaceutical Formulary
PTOR	Prontuario Terapeutico Ospedaliero Regionale / Regional Hospital Pharmaceutical Formulary
QALY	Quality-Adjusted Life Year
RP	Reference Pricing
S.O.	Supplemento Ordinario della G.U. / Ordinary Supplement of the Official Journal (G.U.)
SMR	Standardised Mortality Rate
SOP	Senza Obbligo di Prescrizione / Non-prescription pharmaceuticals with advertising prohibition
SPC	Supplementary Protection Certificate
THE	Total Health Expenditure
TPE	Total Pharmaceutical Expenditure

UH	University Hospital(s)
VAT	Value-Added Tax
WHO	World Health Organization

Introduction

The Pharmaceutical Pricing and Reimbursement Information (PPRI) project is a 31 month-project (2005-2007) commissioned by the Health and Consumer Protection Directorate-General (DG SANCO) of the European Commission (EC) and co-funded by the Austrian Federal Ministry of Health, Family and Youth (*Bundesministerium für Gesundheit, Familie und Jugend*, BMGFJ). The project was coordinated by the main partner Gesundheit Österreich GmbH / Geschäftsbereich ÖBIG (GÖG/ÖBIG) and the associated partner World Health Organization (WHO) Regional Office for Europe. The PPRI project has established a network of 46 participating institutions (competent authorities and other relevant organisations) in the field of pharmaceuticals.

The PPRI project seeks to increase transparency and knowledge and facilitate the exchange of experience in the field of pharmaceuticals by

- establishing and maintaining a network of relevant institutions in the field of pharmaceuticals in the enlarged European Union (EU), in order to facilitate a regular exchange of information and allow a process of learning from each other,
- producing country reports on pharmaceutical pricing and reimbursement systems, the "PPRI Pharma Profiles",
- developing indicators for the comparison of pharmaceutical pricing and reimbursement information,
- providing a comparative analysis on pharmaceutical pricing and reimbursement in the European Union (EU) and,

disseminating the outcomes of the project.

The PPRI Pharma Profiles are country-specific reports that provide detailed descriptions of the countries pharmaceutical systems and policies. The profiles are written by PPRI participants (country experts from competent authorities, Medicines Agencies, Social Insurance Institutions, research institutes) and edited by experts of the PPRI project coordination.

This Pharma Profile is one of the many PPRI Pharma Profiles, which all are available on the PPRI web site at http://ppri.oebig.at. The information and data provided in the PPRI Pharma Profiles refer, in general, to the year 2006.

In order to improve readability and allow for comparisons between countries, the structure of the Pharma profiles follows a template, which was developed by the project coordination team and the PPRI participants. The template is based on a large needs assessment of both national and international stakeholders. In addition to the template a glossary was developed to facilitate the writing process and the readability. The 70-page PPRI Pharma Profile Template and the PPRI Glossary are available at the PPRI web site.

1 Background

1.1 Demography

At the end of 2005 Italy had a population of 58.8 Mio. inhabitants. The country is densely populated (195 inhabitants per km^2, on average); population density is low in inland mountainous areas (with the lowest level of 37 inhabitants per km^2), while it reaches over 8,500 in Naples municipality.

The percentage of elderly people has begun to increase steadily since 1985 and it is now at 20%. A total of 2.5 Mio. people over 65 years live alone and most of them (85%) are women. This ageing trend is sustained by two factors: a decrease in fertility and an increase in life expectancy. Fertility decreased from 2.69 children per woman in 1964 to a minimum of 1.19 in 1995, producing the halving of the newborn cohort from 1 Mio. during the mid-1960s to 550,000. In recent years a slight (but rising) increase took the fertility level up to an estimated 1.34 in 2004. Life expectancy has also seen had a substantial increase, starting after the end of the Second World War, life expectancy at birth increased by 16.7 years (+25%) for females and 14.4 years (+23%) for males. The improvement has been particularly relevant in older ages: life expectancy at 65 years increased by 8.1 years (+62%) in females and 6.5 years (+68%) in males.

Table 1.1: Italy – Demographic indicators 1995, 2000-2005

Variable	1995	2000	2001	2002	2003	2004	2005
Total population in Mio.	56.8	57.0	57.0	57.3	57.9	58.5	58.8
Population density per km^2	188.6	188.0	189.1	190.2	192.1	194.0	195.0
Population aged 0-14 (as a % of total)	14.6	14.3	14.2	14.2	14.1	14.1	14.1
Population aged 15-64 (as a % of total)	68.5	67.3	67.1	66.8	66.6	66.4	66.2
Population aged > 64 (as a % of total)	16.9	18.4	18.7	19.0	19.2	19.5	19.7
Life expectancy at birth (in years)							
Life expectancy at birth, females	81.3	82.5	82.8	83.0	82.8	83.7	83.4
Life expectancy at birth, males	74.9	76.6	77.0	77.1	77.2	77.8	77.8
Life expectancy at 65, females	19.6	20.4	20.7	20.8	20.6	n.a..	21.2
Life expectancy at 65, males	15.8	16.5	16.9	16.9	16.8	n.a..	17.4
Disability-free life expectancy at 65, females	14.2[(a)]	15.2	n.a.	n.a.	n.a.	n.a.	16.1
Disability-free life expectancy at 65, males	12.7[(a)]	13.7	n.a.	n.a.	n.a.	n.a.	14.9

[(a)] 1994, n.a. = not available

Source: Italian National Institute for Statistics (ISTAT) – Database Health for All, Italian version 2007

The leading causes of death are diseases of the circulatory system (International Classification of Diseases (ICD) ICD9 390-459), neoplasms (ICD9 140-239) and diseases of the respiratory system (ICD9 460-519).

Recent trends (1990-2002) show important reductions in the standardised mortality rate (SMR) per 10,000 for cardiovascular causes (–30% for women and –27% for men) and lower reductions for cancer (–10% for women and –12% for men). In the period 1990-2002, the standardised mortality rate (SMR) for cardiovascular diseases decreased from 51.3 to 37.6 in males and from 36.0 to 25.2 in females. In the same period the standardised mortality rate (SMR) for cancer decreased from 37.2 to 32.6 in males and from 18.9 to 17.0 in females.

Causes of death have a different distribution by age: road accidents are the first cause in the age group (10-34 years) and breast cancer is the first cause of death in females 35-69 years old, but this is replaced by coronary heart disease and cerebrovascular disease in older age groups. In males road accidents are replaced in older age by lung cancer, liver diseases, coronary heart disease and cerebrovascular diseases.

1.2 Economic background

Italy's economy is the world's 8th largest, with a gross domestic product (GDP) of € 1,417 billion in 2005. The economy's overall structure consists of a small and shrinking primary sector accounting for approximately 3% of total value added, and a large service sector contributing more than two thirds.[1]

Large differences in economic development exist across geographical areas, with per-capita gross domestic product (GDP) in southern Italy below 70% of the national average.[2]

Government spending is close to 50% of gross domestic product (GDP) and government debt still exceeds 100% of gross domestic product (GDP). Net borrowing has breached the 3% threshold set by the Economic and Monetary Union (EMU) Growth and Stability Pact. Public policy is thus dominated by the need to constrain expenditure and deficits, including in sectors such as health care, where government spending is already fairly low by international standards.

Since the late 1990s, gross domestic product (GDP) growth, unemployment and inflation rates have been systematically worse than the averages for the countries belonging to the European Union (EU) before May 2004 (EU15) / the Eurozone. In real terms, the economy grew at an average annual rate of 1.9% in the period 1995-2000 and 0.9% in the period 2001-2004.[3]

[1] OECD Factbook 2006: Economic, Environmental and Social Statistics (2003 data), http://stats.oecd.org/WBOS/ViewHTML.aspx?QueryName=187&QueryType=View&Lang=en, accessed 2 October 2006.
[2] Eurostat general and regional statistics (2003 data), http:\\epp.eurostat.ec.europa.eu, accessed 2 October 2006.
[3] http:\\www.economist.com/countries/Italy, accessed 2 October 2006.

Table 1.2: Italy – Macroeconomic indicators 1995, 2000-2005

Variable	1995	2000	2001	2002	2003	2004	2005
GDP in €, Mio.	947,339	1,191,057	1,248,648	1,295,226	1,335,354	1,388,870	1,417,241
GDP / capita[1] in €	16,695	20,827	21,773	22,536	23,232	24,132	n.a.
GDP / capita in PPPa, US$	n.a.	25,759	26,586	27,320	27,537	28,352	n.a.
Annual economic growth rate in % 1995-2000	n.a.	1.9%	n.a.	n.a.	n.a.	n.a.	n.a.
GGE, Mio. €	497,487	550,032	599,587	613,734	644,603	663,443	n.a.
GGE as a % of GDP	52.5%	46.2%	48.0%	47.4%	48.3%	47.8%	n.a.
Exchange rate (Italian Lire per €), annual rate	n.a.	n.a.	1,936.27	1,936.27	1,936.27	1,936.27	1,936.27

GDP = gross domestic product, GGE = general government expenditure, PPPa = purchasing power parity, n.a. = not available

Source: OECD Health Data 2006 and OECD Factbook 2006: Economic, Environmental and Social Statistics

1.3 Political context

The Italian public sector is organised into four levels: the central Government, 21 Regions, 103 provinces (including the two Autonomous Provinces of Trento and Bolzano) and more than 8,000 municipalities. Each level has a legislative/representative body (Parliament, Council), an executive body and a professional bureaucracy.

The 1948 Constitution introduced as part of its fundamental principles an initial course of action aimed at developing larger local autonomies (the "Regions"), which were established in 1970 and have received significant powers since 1992.

Between 2001 and 2005 the Regions accumulated deficits of nearly € 20 billion, of which 51% belongs to the two Regions of Lazio and Campania.[4]

1.4 Health care system

This section provides an overview of the organisation of the Italian health care system as well as outlining the main actors, their roles and their decision-making powers within the health care system.

[4] Ministry of Economics – Annual Report on the national economic condition 2005 [*Ministero dell'Economia e delle Finanze. 2006. Relazione Generale sulla Situazione Economica del Paese 2005. Roma*]

1.4.1 Organisation

Since 1978[5] Italy has had a National Health Service (NHS) based on the Beveridge model. The Italian National Health Service (NHS) covers the entire population, provides uniform and comprehensive care, is tax-funded and delivers most care free of charge at the point of service.

Services provided by the National Health Service (NHS) include preventive services (such as food and water control, vaccination and screening) health care (primary care and hospital care) and rehabilitation.

Figure 1.1: Italy – Organisation of the Italian National Health Service (NHS) in Regions and Local Health Units (ASL)

Source: Istituto di ricerca sulla popolazione e le politiche sociali – Consiglio Nazionale delle Ricerche (CNR)

[5] Law no. 833/1978 Institution of the National Health Service [*Legge 23 dicembre1978, n. 883 "Istituzione del servizio sanitario nazionale". G.U. 28 dicembre 1978, S.O. n. 360*]

The Italian National Health Service (NHS) is organised into three levels:

- **The central Government:**

  Following a 2001 amendment to the Constitution,[6] health care is currently a matter of shared jurisdiction between the central Government and the Regions. The central Government has the exclusive power to set out a framework of basic principles, including the "Essential levels of care" (LEA)[7] which must be guaranteed in the same way to every citizen throughout the country.
- **21 regional authorities ("Regions"):**

  Every Region has the power to legislate within the framework established by the central Government and has exclusive responsibility for the organisation of health care services within its jurisdiction.
- **195 Local Health Units (ASL), and 147 Independent Hospitals (AO) and University Hospitals (UH), mainly at the tertiary care level:**

  Within each Region, each Local Health Unit (ASL) is responsible for the health of the entire population within the given area. To carry out such responsibility, a Local Health Unit (ASL) can provide services directly or reimburse the Independent Hospitals (AO) and University Hospitals (UH) and accredited private providers for care delivered to its residents. Accreditation is subject to specific requirements and ensures that private providers are eligible for National Health Service (NHS) reimbursement. Non-accredited private providers, on the other hand, must charge their own patients or the latter's voluntary health insurance policies, if applicable.

1.4.2 Funding

The Italian National Health Service (NHS) is financed by general taxation (97%) at both national and regional levels, as well as by patient co-payments. In June each year the central Government defines a proposal for the next calendar year's budget and a planning schedule for that of the next three calendar years. This document is then discussed, amended and approved by Parliament within December and becomes the annual Budget Law ("*Legge Finanziaria"*). The *Legge Finanziaria* establishes the amount to be spent by the Government on health care. This amount is then allocated among the Regions, mostly on an age-adjusted capitation basis.

The funds assigned to the Regions are intended to cover the provision of the Essential levels of care (LEA). The Regions are free to provide further services that are not included in the Essential levels of care (LEA), but must finance them with revenue from their own sources. The presence of the National Health Service (NHS) does not prevent patients from seeking care on a purely private basis. Private expenses are a significant share of total health expenditure (THE). Only 15% of Italians have private health insurance; most private outlays are consequently out-of-pocket payments.

[6] Constitutional Law no. 3/2001 Amendment to the Title V of the Italian Constitution [Legge costituzionale 18 ottobre 2001, No. 3 "Modifiche al titolo V della parte seconda della Costituzione" *G. U.* del 24 ottobre 2001, No. 248

[7] Definition of the Essential levels of care Act [*DPCM del 29 novembre 2001 "Definizione dei Livelli essenziali di assistenza" G.U n.33 - 8 febbraio 2002, S.O. n. 26*]

Health care on average exceeds 80% of regional spending[8] at the time of writing and the regionalisation of health care was expected to act as a "picklock" for the decentralisation of the Italian public sector as a whole. In practice, however, the regionalisation process has been hindered by large interregional differentials in fiscal and administrative capacity and by conflicts between the central and regional governments on matters of jurisdiction and funding.

Table 1.3: Italy – Health expenditure (HE) 1995, 2000-2005

Health expenditure (HE)	1995	2000	2001	2002	2003	2004	2005
THE in €/ Mio.	67,473	94,272	100,475	106,002	109,649	117,194	n.a.
THE as a % of GDP	7.1	7.9	8.0	8.2	8.2	8.4	n.a.
THE per capita in €	1,189	1,648	1,752	1,844	1,908	2,036	n.a.
Public HE as a % of THE	71.9	73.5	75.8	75.4	75.1	76.4	n.a.
Private HE as a % of THE	28.1	26.5	24.2	24.6	24.9	23.6	n.a.

n.a. = not available, HE = health expenditure, THE = total health expenditure, GDP = gross domestic product

Source: OECD HEALTH DATA 2006, June 2006

The funding system varies across Regions, but its general template can be summarised as follows. Local Health Authorities are funded by the Regions, mostly on an adjusted capitation basis. Part of these funds are used for the direct provision of in-patient and out-patient care by the Local Health Unit (ASL), part for the remuneration of general practitioners (GP) and the reimbursement of pharmaceuticals dispensed by retail pharmacies, and part for the reimbursement of care provided to Local Health Unit (ASL) residents by Independent Hospitals (AO) and accredited private providers. These latter reimbursements are based on diagnosis-related groups (DRG) for in-patient care. Moreover, over time all the Regions have tried to limit the incentives for Independent Hospitals (AO) and private providers to increase the volumes of services. The main intervention has been the introduction of automatic mechanisms to cut tariffs when volumes exceed pre-established thresholds for the regional hospital sector as a whole, individual hospitals, and/or specific sets of diagnosis-related groups (DRG).

1.4.3 Access to health care

This section describes the level of access to services provided by the health care system, which is based on the "freedom of choice" principle, i.e. the freedom for every patient to choose the doctor and/or hospital from which they receive care.

1.4.3.1 Out-patient care

Primary care is provided by general practitioners (GP), on average one per 1,000 inhabitants. Each Italian resident must enrol with a general practitioner (GP) of her/his choice and can freely change subject to availability. General practitioners (GP) are also responsible for referring patients to secondary and tertiary levels of care and are thus expected to act as gatekeepers to the

[8] Court of Auditors Deliberation no. 7/2005 [*Corte dei Conti - Sezione delle autonomie (2005). Relazione sulla gestione finanziaria delle Regioni. Esercizi 2003 – 2004. Deliberazione 7/2005. Roma*]

health system, although they lack both the powers and the incentives to do so effectively. General practitioners (GP) are not National Health Service (NHS) employees, but rather independent contracted doctors, and are paid according to the (unadjusted) number of patients on their lists. There are also some incentives for grouping together, to use computerised systems and to provide epidemiological data.

Out-patient specialist care is delivered by public (Local Health Units (ASL), Independent Hospitals (AO) and private providers in hospital out-patient departments, clinics and doctors' practices.

Table 1.4: Italy – Out-patient care 1995, 2000-2005

Variable	1995	2000	2001	2002	2003	2004	2005
Total no. of doctors[1(*)]	221,000	237,000	n.a.	253,000	n.a.	241,000	224,000
No. of doctors[1] per 1,000 inhabitants [(*)]	3.9	4.1	n.a.	4.4	n.a.	4.2	n.a.
Total no. of NHS out-patient doctors (**)	52,844	54,303	54,226	54,764	54,469	54,477	54,481
of which GPs	47,157	47,148	47,027	46,907	47,111	47,061	47,022
of which Paediatricians	5,687	7,155	7,199	7,857	7,358	7,416	7,459
No. of NHS GPs per 1,000 inhabitants [(**)]	0.83	0.83	0.83	0.82	0.82	0.81	0.80
No. of out-patient clinic departments[2] per 100,000 population(**)	7.17	12.54	12.59	12.59	12.56	7.79	7.80

[1] excluding retired and non-practising doctors; [2] also includes laboratories; n.a. = not available, GP = general practitioner, NHS = National Health Service

Sources: (*)OECD HEALTH DATA 2006, June 2006; and (**)Italian National Institute for Statistics (ISTAT)– Database Health for All Italia version 2007

1.4.3.2 In-patient care

In-patient care is provided by a network of public and private hospitals. Public hospitals can be either run by Local Health Units (ASL) or set up as Independent Hospitals (AO). Private hospitals can be profit-making or non-profit-making. The relative weight of private hospitals has showed large cross-regional variations in the past but the number of beds per 1,000 inhabitants is quite evenly weighted at the time of writing (3.6 in the North and 3.5 in the South). Hospitals can also be classified according to other criteria, the most important being the number of beds, the presence of an emergency department, and the presence of tertiary care units.

Access to hospital care is free of charge and can occur on a planned basis (i.e. elective surgery or other planned care) or as a result of an emergency (i.e. myocardial infarction, road accidents, etc). For planned hospitalisations, general practitioners (GP) are expected to act as gatekeepers.

All doctors and other health professionals working in hospitals are National Health Service (NHS) employees and are consequently salaried and granted civil service status. A 1999 reform[9] has linked approximately 20% of a doctor's salary to position and performance. Doctors may work in public hospitals on a full-time or part-time basis, and those working on a part-time basis are allowed to have a private practice.

Table 1.5: Italy – In-patient care 1995, 2000-2005

Variable	1995	2000	2001	2002	2003	2004	2005
No. of in-patient doctors (*)	99,589	96,313	99,707	102,798	104,704	102,989	105,652
No. of in-patient doctors per 1,000 inhabitants (*)	1.75	1.69	1.75	1.79	1.81	1.77	1.80
No. of hospitals (***)	n.a.	1,425	n.a.	1,377	n.a.	1,296	n.a.
No. of acute care beds (**)		232,516	226,756	216,997	204,166	n.a.	n.a.
of which in private sector (%)	n.a.	14	15	16	16	n.a.	n.a.
Acute care beds per 1,000 inhabitants (**)	n.a.	4.1	3.9	3.8	3.5	n.a.	n.a.
Average length of stay in hospital (**)	n.a.	7.7	7.6	7.6	7.7	n.a.	n.a.

n.a. = not available

Sources: (*)Italian National Institute for Statistics (ISTAT) Database Health for All Italia version 2007; (**) OECD HEALTH DATA 2006, June 2006, and (***) Ministero della Salute. Direzione generale del Sistema Informativo. Ufficio di Direzione Statistica: *Attività gestionali ed economiche delle ASL. ed aziende ospedaliere. Annuario statistico del Servizio Sanitario Nazionale. Anno 2004*. Rome, May 2005

[9] Legislative Decree no. 229/1999 [*Decreto legislativo n. 229 del 19 giugno 1999 "Norme per la razionalizzazione del Servizio sanitario nazionale, a norma dell'articolo 1 della legge 30 novembre 1998, n. 419" G.U. n. 165 del 16 luglio 1999 – S.O. n. 132*]

2 Pharmaceutical system

2.1 Organisation

Since July 2004 Italy has had a Medicines Agency (AIFA).[10] The Italian Medicines Agency (AIFA) is responsible for market authorisation, pharmacovigilance, pricing and reimbursement of all pharmaceuticals for human use, along with governance of pharmaceutical expenditure (PE). Veterinary products and medical devices are the responsibility of the Ministry of Health.

2.1.1 Regulatory framework

The section includes a description of the legal framework for the country's pharmaceutical policy, along with the principal authorities and important players within this framework and their role(s).

2.1.1.1 Policy and legislation

A number of laws and ministerial decrees have been produced over the years with the aim of rationalising the sector and containing pharmaceutical expenditure (PE).

The main steps are:

- a threshold to public pharmaceutical expenditure (PE) (13% of public health expenditure (HE))[11] since 2001;
- a reference price for off-patent pharmaceuticals;[12]
- the National Pharmaceutical Formulary (PFN 2003), which introduced the cut-off methodology for defining the reference price (cf. 4.6.1);
- the creation of the Italian Medicines Agency (AIFA) in 2004;[13]
- several price cutting measures (refer to Table 3.9 in 3.6);
- the transposition of the European Union (EU) Community Code in 2006;[14]
- the introduction of a pay-back system as an alternative to price cutting in 2006[15] (refer to Table 3.9 in 3.6).

[10] Law No. 326/2003 [*Legge 24 novembre 2003, No. 326 "Conversione in legge, con modificazioni, del decreto-legge 30settembre 2003, No. 269, recante disposizioni urgenti per favorire lo sviluppo e per la correzione dell'andamento dei conti pubblici" Pubblicata nella G. U. No. 274 del 25 novembre 2003 – S. O. No. 181*]

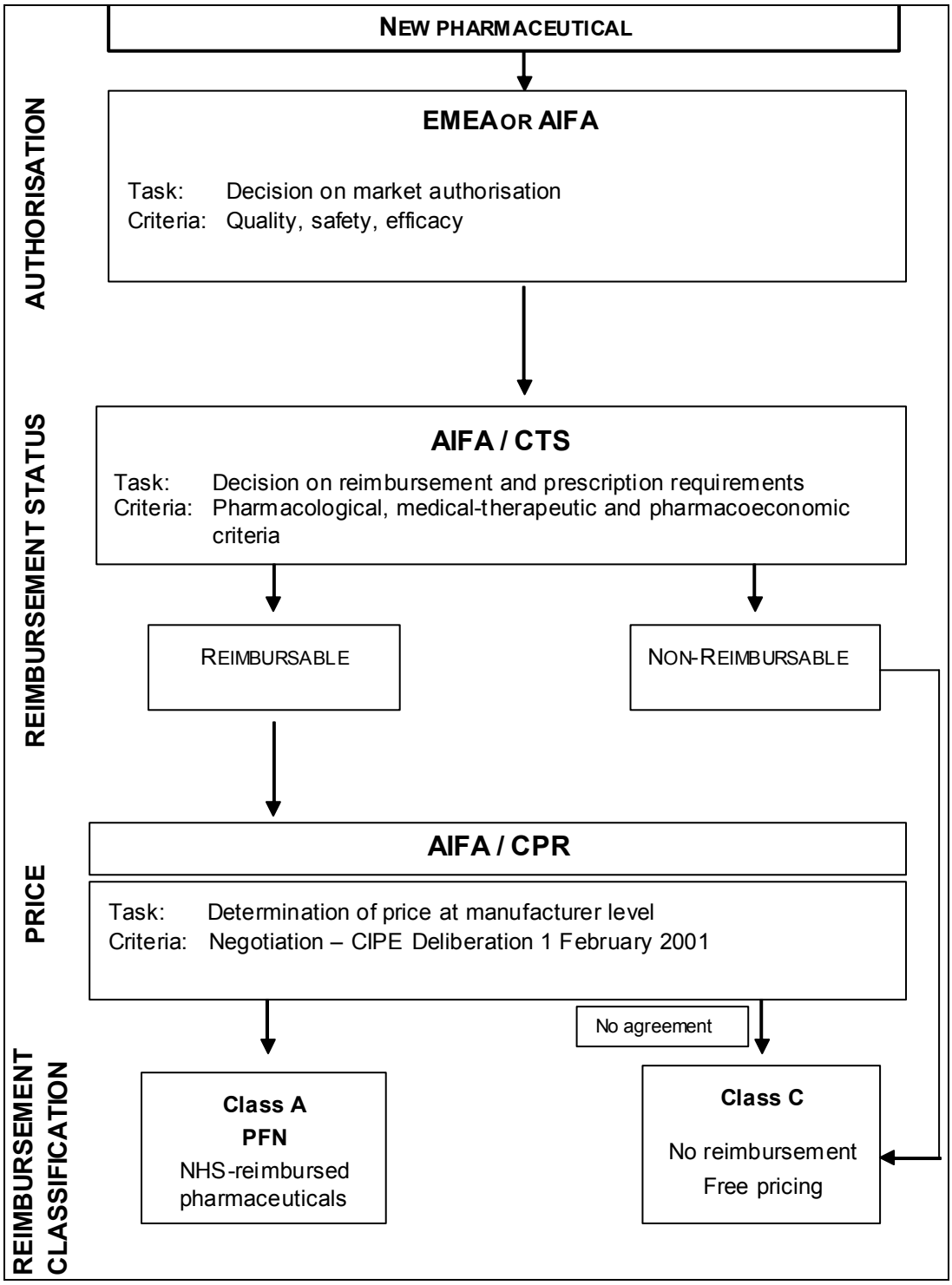
[11] Law No. 405/2001 [*Legge 16 novembre 2001, No. 405 "Conversione in legge, con modificazioni, del decreto-legge 18 settembre 2001, No. 347, recante interventi urgenti in materia di spesa sanitaria" G.U. del 27 novembre 2001, No. 268*]

[12] Law Decree No. 347/2001 [*Decreto Legge 18 settembre 2001, No. 347 "Interventi urgenti in materia di spesa sanitaria." G. U. del 19 settembre 2001, S.O. No. 218]*

[13] Refer to footnote 10

[14] Legislative Decree No. 219/2006, implementing the European Directive 2001/83/EC on the Community Code relating to pharmaceuticals for human use and Directive 2003/94/EC [*Decreto Legislativo No. 219 del 24 aprile 2006 Attuazione della direttiva 2001/83/CE (e successive direttive di modifica) relativa ad un codice comunitario concernente i medicinali per uso umano, nonché della direttiva 2003/94/CE, G.U. del 21 giugno 2006. No. 142 – S.O. No. 153*]

Figure 2.1: Italy – Flowchart of the pharmaceutical system 2006



AIFA = Italian Medicines Agency, CTS = Technical Scientific Committee, CPR = Committee for Pricing and Reimbursement, CIPE = *Comitato Interministeriale Programmazione Economica* (Interministerial Committee for Economic Planning), EMEA = European Medicines Agency, PFN = National Pharmaceutical Formulary
Source: Centre for Studies of AIFA

[15] Law No. 296/2006 - Budget Law 2007 - [*Legge 27 dicembre 2006, No. 296 "Disposizioni per la formazione del bilancio annuale e pluriennale dello Stato" (Legge Finanziaria 2007),* G.U. *del 27 dicembre 2006, No. 299 – S. O. No. 244*]

2.1.1.2 Authorities

The main actors in the pharmaceutical system in Italy are: the Italian Medicines Agency (AIFA); the Ministry of Health and the Ministry of Economics, the Regions and the Italian Institute of Public Health (ISS).

The Ministry of Health and the Ministry of Economics have functions of control over Italian Medicines Agency (AIFA) activities, and cooperation for the elaboration of pharmaceutical policies, regulation and control of expenditure.

The Ministry of Health is also responsible for control of production, marketing and utilisation of narcotic and psychotropic pharmaceuticals, for the authorisation and control of advertising of over-the-counter (OTC) pharmaceuticals, for the updating of the national official pharmacopoeia, for the national price of galenics, for regulation of wholesalers, pharmacies and retail policies and for advertising regulation and monitoring.

The Italian Medicines Agency (AIFA) was created in 2004 by Law No. 326/2003 (refer to footnote 10). The agency has legal personality and organisational, patrimonial, financial and administrative authority. The Italian Medicines Agency (AIFA) operates autonomously under the direction and vigilance of the Ministry of Health and of the Ministry of Economics, cooperating with the regional authorities and other national organisations such as the Italian Institute of Public Health (ISS), research institutes and patients' associations, health professionals, scientific associations, the pharmaceutical industry, and wholesalers' and pharmacists' associations.

The Italian Medicines Agency (AIFA) is responsible for all matters regarding the chain of pharmaceuticals for human use, from market authorisation to pricing and reimbursement. The main objectives and functions of the Agency (AIFA) are as follows:

- administrative and regulatory functions;
- to guarantee access to pharmaceuticals and their safe and appropriate use, and to promote and protect public health;
- to promote the rational use of pharmaceuticals and the dissemination of information on pharmaceuticals in order to improve pharmaceutical culture and knowledge;
- to provide pharmaceutical expenditure (PE) governance in the framework of economic and financial viability and competitiveness of the pharmaceutical industry;
- to encourage and reward innovation and investments in research and development (R&D) in Italy.

The Agency (AIFA) is structured as follows:

- the Management Board, which consists of the President and four members
- the Executive Director
- the Board of Auditors, consisting of a president and two members.

Table 2.1: Italy – Authorities in the regulatory framework of the pharmaceutical system 2006

Name in local language (Italian)	Name in English	Description	Responsibility
Ministero dell'Economia	Ministry of Economics	Regulatory body	• Control of AIFA activities and cooperation in elaboration of pharmaceutical policy and regulations
Ministero della Salute	Ministry of Health	Regulatory body	• Control of AIFA activities and cooperation in elaboration of pharmaceutical policy and regulations • Regulation of wholesale, pharmacy and retail policies • Authorisation and control of OTC pharmaceuticals advertising • Regulation and control of production, marketing and utilisation of narcotic and psychotropic pharmaceuticals • Updating of national official pharmacopoeia and price of galenics
Agenzia Italiana del Farmaco (AIFA)	Italian Medicines Agency	Regulatory body	• Overall pharmaceutical policy • Market authorisation / licensing • Pharmacovigilance • Legal classification of pharmaceuticals • Pricing procedure • Reimbursement • Inspections of pharmaceutical sites • Inspections of clinical trial sites • Information to health professionals and patients • Control of industry advertising to health professionals • Monitoring of pharmaceutical utilisation • Control of PE • Authorisation to export and import pharmaceuticals • Promotion of orphan pharmaceuticals • Register of clinical trials • Funding of independent research
Regioni	Regions		• Applying national rules • Monitoring PE • Organising services provided in their territories and coordinating the action of ASL and checking their work. Through the State–Regions Conference, Regions nominate some members of the main AIFA Committees (CTS, CPR, CRS and Board of Auditors)

Name in local language	Name in English	Description	Responsibility
Istituto Superiore di Sanità (ISS)	Italian Institute of Public Health	Technical-scientific body of the NHS and National Centre for expert knowledge, epidemiology, infectious disease control, environmental pharmaceuticals, toxicology	• Collaboration in the assessment of registration dossiers of biological pharmaceuticals • Quality control of pharmaceuticals • Evaluation of clinical trials • Pharmacovigilance, pharmacoepidemiologic and pharmacoutilisation studies

AIFA = Italian Medicines Agency, ASL = Local Health Unit, CTS = Technical Scientific Committee, CPR = Committee for Pricing and Reimbursement, CRS = *Commissione per la promozione della Ricerca e dello Sviluppo* (Committee for Research and Development), NHS = National Health Service, OTC = over-the-counter (pharmaceuticals), PE = pharmaceutical expenditure

Source: AIFA - Centre for Studies

The basic organisational structure is as follows:

- five technical-scientific departments
- one Administrative, Personnel and Legal Affairs department
- the Press and Communication Office.

The activity of each of the five technical-scientific departments is described here.

- The **Market Authorisations and Pharmacovigilance** department (*Registrazione e Farmacovigilanza*) is responsible for the market authorisation of pharmaceuticals through national or European procedures according to quality, safety and efficacy criteria set out by community legislation. The area is also responsible for continuous monitoring of adverse reactions (pharmacosurveillance activities) and the benefit/risk profiles of pharmaceuticals, through the National Network of Pharmacovigilance, linked to the European database “EUDRAVigilance”.

- The **Manufacturing and Control** department (*Produzione e Controllo*) surveys and inspects pharmaceuticals manufacturing sites in order to guarantee the quality of the manufacturing of pharmaceuticals and raw materials. It verifies the implementation of national and European laws on distribution, import/export and the proper management of rapid alert procedures and emergencies and it also assures the equivalence of the Italian inspection system with those of the other European Union (EU) Member States and with mutual recognition agreements with third countries. The area also manages inspection activities: the establishment of pharmaceutical companies in order to check compliance with quality standards of the products and starting materials, as well as assuring compliance with national and European legislation.

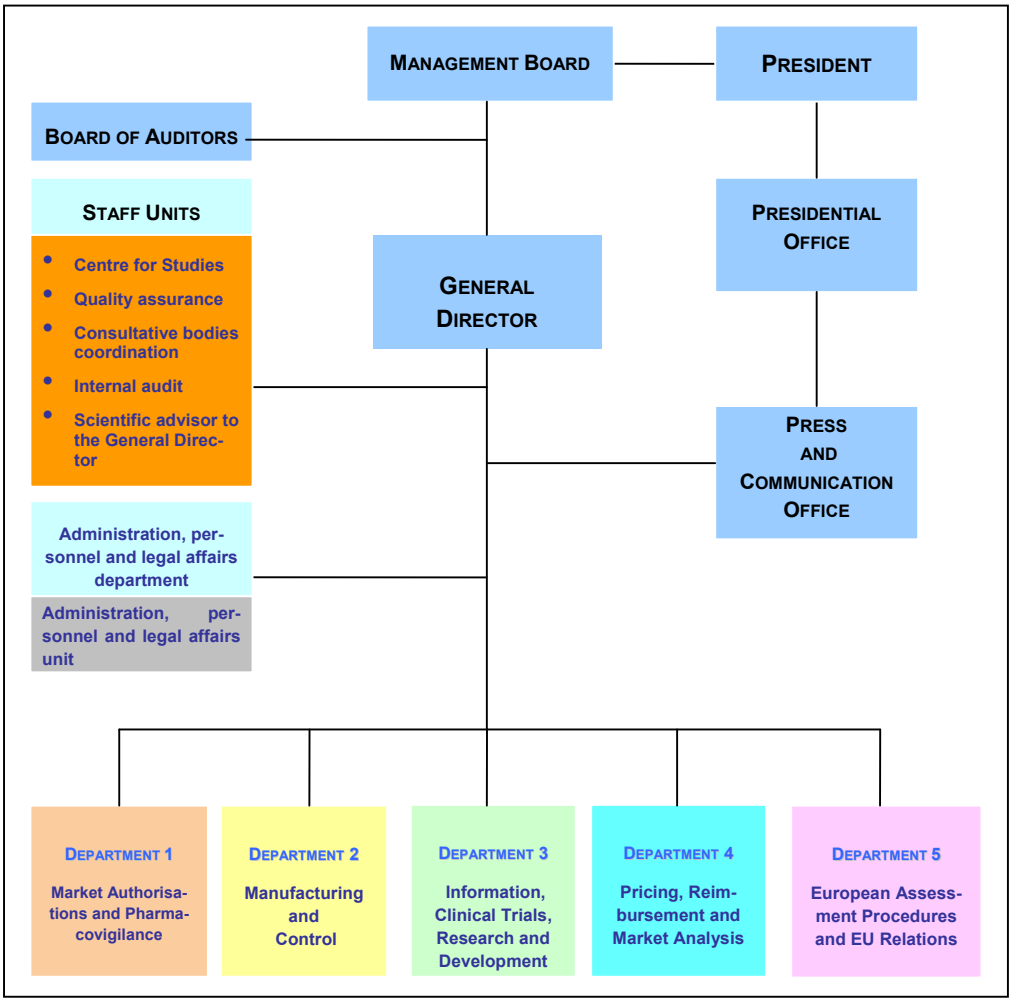
- The **Information, Clinical Trials, Research and Development** department (*Informazione, Sperimentazione, Ricerca*) enforces the national and European provisions on clinical trials and coordinates with the National Observatory on Clinical Trials. It supervises and verifies the implementation of good clinical practice (GCP) in clinical trials, and promotes comparative non-profit-making clinical trials in order to prove the improved

efficacy of new pharmaceuticals, through a specific fund (established for this purpose) consisting of 5% of the expenditure of pharmaceutical companies engaged in promotional activities. Furthermore, the area provides public and independent information in order to promote the appropriate use of pharmaceuticals; in addition the department undertakes updating activities addressed to practitioners, through the press and e-learning programmes (*Formazione a Distanza*, FAD).

- The **Pricing, Reimbursement and Market Analysis** department (*Prezzi, Rimborso e Mercato*) is in charge of preliminary evaluation activities for reimbursement classification and setting the price of reimbursable pharmaceuticals. The department contributes to the control of expenditure by means of a periodic revision of the list of reimbursable pharmaceuticals, and the negotiation of prices of pharmaceuticals. With the help of the Italian National Observatory for Pharmaceutical Use (OsMed), it also monitors national, regional and local pharmaceutical expenditure (PE) and consumption, and provides the relevant data to the Regions on a monthly basis.

- The **European Assessment Procedures and European Union (EU) Relations** department (*Assessment europeo e Rapporti con l'EMEA*) coordinates the participation of the Italian Medicines Agency (AIFA) within the European Committees, within the European Medicines Agency (EMEA) Working Groups and at international level, as well as providing for the assessment of centralised authorisation procedures.

Figure 2.2: Italy – Italian Medicines Agency (AIFA) organisational structure



EU = European Union

Source: AIFA

The Agency is supported by the activities of four technical-scientific consultative committees composed of well-established experts with experience.

- The **Technical Scientific Committee (*CTS*)**, has taken over from the previous National Medicine Evaluation Board (*Commissione Unica del Farmaco*, CUF). It assesses the national and European market authorisation applications, delivers a consultative opinion on them and provides the classification for reimbursement.

- The **Committee for Pricing and Reimbursement (CPR)** is in charge of negotiation activities with pharmaceutical companies for the prices of pharmaceuticals reimbursed by the National Health Service (NHS), according to procedures established by the Intermin-

isterial Committee for Economic Planning (*Comitato Interministeriale Programmazione Economica*, CIPE) deliberation of 1 February 2001.[16]

- The **Italian Medicines Agency (AIFA) Regional Authorities Coordination Centre** (*Centro di Coordinamento AIFA – Regioni*) provides the linkage and cooperation between the Agency (AIFA) and the Regions and conducts a unified process within a decentralised framework. It also analyses national and regional expenditure and utilisation trends.

- The **Committee for Research and Development** (*Commissione per la promozione della Ricerca e dello Sviluppo*, CRS) promotes public and international scientific research in the strategic sectors of health care; fosters private investments within the national territory and promotes the integration of different bodies and clinical research projects at national level.

Recent legislation has transferred several administrative and organisational responsibilities and authorities from the central Government to the Regions, which are responsible for controlling expenditure and promoting efficiency and quality.

Each Region defines a plan in accordance with central government guidelines, and each regional activity must be covered by regional laws as approved by Parliament. These activities comprise:

- assuring a set of essential health care services in accordance with national laws;
- organising services for their specific populations;
- allocating financial resources to the Local Health Units (ASL) within their territories, monitoring Local Health Units' (ASL) health care services and activities and assessing their performance.

Another body dealing with pharmaceuticals is the Italian Institute of Public Health (ISS), which is the technical-scientific body of the National Health Service (NHS) and collaborates with the Italian Medicines Agency (AIFA) for the assessment of the authorisation dossiers associated with new pharmaceuticals and the evaluation of clinical trials, for the quality control of pharmaceuticals and for the realisation of studies on pharmaceuticals matters.

2.1.2 Pharmaceutical market

This section gives an overview of the availability of pharmaceuticals, along with market figures.

[16] CIPE Deliberation No. 3/2001 [*Deliberazione del Comitato Interministeriale per la Programmazione Economica del 1° febbraio 2001, No. 3 "Individuazione dei criteri per la contrattazione del prezzo dei farmaci" G.U. del 28 marzo 2001, No. 73*]

2.1.2.1 Availability of pharmaceuticals

On 1 January 2006 a total of 33,490 pharmaceuticals were authorised in Italy (including different pharmaceutical forms, dosages and pack sizes).

The increase of generics observed in the period 2003-2006 is mainly due to the country's policy of promoting the off-patent market (cf. 5.5).

Prescription-only medicines (POM) represent the greater share of the market and have increased significantly over the years, as have hospital-only medicine(s) (HOM). This was due in part to the expiration of patent protection of a great number of active ingredients and in part to the approval of some new active ingredients, especially in the oncology field.

Parallel imports represent a very small proportion of the market in Italy: there were as few as three market authorisations of this type in 2002.

Table 2.2: Italy – Number of pharmaceuticals 1995, 2000-2006

Pharmaceuticals	1995	2000	2001	2002	2003	2004	2005	2006
Authorised	12.631	21.801	24.059	25.408	26.670	28.660	31.026	33.490
On the market	6.426	10.179	11.641	11.861	12.396	12.261	12.445	13.070
POM	10.188	19.360	19.419	20.770	21.880	23.816	26.075	28.630
Reimbursable	3.882	6.187	7.265	7.943	8.370	8.421	9.057	9.567
Generics (only reimbursable)[1]	2	84	174	318	397	629	875	1,230
Parallel traded	n.appl.	n.appl.	n.appl.	3	3	3	4	13
Hospitals-only	740	1.283	1.430	1.906	2.074	2.062	2.267	2.601

[1]Data as of 1 January
POM = prescription-only medicine(s), n.appl. = not applicable
Source: Federfarma; [1] Assogenerici

2.1.2.2 Market data

The market data presented in Table 2.3 are based on different sources available in Italy to monitor and evaluate utilisation and sales of pharmaceuticals. Data on prescription are provided by the Italian National Observatory for Pharmaceutical Use (OsMed), which publishes an annual National Report on pharmaceutical consumption and expenditure.

The number of prescriptions increased by 21% in the period 2000-2005 and the expenditure for prescriptions increased by 34% in the same period. Similar trends are observed for sales both at ex-factory price level (+22%) and at pharmacy retail price (PRP) level (+24%).

Table 2.3: Italy – Market data 1995, 2000-2005

Pharmaceutical industry	1995	2000	2001	2002	2003	2004	2005
Prescriptions reimbursed by the NHS [1]							
No. of annual prescriptions by volume (Mio. packs)	n.a.	745	856	862	843	890	899
No. of annual prescriptions by value (Mio. €)	6,087	10,041	12,154	12,644	12,354	13,491	13,408
Pharmaceutical sales in Mio. €							
Sales at ex-factory price level [2]	6,437	9,509	10,728	11,042	11,292	11,642	11,642
Sales at wholesale price level	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Sales at PRP level[2]	9,940	15,254	17,167	17,619	18,020	18,721	18,870
Sales at hospitals	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Sales of reimbursable generics (ex-factory price level)[3]	n.a.	n.a.	76	153	201	241	263
Sales of parallel traded pharmaceuticals	n. app.	n. app.	n. app.	n. app.	n. app.	n. app.	n.app.
Exports and import [2] in Mio. €							
Total pharmaceutical exports	3,680	7,662	8,939	10,140	9,741	9,660	11,138
Total pharmaceutical imports	3,884	7,101	8,540	10,280	10,769	11,503	12,444
Difference between export and import	-204	561	399	-140	-1,028	-1,843	-1,306

n.a.= not available, n. app.= not applicable, PRP = pharmacy retail price, NHS = National Health Service

Source: [1]OsMed – National Report 2001-2005; [2]Farmindustria - Indicatori Farmaceutici 2006; [3] Assogenerici

Table 2.4 and 2.5, respectively, present data on the top ten most active ingredients according to National Health Service (NHS) expenditure and National Health Service (NHS) consumption in 2005.

Table 2.4:Italy – Top 10 active ingredients by National Health Service (NHS) expenditure 2005

Anatomic Therapeutic Chemical (ATC) 1st level	Pharmaceutical, by active ingredient	Expenditure Mio. €	%	Rank 2005
A	Omeprazole	383	2.9	1
C	Atorvastatin	351	2.6	2
C	Simvastatin	321	2.4	3
C	Amlodipine	284	2.1	4
A	Esomeprazole	269	2.0	5
R	Salmeterol + Fluticasone	253	1.9	6
J	Amoxicillin + Clavulanic Acid	234	1.7	7
C	Ramipril	189	1.4	8
J	Clarithromycine	179	1.3	9
C	Doxazosin	175	1.3	10
	Total	2,638	19.6	-
	Total NHS PE	13,408	100.0	-

NHS = National Health Service, PE = pharmaceutical expenditure

Source: OsMed– National Report 2005

Table 2.5: Italy – Top 10 active ingredients by National Health Service (NHS) consumption 2005

Anatomic Thera-peutic Chemical (ATC) 1st level	Pharmaceutical, by active ingredient	Volume (defined daily dose DDD))/100(inh die	%	Rank 2005
B	Acetylsalicylic acid	31.8	3.9	1
C	Ramipril	28.7	1.4	2
C	Amlodipine	24.7	3.1	3
C	Glyceryl trinitrate	19.9	2.5	4
C	Enalapril	19.4	2.4	5
C	Atorvastatin	19.4	2.4	6
C	Simvastatin	17.0	2.1	7
C	Furosemide	16.5	2.0	8
H	Levotyroxin sodium	15.2	1.9	9
R	Ferrous Sulphate	12.1	1.5	10

ATC = Anatomic Therapeutic Chemical classification, inh die = inhabitants per day

Source: OsMed– National Report 2005

2.1.2.3 Patents and data protection

In Italy patents of pharmaceuticals may often have a longer duration as compared to other countries. Patent protection of pharmaceuticals was introduced in Italy in 1978 by a judgement of the Constitutional Court.[17]

In 1991 the Complementary Protection Certificate (*Certificato Complementare di Protezione*, CCP) was created, extending the previous 20-year patent coverage for pharmaceuticals by a maximum of a further 18 years, for a total coverage period of 38 years.[18] At European Union (EU) level the Supplementary Protection Certificate (SPC) was developed in 1992, and its maximum duration cannot exceed five years.[19] As the Complementary Protection Certificate (CCP) became effective before the institution of the Supplementary Protection Certificate (SPC), the patent coverage of approximately 80% of active ingredients on the market in Italy had a particularly long duration – longer than coverage of the other European Union (EU) Member States – leading to deep disparities in the matter of complementary patent protection between Italian and European law.

Table 2.6 summarises some differences between patent expiration in Italy and in selected other European Union (EU) Member States.

Table 2.6: Italy – Expiration of patent protection for selected active ingredients in Italy and selected other European countries

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
Source: AIFA - Centre for Studies – Scadenza dei diritti di brevetto sui farmaci – January 2007

Subsequently, in 2002, Law No. 112/2002 was promulgated in order to harmonise the Italian law to the European law, to remove obstacles to the free movement of pharmaceuticals within the European Community (EC) and to promote the development of the generics market. The law

[17] Judgement of the Constitutional Court No. 20 /1978 [*Sentenza della Corte Costituzionale del 20 marzo 1978, No. 20*].

[18] Law No. 349/2001 [*Legge 19 Ottobre 1991, No. 349 "Disposizioni per il rilascio di un Certificato Complementare di Protezione per i medicamenti o i relativi componenti, oggetto di brevetto", G.U. No. 258 del 4 novembre 1991*]

[19] Council Regulation EC No. 1768/1992 "Concerning the Creation of a Supplementary Protection Certificate for Medicinal Products"- EC O.J. 2 july 1992, N.L 182

establishes a gradual reduction of the duration of patent protection, calculated as six months every year since 1 January 2004.[20]

Table 2.7 collects the expiration date of the patent protection for the top ten active ingredients by National Health Service (NHS) health expenditure (HE) (year 2005), and in Figure 2.3 the number of active ingredients per year expiring in Italy in the period 1996-2017 are reported. The highest number of patents expire in the period 2006-2009.

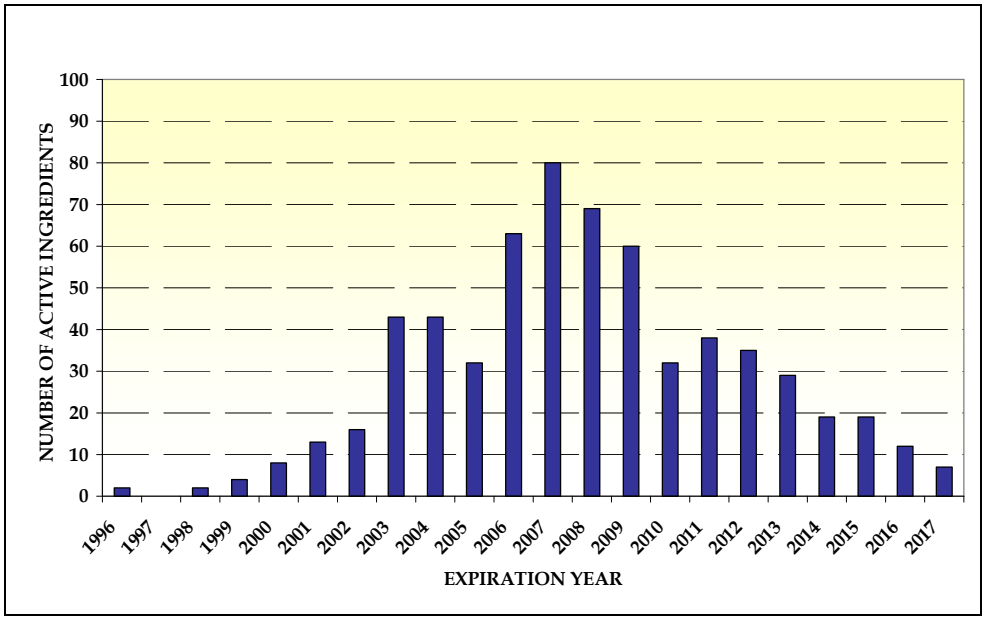
Table 2.7: Expiration of patent protection for the top 10 active ingredients (by National Health Service (NHS) expenditure in 2005)

Rank	Anatomic Therapeutic Chemical	Active ingredient	Expiration of patent protection
1	A02BC01	Omeprazole	2007
2	C10AA05	Atorvastatin	2011
3	C10AA01	Simvastatin	2007
4	C08CA01	Amlopidine	2007
5	A02BC05	Esomeprazole	2009
6	R03AK06	Salmeterol + Fluticasone	2015
7	J01CR02	Amoxicill. + Clavulanic Acid	2006
8	C09AA05	Ramipril	2007
9	J01FA09	Clarithromycine	2007
10	C02CA04	Doxazosin	2007

Source: AIFA - Centre for Studies – Scadenza dei diritti di brevetto sui farmaci – January 2007

[20] Law No. 112/2002 [*Legge "Conversione in legge, con modificazioni, del decreto-legge. 15 aprile 2002, No. 63, recante disposizioni finanziarie e fiscali urgenti in materia di riscossione, razionalizzazione del sistema di formazione del costo dei prodotti farmaceutici, adempimenti ed adeguamenti comunitari, cartolarizzazioni, valorizzazione del patrimonio e finanziamento delle infrastrutture." G.U. No. 139 del 15 giugno 2002*]

Figure 2.3: Italy – Number of active ingredients expiring per year 1996-2017



Source: AIFA - Centre for Studies – Scadenza dei diritti di brevetto sui farmaci – January 2007

2.1.3 Market players

This section describes the key players in the pharmaceutical system, except for the authorities which have been introduced in 2.1.1.2. It gives an overview of the key players in the production, distribution, dispensing, prescription and use of pharmaceuticals and their influence on pharmaceutical policy-making.

2.1.3.1 Industry

There are 229 pharmaceutical companies based in Italy, represented by the manufacturers' association "Farmindustria". There are 61 companies specialising in generics and these are members of the "AssoGenerici" association.

The generics industry is very small in Italy, with low revenue and a low number of employees. Generics companies comprise only a quarter of the total. Of the first 15 generics companies by sales, only two are Italian and they account for only approximately a quarter of the generics market.

The manufacturing industry employed 74,000 people in 2005 and 70,770 in the year 2000, with a percentage increase of 4.6% since the early 2000s.

The three leading companies by market share are Pfizer, Glaxo Smith Kline and Roche (2006 sales, AIDA database Bureau van Dijk).

Table 2.8: Italy – Key data on the pharmaceutical industry 1995-2005[1]

Pharmaceutical industry	1995	2000	2001	2002	2003	2004	2005
Total no. of companies[2]	293	290	294	295	262	241	229
- research-oriented	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
- biotech	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Generic producers*	2	13	16	31	35	43	61
No. of persons employed[3]	66,945	70,770	70,356	72,007	72,088	73,266	74,000
No. of persons employed working in R&D	5,555	5,190	5,242	5,360	5,522	5,798	6,030

[1] as 1 January [2] companies with manufacturing activities in Italy [3] counted per head; n.a.= not available, R&D = research and development

*Source: Farmindustria - Indicatori farmaceutici 2006 & *Assogenerici*

2.1.3.2 Wholesalers

In Italy there are approximately 250 wholesale companies. Table 2.9 provides information on the number of wholesale companies.

Table 2.9: Italy – Key data on pharmaceutical wholesale 1995-2005[1]

Wholesalers	1995	2000	2001	2002	2003	2004	2005
Total no. of wholesale companies	319	283	305	252	314	247	246

[1] as of 1 January

Source: ADF (2006)

2.1.3.3 Pharmaceutical outlets / retailers

In Italy only registered pharmacists are allowed to dispense pharmaceuticals. Dispensing of any pharmaceutical to the public may take place in community pharmacies (private or public), in some hospital pharmacies, and since July 2006 in devoted areas in large-scale retail outlets (supermarkets). Pharmacies are allowed to dispense any pharmaceutical. Supermarkets are only allowed to sell over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP) (i.e. these products (SOP) do not need a prescription but are not allowed to be advertised). The dispensing of pharmaceuticals through Internet pharmacies is not allowed in Italy.

2.1.3.3.1 Pharmacies

Dispensing of reimbursable and prescription-only pharmaceuticals to patients is allowed exclusively through pharmacies and their subsidiaries.

Pharmacies are public or private, the latter representing 92% of the total. Private pharmacies are owned by pharmacists who act as independent contractors under the National Health Ser-

vice (NHS). Public pharmacies continue to be mainly municipal, although the privatisation process has affected many of them.

The number of pharmacies is determined by law and according to demographic and geographical criteria and the minimum distance between retailers (one pharmacy per 4,000 inhabitants in towns with more than 12,500 residents, one pharmacy per 5,000 inhabitants in towns with fewer citizens). Private pharmacists are represented by the Italian Pharmacists Union ("Federfarma"), while the association of public pharmacies is named "Assofarm".

Hospital pharmacies in Italy primarily focus on the distribution of pharmaceuticals and medical devices to patient care units but some hospital pharmacies may also have a section open to the public.

Table 2.10: Italy – Retailers of pharmaceuticals 1995, 2000-2006[1]

Retailers	1995	2000	2001	2002	2003	2004	2005	2006
No. of community pharmacies	16,040	16,454	16,525	16,420	16,659	16,928	17,274	17,404
No. of private pharmacies	n.a.	15,256	15,324	15,397	15,435	15,692	16,018	16,103
No. of public pharmacies	n.a..	1,198	1,201	1,023	1,224	1,236	1,256	1,301
No. of hospital pharmacies for out-patients	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
No. of other POM dispensaries	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.
Total no. of POM dispensaries	16,040	16,454	16,525	16,420	16,659	16,928	17,274	17,404
No. of Internet pharmacies	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.
No. of OTC dispensaries, such as pharmacies	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.	n.app.	< 300 [2]

OTC = over-the-counter (pharmaceuticals), POM = prescription-only medicine(s); POM dispensaries include branch pharmacies, self-dispensing doctors, and other university pharmacies, policlinic pharmacies and hospital pharmacies acting as community pharmacies; n.app. = not applicable, n.a.= not available

[1] as of 1 January, [2] since August 2006

Source: Federfarma

2.1.3.3.2 Other pharmacy outlets

In the Italian pharmaceutical distribution system no other pharmacy outlets are allowed to dispense pharmaceuticals, apart from large-scale retail outlets complying with some specific rules (Law Decree No. 223/2006)[21], which can dispense only over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP). Some products can be also be sold in specific shops *(parafarmacie).*

[21] Law Decree No. 223/2006 [*Decreto Legge 4 luglio 2006, No. 223 "Disposizioni urgenti per il rilancio economico e sociale, per il contenimento e la razionalizzazione della spesa pubblica, nonché interventi in materia di entrate e di contrasto all'evasione fiscale" G.U. del 4 luglio 2006, No. 153*]

2.1.3.3.3 Internet pharmacies

Neither Internet pharmacies/e-commerce, nor sale of pharmaceuticals by e-mail or mail orders are allowed in Italy.

2.1.3.3.4 Dispensing doctors

Doctors are not allowed to dispense pharmaceuticals.

2.1.3.4 Hospitals

Hospitals work with a limited list of products, in compliance with the Hospital Pharmaceutical Formulary (*Prontuario Terapeutico Ospedaliero Aziendale*, PTOA). The Hospital Pharmaceutical Formulary (PTOA) is an updated list of pharmaceuticals which are part of the Regional Hospital Pharmaceutical Formulary (*Prontuario Terapeutico Ospedaliero Regionale*, PTOR) and the National Pharmaceutical Formulary (PFN). The Hospital Pharmaceutical Formulary (PTOA) guarantees the pharmacological therapy necessary in each hospital, and is a versatile and ever-evolving tool, aimed at including innovative and new pharmaceuticals. The criteria for inclusion of new pharmaceuticals are: clinical efficacy, risk/benefit evaluation, cost/efficacy evaluation, pharmacovigilance and patient compliance.

However, in some cases, hospitals can decide to autonomously purchase pharmaceuticals that may not be among those on the national list or may not even have a recognised national authorisation, according to Law No. 648/1996.[22]

Pharmaceutical companies may have a strong interest in the inclusion of new pharmaceuticals on the hospital list as a way of enhancing primary care prescribing of those particular pharmaceuticals. For this reason the prices of some pharmaceuticals during tenders can be very low.

In 2001, Law No. 405/2001 (cf. 3.6 and footnote 11) established that National Health Service (NHS) pharmaceutical expenditure (PE) could not exceed 13% of the total health expenditure (THE) at either national or regional level. The various Regions therefore implemented initiatives for containing expenditure and, in order to keep pharmaceutical expenditure (PE) under the 13% ceiling, direct distribution was expanded through different channels:

- direct distribution by Local Health Units (ASL)
- direct distribution by community pharmacies (*distribuzione per conto)*
- direct distribution of the first cycle of therapy by hospitals.

Regions can provide reimbursable pharmaceuticals for patients that require specialised medical visits on a regular basis, through Local Health Units (ASL). The specific pharmaceuticals affected by this legislation are listed in the Direct Distribution Formulary (*Prontuario della Distribuzione Diretta*, PHT). The aim of the Direct Distribution Formulary (PHT) is to guarantee a

[22] Law No. 648/1996 [*Legge 23 dicembre 1996, No. 648 "Conversione in legge del decreto-legge 21 ottobre 1996, No. 536, recante misure per il contenimento della spesa farmaceutica e la rideterminazione del tetto di spesa per l'anno 1996"* G. U. *del 23 dicembre 1996, No. 300*]

balance in pharmaceuticals distribution, in the overall framework of improved health care and cost-containment.

In addition, another form of direct distribution named "*Distribuzione per conto*" has been implemented in order not only to lower pharmaceutical expenditure (PE) but also to overcome geographic difficulties and allow patients to reach any of the capillary distributed pharmacies, especially patients undergoing treatments that require specialised medical visits on a regular basis. In this modality of distribution the Regions can stipulate agreements with wholesalers and pharmacy associations, for the purchase and the distribution of pharmaceuticals listed in the Direct Distribution Formulary (PHT). Through the Local Health Units (ASL), Regions can acquire Direct Distribution Formulary (PHT) pharmaceuticals at a reduced price; the wholesalers supply the products to the pharmacies, and these are then directly distributed to the patients. As a consequence, pharmacies and wholesalers earn less for pharmaceuticals distribution, constituting a saving for the National Health Service (NHS) compared to the costs of the traditional means of distribution. Expenditure for pharmaceuticals distributed through the *distribuzione per conto* represented 9.5% of the total pharmaceutical expenditure (TPE) in 2006.

In addition to the previous direct distribution methods, another form of direct distribution has been implemented for patients being discharged from hospital or those undergoing specialised out-patient visits. The first cycle of therapy is provided through direct distribution by the hospital. However, this procedure varies according to the Region, which defines the maximum duration of this first cycle and establishes the pharmaceutical categories subject to this type of distribution.

The pharmaceuticals subject to direct distribution are purchased by the National Health Service (NHS) at a discount of either 50% (for pharmaceuticals authorised according to Italian procedure yet not subject to negotiation) or 33.35% (for pharmaceuticals authorised according to European Union (EU) procedures, centralised or mutual recognition). Higher discounts can be obtained through purchase by tender, especially for Local Health Units (ASL) forming a consortium or covering a vast area. The specific discount depends on the pharmaceutical type, on whether or not other generic products are commercially available, and on the potential market for the pharmaceutical.

Nonetheless, in order to calculate the actual savings for the National Health Service (NHS) through purchase by tender (and thus direct distribution) as opposed to distribution through pharmacies, the discount that community pharmacies are legally required to apply to pharmaceuticals purchased by the National Health Service (NHS) must be taken into account (this evaluation is limited to pharmaceutical prices, excluding the costs of managing this system). The discount, which is calculated regressively, is inversely proportional to the price of the pharmaceutical for the public. Given that most of the pharmaceuticals included in the Direct Distribution Formulary (PHT) are those with a high cost and that the purchase price of these pharmaceuticals for the National Health Service (NHS) is in most cases discounted by pharmacies by between 12.5% and 19%, the actual savings through direct distribution (tender purchase price) must be compared with the price discounted as above by National Health Service (NHS)-recognised pharmacies.

2.1.3.5 Doctors

In Italy doctors are completely autonomous in the choice of more appropriate pharmaceuticals for the treatment of their patients (including reimbursable products), both in terms of community care and in-patient care.

There are many associations of doctors at syndicate level and at scientific level, both for general practitioners (GP) and hospital doctors. The associations are able to influence health policies (in general) and pharmaceutical policies (in particular) through their institutional channels.

2.1.3.6 Patients

Patients have a primary role in deciding which pharmaceuticals will be prescribed or dispensed in the case of over-the-counter (OTC) pharmaceuticals and Non-prescription pharmaceuticals with advertising prohibition (SOP), or in the substitution of off-patent pharmaceuticals. Patients may have some influence on the prescribing doctors, e.g. in the case of a parent's role in paediatric prescriptions.

Pharmaceutical prices are the same in every pharmacy for prescription-only medicine(s) (POM). For over-the-counter (OTC) pharmaceuticals the pharmacists are allowed to provide discounts, which are higher than those of supermarkets, thus patient sensitivity to prices is stimulated.

Patients receive information on pharmaceuticals and their prices directly from the practitioner and/or pharmacist and from the publication of prices on the web site of the Italian Medicines Agency (AIFA) and on the web site of the Ministry of Health, directly in pharmacies, from the National Pharmaceutical Formulary (PFN), from the Transparency List in the case of off-patent pharmaceuticals or from the Official Journal of the Italian Republic (*Gazzetta Ufficiale*, G.U.).

2.2 Funding

This section provides an overview on the funding of pharmaceuticals. This includes pharmaceutical expenditure (PE) and the allocation of funds for pharmaceuticals.

2.2.1 Pharmaceutical expenditure

This section contains data on pharmaceutical expenditure (PE) provided by the Organisation for Economic Co-operation and Development (OECD), which will allow international comparisons. Other data used include those provided by the Italian National Observatory for Pharmaceutical Use (OsMed) National Report, which mainly covers public expenditure data (general practice and hospital data since 2006).

According to Organisation for Economic Co-operation and Development (OECD) data in 2005 the total pharmaceutical expenditure (TPE) amounted to 25,440 Mio. €, which is +78% compared to 1995 and –0.1% compared to 2004.

In Italy (total) pharmaceutical expenditure (TPE) accounts for approximately 20% of the total health expenditure (THE), a value lower than Spain but higher than most countries belonging to the European Union (EU) before May 2004 (EU15).

Public pharmaceutical expenditure (PE) has grown faster than public health expenditure (HE) and gross domestic product (GDP). From 1995 to 2004 gross domestic product (GDP), public health expenditure (HE) and public pharmaceutical expenditure (PE) increased (current values) by +51%, +81% and +135%, respectively.

Table 2.11a: Italy – Total pharmaceutical expenditure (TPE) 1995, 2000-2005

Pharmaceutical expenditure (PE)	1995	2000	2001	2002	2003	2004	2005
TPE in Mio. €	14,254	21,129	22,668	23,547	24,291	25,475	25,440
TPE as a % of THE	21.1	21.9	22.1	21.8	21.6	21.1	20.3
TPE per capita[1] in €	251	370	403	422	423	445	439
Public PE as a % of THE	8.1	9.7	12.1	11.6	10.6	10.6	10.2
Private PE as a % of THE	13.0	12.2	10.0	10.3	11.0	10.4	10.1

PE = pharmaceutical expenditure, THE= total health expenditure, TPE = total pharmaceutical expenditure
Source: OECD Health Data 2006

According to Italian National Observatory for Pharmaceutical Use (OsMed) data, expenditure for pharmaceuticals prescribed in general practice increased in the period 1995-2005 from € 6,087 Mio. to € 13,408 Mio. (+120%); in the same period private expenditure increased from € 3,785 Mio. to € 6,046 Mio. (+60%).

Public pharmaceutical expenditure (PE) in general practice accounts for approximately 70% of total pharmaceutical expenditure (TPE) in the country.

Table 2.11b: Italy – Total out-patient pharmaceutical expenditure (PE) 1995, 2000-2005

Pharmaceutical expenditure (PE)	1995	2000	2001	2002	2003	2004	2005
TPE in Mio. € (excluding in-patient exp.)	**9,872**	**15,725**	**17,483**	**18,185**	**19,017**	**19,787**	**19,974**
Public PE in Mio. € (excluding in-patient PE)	6,087	10,041	12,154	12,644	12,354	13,491	13,408
Private PE in Mio. € (including OPP)	3,785	5,684	5,329	5,541	6,483	6,296	6,566
Public PE in % of TPE (excluding in-patient PE)	61.7	63.9	69.5	70.5	65.9	68.2	67.2
Private PE in % of TPE (including OPP)	38.3	36.1	30.5	30.5	34.1	31.8	32.8

OPP = out-of-pocket payment(s), PE = pharmaceutical expenditure, TPE = total pharmaceutical expenditure
Source: OsMed – National Report 2005

2.2.2 Sources of funds

The main funding source for public pharmaceutical expenditure (PE) is general taxation, at national and regional levels.

Approximately 50% of private pharmaceutical expenses comprise payments for non-reimbursed prescription pharmaceuticals (Class C with prescription), while self-medication expenses (over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP)) amount to 35%. The majority of the remaining 15% derives from expenses for pharmaceuticals which are reimbursable but are bought privately and from out-of-pocket payments (OPP). The out-of-pocket payment (OPP) proportion includes fixed fees (only in some Regions) and payments deriving from the reference price system: if patients refuse substitution of a pharmaceutical within the system for generic substitution (refer to 5.5.1) and/or if the doctor prescribes a pharmaceutical with a price higher than the reference price, the difference is paid by patients.

Table 2.12: Italy – Private pharmaceutical expenses 2000-2005

Pharmaceutical expenditure (PE) (Mio. €)	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**
Private expenditure (1)	5,684	5,316	5,204	5,841	5,694	6,051
Expenses for pharmaceuticals reimbursable by the NHS and bought privately	784	703	569	674	619	837
Expenses for non-reimbursed prescription pharmaceutical (Class C with prescription)	n.a.	2,734	2,738	3,100	3,035	3,102
Expenses for self-medication (SOP and OTC)	n.a.	1,879	1,897	2,067	2,040	2,113
OPP (fixed co-payment) (2)	n.a.	13	337	642	602	515
Total Private Expenditure (1)+(2)	n.a.	5,329	5,541	6,483	6,296	6,566

n.a. = not available, NHS = National Health Service, PE = pharmaceutical expenditure, SOP = Non-prescription pharmaceuticals with advertising prohibition, OTC = over-the-counter (pharmaceuticals), OPP = out-of-pocket payment(s)
Source: OsMed – National Report 2001-2005

3 Pricing

This chapter gives an overview of the pricing system by describing the process and the regulations involved in the pricing of pharmaceuticals.

3.1 Organisation

In Italy prices of pharmaceuticals reimbursed by the National Health Service (NHS) are regulated at central level and are the same across the whole country. Prices of non-reimbursed pharmaceuticals are freely established, with some limitations, by pharmaceutical companies. Prices of over-the-counter (OTC) pharmaceuticals may be rebated by pharmacists, thus the actual price may differ (a) from the official maximum price and (b) across the country.

The criteria for setting prices of pharmaceuticals are established by law, in consultation with the Italian Medicines Agency (AIFA), which is also responsible for managing pricing and reimbursement procedures.

Two substantial changes have occurred in recent years within the legal framework and organisation of pricing in Italy:

- a change in the criteria for the setting of prices of pharmaceuticals in 2003
- the establishment of the Italian Medicines Agency (AIFA) in 2004.

The new price setting system introduced in January 2004[23] has significantly modified the criteria used to define the prices of pharmaceuticals reimbursed by the National Health Service (NHS). The main variation is the withdrawal of the old system based on the Average European Prices (AEP) and the utilisation of the negotiation system for all pharmaceuticals, whatever the procedure of market authorisation (cf. 3.2.2).

At the time of writing, the Italian Medicines Agency (AIFA), established in 2004, is in charge of the pricing and reimbursement of every authorised reimbursable pharmaceutical, including each strength and dosage form. The Committee for Pricing and Reimbursement (CPR) supports the Italian Medicines Agency (AIFA) in the procedure for establishing a price through a negotiation procedure with pharmaceutical companies. The Committee for Pricing and Reimbursement (CPR) is chaired by the Executive Director of the Italian Medicines Agency (AIFA) and composed of 12 well-established members with experience in pricing methodology, health economy and pharmacoeconomy. The members are designated by the Minister of Health, the Minister of Economy, the Minister of Industry and by the State-Regions Conference. The members serve a 5-year term and meet on a monthly basis.

The process takes approximately 90 days (Interministerial Committee for Economic Planning (CIPE) Deliberation 1 February 2001, No.3).[24] Table 3.1 summarises the arithmetic mean and the 75th percentile of the number of days necessary to complete the procedure for different ty-

[23] Refer to footnote 10
[24] Refer to footnote 16

pologies of application submitted during the year 2006 (the number of days is calculated from the start of the procedure to the Management Board deliberation).

Table 3.1: Italy – Number of days needed for pricing and reimbursement decisions 2006

	No. of procedures	No. of days	
		Mean	75th percentile
New Chemical Entities	25	131	161
Generics and Copies	270	26	36
New Packs	29	27	23
New Dosage Forms	6	83	79
Therapeutic Indication Extension	5	73	99
Orphan Drugs	6	39	39
Reimbursement Classification Changes	9	60	79

Source: AIFA - Pricing, Reimbursement and Market Analysis Unit

Table 3.2 summarises the differences between the timetable for pricing and reimbursement framework actually used by the Italian Medicines Agency (AIFA) with respect to the timetable of the Ministry of Health before the establishment of the Agency.

Table 3.2: Italy – Pricing and reimbursement timetable before and after 2004

Pricing and reimbursement timetable	Italian Medicines Agency (AIFA) (after 2004)	Pharmaceutical Department at the Ministry of Health (before 2004)
Starting procedure	0	0
CPR	33	60
CTS	60	90
Ministry of Economics		125
State-Regions Conference		155
Signature by the Minister		255
Court of Auditors		265
Management Board	76	n.a.
Publication in the G.U.	90	300
Total no. of days	**90**	**300**

CTS = Technical Scientific Committee, CPR = Committee for Pricing and Reimbursement, G.U. = Official Journal of the Italian Republic, n.a. = not available

Source: AIFA

According to European Community (EC) Directive 89/105/EEC relating to the transparency of measures regulating the pricing of pharmaceuticals for human use and their inclusion in the

scope of national health insurance systems, the Italian Medicines Agency (AIFA) has recently shortened the average length of time taken for the pricing process (cf. 3.2.2) through the implementation of an electronic system of negotiation available online. The manufacturer submits the application and the documents requested online and then can follow up the next phase of the procedure.

Pricing and reimbursement decisions are strongly interlinked, not only because they are the responsibility of the same body but also because both types of decision are made in a single procedure and then accepted by the National Health Service (NHS). The negotiation process takes place after the reimbursement decision expressed by the Technical Scientific Committee (CTS). In the case of absence of an agreement about the price, the reimbursement decision made by the Technical Scientific Committee (CTS) is amended and the pharmaceutical is classified as non-reimbursable and listed in Class C (cf. Figure 2.1 and 4.2.2).

3.2 Pricing policies

Two different methods for setting prices of pharmaceuticals are used:

- a Price Negotiation (for reimbursable pharmaceuticals);
- a Free Price, with some limitations (for non-reimbursable products, including all over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP)[25] and a minority of prescription-only medicine(s) (POM), such as benzodiazepines).

Pricing decisions are made at the manufacturer level, then wholesale and pharmacy prices are calculated by formula (cf. 3.5.1 and 3.5.2).

[25] Non-prescription pharmaceuticals with advertising prohibition (SOP) are a particular subclass of over-the-counter (OTC) pharmaceuticals; these pharmaceuticals do not require a prescription but their advertising is not permitted.

Table 3.3: Italy – Ways of pricing pharmaceuticals

	Manufacturer level	Wholesale level	Pharmacy level
Free pricing	Free pricing for all non-reimbursable products, with definition of a maximum retail price.	Not applied	Not applied
Statutory pricing	Not applied	Statutory wholesale mark up (as a % of net PRP) for reimbursable pharmaceuticals	Statutory wholesale mark up (as a % of net PRP) for reimbursable pharmaceuticals
Price negotiations	Not applied. Prices are negotiated (a manufacturer mark-up is defined only calculation of the PRP)	Not applied	Not applied
Discounts / rebates	Yes, cost-related discounts	Yes, cost related discounts (however limited to the hospital sector).	Yes, regressive discounts by pharmacists related to the National Health Service. Discounts to costumers are allowed.
Public procurement	Mainly relevant for products used in hospitals Not applied in the out-patient sector, except for vaccinations and certain blood products and direct distribution.		
Price-volume agreements	For a limited number of pharmaceuticals. The agreement is negotiated during the pricing procedure.	Not applied	Not applied
Institution in charge of pricing	AIFA		
Legal basis	• CIPE Deliberation No.3/ 2001[26] provides the procedures and criteria for pricing and reimbursement listing • Law Decree No. 390/1995[27], pricing of OTC and SOP pharmaceuticals • Law No. 326/2003 (cf. footnote 10)		

AIFA = Italian Medicines Agency, CIPE = Interministerial Committee for Economic Planning, PRP = Pharmacy Retail Price, NHS = National Health Service, OTC = over-the-counter (pharmaceuticals), SOP = Non-prescription pharmaceuticals with advertising prohibition

Source: AIFA – Centre for Studies

3.2.1 Statutory pricing

At the time of writing no statutory price system is in place in Italy at the manufacturer level.

There are statutory wholesale and pharmacy mark ups (both expressed as a percentage of net pharmacy retail price (PRP)) for reimbursable pharmaceuticals.

[26] CIPE Deliberation No. 3/2001 [*Deliberazione del Comitato Interministeriale per la Programmazione Economica del 1° febbraio 2001, No. 3 "Individuazione dei criteri per la contrattazione del prezzo dei farmaci" G.U. del 28 marzo 2001, No.73] Refer footnote 16*

[27] Law Decree No. 390/1995 [*Decreto Legge 20 settembre 1995, No. 390 "Provvedimenti urgenti in materia di prezzi di specialità medicinali, nonché in materia sanitaria," G.U. 21 settembre 1995, No. 221*]

3.2.2 Negotiations

A negotiation procedure has been introduced since 1998 for setting the price of pharmaceuticals authorised through a European procedure (centralised or mutual recognition) and since January 2004 the same procedure has been employed for establishing prices of all pharmaceuticals reimbursable by the National Health Service (NHS), including products with national authorisation. The procedure used is described in the flowchart shown in Figure 3.1.

The Italian Medicines Agency (AIFA) is responsible for managing the pricing and reimbursement process and is assisted by the Committee for Pricing and Reimbursement (CPR) and the Technical Scientific Committee (CTS) (cf. 2.1.1.2).
The process is characterised by five stages, described here.

1) The manufacturer applies for reimbursement and pricing, submitting a specific request to the Pricing and Reimbursement Unit (PRU) of the Italian Medicines Agency (AIFA). The request must be accompanied by the dossier referred to in Annex 1 of the Interministerial Committee for Economic Planning (CIPE) Deliberation 1 February 2001, No. 3. During this stage the Pricing and Reimbursement Unit (PRU) checks the completeness of the application.

2) The request is communicated to the Technical Scientific Committee (CTS), which expresses an opinion on reimbursement classification (cf. 4.2.2) through an evaluation of the clinical-therapeutic value, declares the start of the procedure and issues the writ for the negotiation process to the Committee for Pricing and Reimbursement (CPR).

3) Before the meeting of the Committee for Pricing and Reimbursement (CPR) a preliminary evaluation is carried out by the Pricing and Reimbursement Unit (PRU). The Committee for Pricing and Reimbursement (CPR) provides an evaluation of the manufacturers' dossiers (requests, reimbursement application) and also considers consumption and expenditure data provided by the Italian National Observatory for Pharmaceutical Use (OsMed), along with the hearing of the market authorisation holder company.

4) The outcome of the negotiation is submitted to the Technical Scientific Committee (CTS) and then to the Italian Medicines Agency (AIFA) Management Board for the final decision and approval.

5) The procedure is concluded by publication in the Official Journal of the Italian Republic (G.U.).

The pricing procedure should be completed within 90 days. It can be stopped once in order to request further information or it can be suspended at the company's request.

The method of determining the price of reimbursable pharmaceuticals is based on an evaluation performed in accordance with criteria set out in the Interministerial Committee for Economic Planning (CIPE) Deliberation No.3/2001:

- the results of a cost-benefit analysis;
- international prices of the pharmaceuticals;

- planned expenditure ceiling;
- expected sales in the country;
- prevalence of the indication and likelihood of pharmaceutical usage by patients;
- financial impact, such as regional investment and employment by the company related to the introduction of the new pharmaceutical;
- the product's efficacy (comparative data among similar therapeutics, degree of innovation, improvements in quality of life, impact on incidence and hospitalisation, and impact on the budget).

The criteria applied to determine the price:

- the product's therapeutic characteristics (therapeutic indications; posology and method of administration; duration of treatment or length of course/therapy cycle/no. of cycle; mechanism of action);
- therapeutic value compared to older products of the same therapeutic group (comparative clinical trials);
- pharmacovigilance data;
- price of the product in other European Union (EU) Member States;
- price of similar products within the same pharmacotherapeutic group;
- internal market forecasts (next three years) and market value of all pharmaceuticals ina given pharmacotherapeutic group;
- number of potential patients (annual basis; disease prevalence);
- savings for National Health Service (NHS) (pharmacoeconomy studies; quality-adjusted life years (QALY); number of hospitalisation days).

During the pricing procedure the manufacturers provide data on:

- information on production cost
- expected sales
- price of the pharmaceutical products in other countries
- the therapeutic value
- cost-effectiveness
- innovativeness grade.

Innovativeness Grade Evaluation

Prices are also negotiated on the basis of therapeutic innovation. The evaluation of the innovativeness grade takes into account:

1. disease seriousness (seriousness of the disease, risk factors);
2. relevance of therapeutic effect;
3. available treatments:
    - product for the treatment of a disease with no adequate therapy;
    - product for the treatment of a disease with available therapy not adequate for a particular subgroup of patients;
    - product with improved efficacy and/or safety profile for the treatment of a disease with an available adequate therapy;
    - product more manageable or with improved compliance for the treatment of a disease with an available adequate therapy;

- treatment of equal efficacy compared to the available treatments.

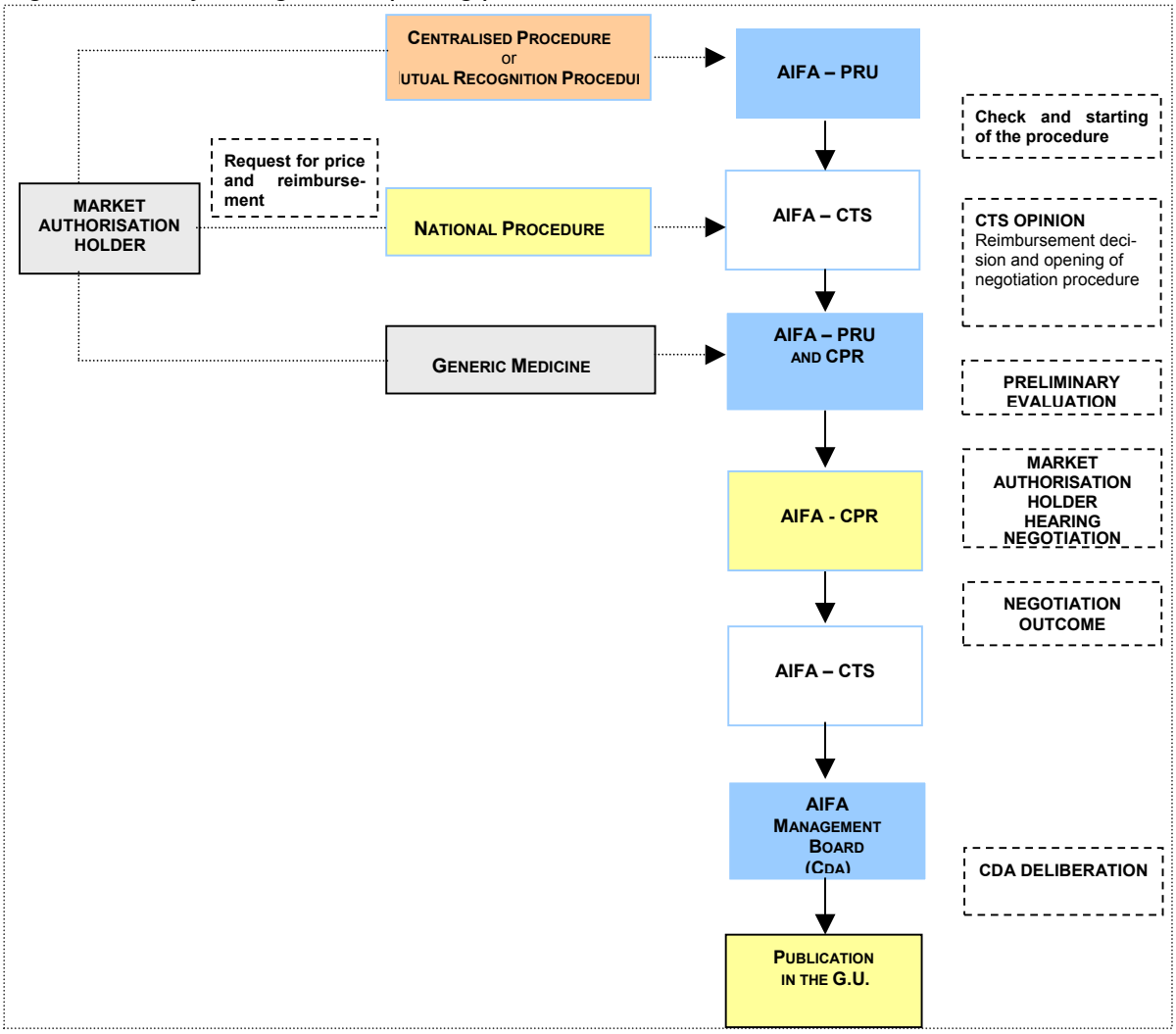
The relevance of the criteria listed is of importance both to reimbursement and to pricing.

The price negotiated is the ex-factory price. To determine the pharmacy retail price (PRP) the wholesale and the pharmacy margin value and the value-added tax (VAT) are added (cf. 3.5).

If the negotiation procedure fails, the pharmaceutical is reclassified as non-reimbursable and assigned to Class C (cf. 4.2.2); consequently, the price of the product is free and set by the market authorisation holders.

The ex-factory price negotiated is normally established for 24 months. Excluding exceptions for specific contractual conditions, the negotiated price is implicitly confirmed for a further 24 months with the previously agreed conditions, but manufacturers may always renegotiate the price after the first 24 months.

Figure 3.1: Italy – Negotiation pricing procedure flow chart



AIFA = Italian Medicines Agency, CPR = Committee for Pricing and Reimbursement, CTS = Technical Scientific Committee PRU = Pricing and Reimbursement Unit, G.U. = Official Journal of the Italian Republic, CDA = Manage-ment Board of AIFA

Source: AIFA – Centre for Studies

The manufacturer may also renegotiate the price after a variation in indication and/or reimbursement classification, in order to set an adequate price.

3.2.3 Free pricing

The free pricing method is used for products included in Class C (non-reimbursable pharmaceuticals). The method of pricing at the time of writing for over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP) was introduced in 1995.[28] The system for free pricing provided that prices are assigned by market authorisation holders and that the price is applied nationally and is the maximum price. Over-the-counter (OTC) prices may be solely increased in January every other year (odd years), while reductions in price are allowed at any time. At the time of writing, prices are fixed until January 2007.

3.2.4 Public procurement / tendering

In Italy, tendering procedures are used only for the hospital sector.

Public hospitals buy pharmaceuticals on the basis of a tendering procedure, granting the contract to the best tender, whether pharmaceutical company or importer (cf. 2.1.3.4).

3.3 Pricing procedures

The negotiation pricing procedure adopted in Italy uses a “mixed” methodology, the criteria for which are based on an evaluation of:

- external price referencing
- internal price referencing

[28] Refer to footnote 27

Table 3.4: Italy – Pricing procedures

Pricing procedure	In use: Yes / No	Level of pricing[1]	Scope[2]
External price referencing	YES	Ex-factory price during negotiation procedure	Reimbursable pharmaceuticals (only as one additional piece of information in pricing)
Internal price referencing	YES	Ex-factory price during negotiation procedure	Reimbursable pharmaceuticals (only used in the reimbursement decision)
Cost-plus pricing	NO	NO	NO
Other, e.g. indirect profit control	NO	NO	NO

[1] Level of pricing = the stage of the pricing process at which the pricing takes place (e. g. at the pharmacy retail price (PRP) level)

[2] Scope = a pricing procedure does not always refer to all pharmaceuticals: e.g. a pricing procedure could only refer to reimbursable pharmaceuticals, whereas for over-the-counter pharmaceuticals there is free pricing.

Source: AIFA – Centre for Studies

3.3.1 External price referencing

At the time of writing external price referencing is only used as additional information during the negotiation procedure, whilst in the past it has been used as the main criterion for the pricing of reimbursable pharmaceuticals which were authorised under the national market authorisation procedure.

From 1994 to January 2004, Italy applied a method of setting prices of reimbursable pharmaceutical products based on the Average European Price (AEP) (used as external reference price applied at the pharmacy retail price (PRP) level). The procedure was managed by the Interministerial Committee for Economic Planning (CIPE) at the Ministry of Economics. The companies were free to set prices on the basis of the estimated cost but without exceeding the Average European Price (AEP) based on the five most sold pharmaceuticals – including generic pharmaceuticals – in France, Germany, Spain and the United Kingdom. The method employed the adjustment of price using the index based on purchasing power parities (PPPa) to change the value of foreign prices into Italian currency.

The country price information was provided by IMS Health international and checked by the Interministerial Committee for Economic Planning (CIPE). Comparisons were made according to the principle of similarity adopted to determine the European equivalents of Italian products: equal active ingredient, route of administration, same or similar therapeutic pharmaceutical form and similar dosage.

In 1997 the system was re-evaluated by the Interministerial Committee for Economic Planning (CIPE) and from 1998 to 2004 the calculation of the Average European Price (AEP) was modified to include all European Union (EU) Member States and using current exchange rates.[29]

The Average European Price (AEP) was employed until 2004 for pharmaceuticals authorised by national procedure, while contemporarily a negotiation procedure has been used for pharmaceuticals authorised under the centralised and mutual recognition procedure. Law No. 326/2003[30] modified the price setting procedure: the pricing of all reimbursable pharmaceuticals authorised via the national registration procedure, centralised procedure and mutual recognition procedure is carried out according to the negotiation procedure managed by the Italian Medicines Agency (AIFA).

3.3.2 Internal price referencing

In 1994, after the abolition of the "old" National Pharmaceutical Formulary (PFN), the criterion of homogeneous categories for reimbursement classification in Classes A, B or C was adopted (cf. 4.2.2.).[31]

The internal price referencing of reimbursable products was introduced in 1996.[32] The method was based on the principle of the same price for the same pharmaceutical: products containing the same active ingredient, with the same method of administration, and the same or comparable pharmaceutical form – on the basis of well-documented bioequivalence – should have the same price per unit of compound.

In 2001 a reference price for off-patent pharmaceuticals was introduced by Decree No.347/2001[33] (cf. 4.3.). The National Health Service (NHS) reimburses the lower price among the prices of off-patent pharmaceuticals with equal composition in active ingredients, with the same pharmaceutical form, the same method of administration, the same number of units and the same unit dosage.

In 2003 the reference price system was modified by the introduction of the new National Pharmaceutical Formulary (PFN). The renewal of the National Pharmaceutical Formulary (PFN) introduced a new methodology for setting the reference price named the "cut-off methodology" which was mainly aimed at narrowing the large price differential existing for similar pharmaceuticals, which had resulted from the Average European Price (AEP) methodology (for details cf. 4.6.1).

[29] Law 27 December 1997, No. 449, article 36 [*articolo 36 della Legge No. 449 del 27 dicembre 1997 "Misure per la stabilizzazione della finanza pubblica (collegato alla Finanziaria 1998)" G.U. 30 dicembre 1997, No. 302, S.O. No. 255/L*]

[30] Refer to footnote 10

[31] Law No. 537/1994 [*Legge No. 537 del 24 dicembre 1993 "Interventi correttivi di finanza pubblica" G.U. del 28 dicembre 1993, S.O. No. 303*]

[32] Law Decree No. 323/1996 [*Decreto Legge No. 323 del 20 giugno 1996, convertito nella legge No. 425 del '8 Agosto 1996, Disposizioni urgenti per il risanamento della finanza pubblica G.U. No. 191 del 16 Agosto 1996]*

[33] Refer to footnote 12

3.3.3 Cost-plus pricing

As discussed in 3.2.2 the negotiation procedure uses a mix of criteria for the evaluation and pricing of reimbursable pharmaceuticals, among which the cost-plus criteria are not applied.

3.3.4 (Indirect) Profit control

At the time of writing indirect profit control is not applied in Italy.

3.4 Exceptions

Potential exemptions to the pricing procedures described above concern hospital-only-medicine(s) (HOM), parallel trade, generics, over-the-counter (OTC) and orphan pharmaceuticals.

3.4.1 Hospitals-only

Hospital pharmaceuticals include products bought by Independent Hospitals (AO), Hospital Trusts and Local Health Units (ASL).

The prices negotiated with the Italian Medicines Agency (AIFA) represent, in the case of hospitals, the maximum sale price for the National Health Service (NHS), but pharmaceutical companies must grant a rebate to hospital: the value of rebate of the individual product is negotiated during the pricing procedure. For pharmaceuticals whose prices are not negotiated, the statutory rebate/discount to hospitals is 50% minimum discount/rebate on the public price (net of value-added tax (VAT)).

The prices of pharmaceuticals in hospitals are monitored by a specific electronic system (named *"Tracciabilità del Farmaco*", cf. 6.1) instituted by Law No. 39/2002.[34] Companies have to deliver monthly information on the pharmaceuticals supplied to hospitals and on the applied prices.

3.4.2 Generics

In general, the procedure for the pricing of generics does not differ from the other pricing methods and procedures. In terms of reimbursement, the decision is the same as that applied to the originator product. Law No. 425/1996[35] states that the price of the generic product should be set at minimum 20% below the price of the comparable originator product.

[34] Law No. 39/2003 [*Legge 1° marzo 2003, No. 39 "Disposizioni per l'adempimento di obblighi derivanti dall'appartenenza dell'Italia alle Comunità europee - Legge comunitaria 2001" G. U. del 26 marzo 2002, No. 72 – S.O. No. 54]*

[35] Law No. 425/1996 [*Legge 8 agosto 1996, No. 425 "Conversione in legge, con modificazioni, del decreto-legge 20 giugno 1996, No. 323, recante disposizioni urgenti per il risanamento della finanza pubblica" G.U. del 16 agosto 1996, No. 191]*

Since 1 January 2005 – as a financial incentive for pharmacists to promote the use of generics and of less expensive equivalent pharmaceuticals – the statutory discount for pharmacists (cf. 3.5.2) is not paid to the National Health Service (NHS) for all dispensed pharmaceuticals (originator or generic) with a price correspondent to the reference price.[36]

3.4.3 Over-the-counter pharmaceuticals

The system for the pricing of non-reimbursable pharmaceuticals (Class C) differs from the pricing method and procedure used for setting the price of reimbursed pharmaceuticals. Class C pharmaceuticals are in fact freely priced (cf. 3.2.3).

Non-reimbursable pharmaceuticals include over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP) (SOP are subgroups of over-the-counter (OTC) products) and a minority of prescription-only medicine(s) (POM) (cf. 3.2).

3.4.4 Parallel traded pharmaceuticals

Parallel traded pharmaceuticals represent a minimal quota of the Italian market. For these pharmaceuticals Italy is more an exporting (e.g. to the United Kingdom and Germany) than an importing country.

The legal basis for authorising parallel trade pharmaceuticals is a Ministerial Decree.[37] It provides that an import market authorisation from the Italian Medicines Agency (AIFA) is required. The importer should demonstrate that the product fulfils given criteria and must provide the appropriate documentation (in Italian language). In particular, it must be proven that no difference in therapeutic effect of a product authorised in Italy exists or that the differences do not affect quality, safety and efficacy. If satisfied with the application, the Italian Medicines Agency (AIFA) issues the authorisation within 45 days.

The system for the pricing of parallel traded pharmaceuticals is similar to the pricing method and procedure employed for the generics sector (cf. 3.4.2).

The parallel importers have to negotiate the price, as described in 3.2.2. The price of a parallel trade pharmaceutical may be lower or the same as the comparable originator (internal reference price). There are no incentives for doctors, patients or pharmacists to use parallel imported products.

3.4.5 Other exceptions

There are no other exceptions in Italy.

[36] Cf. footnote 10

[37] Ministry of Health Decree [*Decreto Ministeriale del 29 agosto 1997 "Procedure di autorizzazione all'importazione parallela di specialità medicinali per uso umano*"]

3.5 Margins and taxes

The margins for reimbursed pharmaceuticals (Class A) for pharmaceutical companies, wholesalers and pharmacies are fixed by law[38] at 66.65%, 6.65% and 26.7%, respectively, of the net pharmacy retail price (PRP). Pharmacists' margins for pharmaceuticals bought by the National Health Service (NHS) are subjected to a rebate/discount calculated according to a regressive method.[39] The value-added tax (VAT) rate for pharmaceuticals is 10%[40] on the net pharmacy retail price (PRP).

Table 3.5: Italy – Regulation of wholesale and pharmacy margins 2006

	Wholesale margin			Pharmacy margin		
	Regulation (Yes / No)	**Content**	**Scope***	**Regulation (Yes / No)**	**Content**	**Scope***
Italy	Yes	Fix	Reimbursable pharmaceuticals	Yes	Fixed margin + regressive element due to the statutory discount (cf. 3.5.2)	Reimbursable pharmaceuticals

*Regulations concerning margins are applied to all reimbursable pharmaceuticals. Free pricing for over-the-counter (OTC) products.

Source: Law No. 662/1996 (cf. footnote 38)

3.5.1 Wholesale remuneration

The wholesale margin for reimbursed pharmaceuticals is established by Law No. 662/1996 (cf. footnote 38) at 6.65% of the net pharmacy retail price (PRP).

The margin for the non-reimbursable market segment is free and is not regulated by the law.

Table 3.6: Italy – Wholesale margin scheme 2006

Pharmacy retail price (PRP) net	Wholesale margin as a % of pharmacy retail price (PRP) net
Reimbursable	6.65
Non-reimbursable	Free

Source: Law No. 662/1996 (footnote 38)

[38] Law No. 662/1996 [*articolo 1, co 40, Legge No. 662 del 23 dicembre 1996 "Misure di razionalizzazione della finanza pubblica" G.U. del 28 dicembre 1996, No. 303*]

[39] Article 40, co 40, Law No. 662/1996 - refer to footnote 38

[40] Article 40, co 39, Law No. 662/1996 - refer to footnote 38

3.5.2 Pharmacy remuneration

Pharmacists are remunerated via margins fixed by government regulation. The pharmacy margin – fixed by Article 1 of Law No. 662/1996 (refer to footnote 38) – is linear but it has been made regressive due to the regressive character of the "statutory discount" which pharmacists have to grant to the National Health Service (NHS).

As of January 1997 the pharmacies' revenue is set as percentage of the overall price of Class A pharmaceuticals.[41] The rate at the time of writing is 26.7% of the net pharmacy retail price (PRP) of reimbursable pharmaceuticals (Class A) (it does not include value-added tax (VAT) of 10%). Since the fixed margin does not take into account the statutory discount and/or the special commercial discounts negotiated with manufacturers, this value is a hypothetical margin.

Since 1992 the pharmacists have been obliged to apply a statutory discount for products reimbursed by the National Health Service (NHS). In the beginning, the discount was set as a fixed percentage of the price (2.5% of the price excluding value-added tax (VAT), 3% since 1995).

The successive method (1997) foresaw different statutory discount rates applied to different price ranges, in order to make pharmacy margins regressive. In 2004 Law No. 289/2002[42] introduced a new discount value of 19% for pharmaceuticals with a price greater than € 154.94. When the total National Health Service (NHS) annual sales are below € 258,228 excluding value-added tax (VAT), the statutory discounts are reduced by 60% to values of 1.5%, 2.4%, 3.6%, 5.0% and 7.6%. When pharmacies receive payment by the National Health Service (NHS) for dispensed reimbursable pharmaceuticals, the National Health Service (NHS) retains a portion as statutory discount (including a prescription fee and excluding value-added tax (VAT)). For pharmacies located in rural areas a residential remuneration is provided (Article 2 of the Law of 8 March 1968, No. 221) and when the total annual sales are below € 387,342 the rebate/discount is reduced at a fixed value of 1.5% (cf. Table 3.7).

As of 1 January 2005 the discount for the National Health Service (NHS) is not applied for oxygen-related medical products and pharmaceuticals with expired patents (branded or unbranded pharmaceuticals) included in the Transparency List (off-patent pharmaceuticals). This amendment was established in order to create a financial incentive to pharmacists to promote the use of generics (cf. 3.4.2).

[41] Law No. 537/1993 [*articolo 8, co 10 Legge 24 Dicembre 1993, No. 537 "Interventi correttivi di finanza pubblica GU del 28 dicembre 1993, S.O. No. 303*]

[42] Law No. 289/2002 - Financial Law 2003 [*Legge 27 dicembre 2002, No. 289 "Disposizioni per la formazione del bilancio annuale e pluriennale dello Stato (legge finanziaria 2003)" G.U. del 31 dicembre 2002, No. 305 – S.O. n. 24*]

Table 3.7: Italy – Pharmacy margin scheme for reimbursable pharmaceuticals 2006

Pharmacy retail price (PRP) gross from … to… in €	Pharmacy margin as a % of PRP net	Pharmacy discount as a % of PRP net	Effective pharmacy margin as a % of PRP net
Urban pharmacies with a total NHS annual turnover < € 258,228			
<25.82	26.70	1.50	25.20
25.83 – 51.65	26.70	2.40	24.30
51.66 – 103.28	26.70	3.60	23.10
103.29 – 154.94	26.70	5.00	21.70
Over 154.94	26.70	7.60	19.10
Urban pharmacies with a total NHS annual turnover > € 258,228			
<25.82	26.70	3.75	22.95
25.83 – 51.65	26.70	6.00	20.70
51.66 – 103.28	26.70	9.00	17.70
103.29 – 154.94	26.70	12.50	14.20
Over 154.94	26.70	19.00	7.70
Rural pharmacies with a total NHS annual turnover < € 387,342			
<25.82	26.70	1.50	25.20
25.82 – 51.64			
51.65 – 103.28			
103.29 – 154.93			
Over 154.94			
Rural pharmacies with a total NHS annual turnover < € 387,342			
<25.82	26.70	3.75	22.95
25.83 – 51.65	26.70	6.00	20.70
51.66 – 103.28	26.70	9.00	17.70
103.29 – 154.94	26.70	12.50	14.20
Over 154.94	26.70	19.00	7.70

NHS = National Health Service, PRP = pharmacy retail price

Source: Financial Law 2003 (cf. footnote 41)

3.5.3 Remuneration of other dispensaries

Since August 2006,[43] non-pharmacy outlets are allowed to dispense over-the-counter (OTC) products and Non-prescription pharmaceuticals with advertising prohibition (SOP), in a specific and opposite area of the store in the presence of a pharmacist. Each vendor is allowed to fix a discount for the price indicated on the product package. The commercial discount must be clearly indicated and applied equally to every consumer.

3.5.4 Value-added tax

Value-added tax (VAT) applied in Italy is set at the rate of 4%, 10% and 20% (the latter is standard value).

[43] Law Decree No. 223/2006 [*Decreto Legge 4 luglio 2006, No. 223 "Disposizioni urgenti per il rilancio economico e sociale, per il contenimento e la razionalizzazione della spesa pubblica, nonché interventi in materia di entrate e di contrasto all'evasione fiscale" G.U. del 4 luglio 2006, No. 153*]

The value-added tax (VAT) for pharmaceutical products (reimbursable and non-reimbursable, including homeopathic) is fixed at 10%.

Since 1 January 1997 the value applied to pharmaceutical products changed from 4% to 10%,[44] with the exception of oxygen (therapeutic gas), to which a value-added tax (VAT) of 4% is applied.

Table 3.8: Italy – Changes in value-added tax (VAT) rates

Legal basis and application period	Reimbursable products (%)	OTC products (%)
Until 24 February 1995	9	19
Since 25 February 1995[45]	4	4
Since 23 October 1996[46]	4	10
Since1 January 1997 (Law No. 662/96)	10	10

OTC = over-the-counter

Source: Cited Laws

3.5.5 Other taxes

In the Italian system there are no further taxes or fees applied to pharmaceuticals.

3.6 Pricing-related cost-containment measures

The main price control mechanisms currently used in Italy are dictated by the provisions of Law No. 405/2001,[47] which introduced an expenditure ceiling for community pharmaceutical care. This expenditure cannot exceed 13% of the overall health expenditure (HE) at national and regional levels. Law Decree No. 269/2003[48] states that the amount of the overall pharmaceutical expenditure (PE), including expenditure for treatment of patients in hospitals (in-patient care), cannot exceed 16% of the total health expenditure (THE).

[44] Refer to footnote 38

[45] Law Decree No.41/1995 [*Decreto Legge 23 febbraio 1995, No. 41 convertito in legge 23 marzo 1995, No. 85 "Misure urgenti per il risanamento della finanza pubblica e per l'occupazione nelle aree depresse" G.U. No. 69 del 23 marzo 1995].*

[46] Law Decree No.536/1996 [*Decreto Legge 21 ottobre 1996, No. 536, No. 536 "Misure per il contenimento della spesa farmaceutica e la rideterminazione del tetto di spesa per l'anno 1996" G.U. No. 248 del 22 ottobre 1996].*

[47] Refer to footnote 11

[48] Law Decree No.269/2003 [*Decreto-legge 30 settembre 2003, No. 269 "Disposizioni urgenti per favorire lo sviluppo e per la correzione dell'andamento dei conti pubblici"G.U. del 2 ottobre 2003 No. 229 – S.O. No. 157]*

In the event that the ceiling is exceeded corrective measures are applied:

- in the positive list of reimbursable pharmaceuticals (National Pharmaceutical Formulary (PFN));
- by reducing the producers' earning margin (named "manufacturer discount") or the pharmacy retail price (PRP) of pharmaceuticals.

(Manufacturers pay for 60% of cases of the expenditure ceiling being exceeded, while for the remaining 40% the regional authorities adopt specific containment measures to deal with their pharmaceutical expenditure (PE) (Law No. 405/2001)).

Table 3.9: Italy – Main pharmaceutical expenditure (PE) containment measures 2004-2006

Provision/ Legal basis	Containment measures	Note and exception
Law Decree of 24 June 2004 No. 156, converted in Law on 2 August 2004, No. 202	• Margin cut at the manufacturer price level by 6.8% of the ex-factory price (corresponding to 4.12% of PRP including VAT) on sales of all reimbursable NHS pharmaceuticals for the period required to restrain the overspending of the first quarter of 2004 • Request for update of the positive list (PFN)	Exclusion of pharmaceuticals dispensed in hospitals, generics, hemoderivatives and DNA recombinant products
AIFA Decision 16 December 2004	On 1 January 2005 the new PFN was published introducing a price reduction (maximum 10%) applied to 53 selected substances (excessive and unjustified increase in consumption higher than the national average of 8.6% for the first semester 2004) equivalent to 296 products	Exclusion of generics and new commercialised active substances
AIFA Decision 26 July 2005	Confirmation of margin cut at the manufacturer price level at 6.8% of the ex-factory price (corresponding to 4.12% of PRP including VAT) until 1 November 2005	Exclusion of pharmaceuticals dispensed in hospitals, generics, hemoderivatives and DNA recombinant products
AIFA Decision 30 December 2005	• Cut of PRP, including VAT, of 4.4% of all reimbursed NHS pharmaceuticals • Additional temporary manufacturer's discount of 0.6% on the recalculated PRP, including VAT	Exclusion of generics, extractive and DNA recombinant hemoderivative products, vaccines and products with a price of less than € 5
AIFA Decision 3 July 2006	• Cut of PRP, including VAT, from 4.4% of the AIFA decision of 30 December 2005 to 5% of all reimbursable NHS pharmaceuticals • Updating of the positive list (PFN), price reduction (maximum 10%) applied to selected active substances (increase in consumption higher than the national average of 9.9% on the first trimester 2006)	Exclusion of generics, extractive and DNA recombinant hemoderivative products, vaccines and products with a price of less than € 5 Exclusion of pharmaceuticals dispensed exclusively in hospitals, pharmaceuticals dispensed by direct distribution, generics, paediatrics, new active substances brought onto the market in 2005 and some antineoplastics
AIFA-CDA Deliberation 27 September 2006	• Further cut of PRP by 5%, including VAT, for all reimbursable NHS pharmaceuticals	Exclusion of hemoderivatives and DNA recombinant products, vaccines and products with a price of less than € 5

Provision/ Legal basis	Containment measures	Note and exception
AIFA Deliberation 20 September and 2006 Financial Law 2007	• Extension to financial year 2007 of price cut of 5% of PRP, including VAT, for all reimbursed NHS pharmaceuticals • Extension to financial year 2007 of PFN price cut	As an alternative the pharmaceutical manufacturers may opt for the pay-back mechanism. This consists of delivering the price cut by making a payment to the Regions equivalent to the estimated amount deriving from the price reduction in each Region

AIFA = Italian Medicines Agency, NHS = National Health Service, PFN = National Pharmaceutical Formulary, PRP = pharmacy retail price, VAT = value-added tax

3.6.1 Discounts / Rebates

In Italy there are statutory regressive discounts for pharmacies (differentiated by urban/rural and the annual National Health Service (NHS) turnover – cf. 3.5) and statutory discounts in the form of "margin cuts" which often target the profit margin of the manufacturer (cf. Table 3.9). Commercial discounts of pharmacies and other retails outlets to consumers are allowed for non-reimbursable medicines.

Commercial rebates/discounts are also possible, but only in the hospital sector. They are statutory and fixed during the negotiation procedure case by case or fixed at a minimum value of 50% of the pharmacy retail price (PRP) for non-negotiated products. Higher discounts are also possible and enforceable on industry, both for the hospital sector and for wholesalers and pharmacies. The legal basis for granting the statutory discounts to hospitals is provided by Law No. 386/1974 (Article 9).[49]

3.6.2 Margin cuts

Cf. 3.6, Table 3.7.

3.6.3 Price freezes / Price cuts

At the time of writing a price freeze is applied only to the specific segment of Class C pharmaceuticals products. The freeze is the result of the agreement of 9 December 2005 between the Ministry of Health and Farmindustria (the manufacturers association) that froze the price of pharmaceuticals belonging to Class C for two years. Law No. 149/2005[50] stipulated that the ma-

[49] Law No. 386/1974 *[Legge 17 agosto 1974, No. 386 "Conversione in legge,con modificazioni,del decreto-legge 8 luglio 1974, No. 264, recante norme per l'estinzione dei debiti degli enti mutualistici nei confronti degli enti ospedalieri,il finanziamento della spesa ospedaliera e l'avvio della riforma sanitaria" G.U. No. 225 del 29 agosto 1974].*

[50] Law No. 149/2005 [*Legge 26 luglio 2005, No. 149 "Conversione in legge, con modificazioni, del decreto-legge 27 maggio 2005, No. 87, recante disposizioni urgenti per il prezzo dei farmaci non rimborsabili dal Servizio sanitario nazionale" G. U. del 29 luglio 2005, No. 175]*

nufacturer must fix the prices of products listed in Class C and C-*bis* as maximum prices and the prices may be increased only in January of every other year (odd years). The Law also stipulated that the community pharmacies may apply a price reduction of up to 20% on over-the-counter (OTC) pharmaceuticals and on pharmaceuticals without obligatory prescription (Non-prescription pharmaceuticals with advertising prohibition (SOP)). The main aim of using this mechanism was to reduce private pharmaceutical expenditure (PE). The effect of the mechanism is under evaluation at the time of writing.

3.6.4 Price reviews

The methods of pricing and the pricing procedures are not reviewed and evaluated on a regular basis in Italy.

4 Reimbursement

This chapter gives an overview of the reimbursement system, the reimbursement procedure and the regulation of reimbursement.

4.1 Organisation

The Italian reimbursement system covers all relevant diseases in the whole country and provides universal pharmaceutical coverage to the whole population (Italian citizens and legal residents).

The system at the time of writing groups pharmaceuticals into two main reimbursement categories according to a combination of relevance in terms of effectiveness and cost: Class A (fully reimbursed) and Class C (not reimbursed).

Reimbursable pharmaceuticals are included in a positive list, named the National Pharmaceutical Formulary (PFN) that comprises pharmaceuticals of well-established therapeutic efficacy and innovative pharmaceuticals.

Seeking to contain growing budgetary pressures, the Italian Government in 2002 implemented a set of interventions at several levels with the general aim of improving pharmaceutical expenditure (PE) governance. Key changes included:

- the restructuring of the positive list of reimbursable pharmaceuticals (implementation of a new National Pharmaceutical Formulary (PFN 2003));
- the reorganisation of categories of reimbursable products;
- pharmaceuticals price reduction;
- generic pharmaceuticals promotion;
- delisting of selected pharmaceuticals;
- direct distribution of pharmaceuticals by hospital services (cf. 2.1.3.4).

The decision-making power in deciding whether or not a pharmaceutical is reimbursed is allocated to the Technical Scientific Committee (CTS) within the Italian Medicines Agency (AIFA) (cf. 3.2.2).

The latest available National Pharmaceutical Formulary (PFN) was published in July 2006.

4.2 Reimbursement schemes

The objectives of the Italian reimbursement scheme are summarised as follows:

- to ensure patients complete pharmaceutical coverage for clinically and epidemiologically relevant diseases;
- to guarantee the reimbursement of pharmaceuticals listed in a non-reimbursable category only for particular and/or chronic conditions (e.g. corticosteroid ointments, atopic dermatitis – psoriasis). In this case the procedure of reimbursement is based on diagnosis and a therapeutic plan put together exclusively by specialised health care centres identified by the Regions. The patient submits the prescription indicated in the therapeutic plan to a pharmacy and the product is dispensed free of charge;
- to ensure general practitioners (GP) the possibility (when prescribing) to choose among different active substances with the same therapeutic indications;
- to identify a reimbursement value in order to save money by trying to minimise the marked price differential among molecules with comparable efficacy and tolerability.

As analysed earlier, prices and reimbursement status are simultaneously determined and therefore the level of prices influences the reimbursement status of a product.

Admission for reimbursement of pharmaceuticals is decided during the pricing procedure on the basis of the opinion given by the Technical Scientific Committee (CTS) (cf. 3.2.2).

4.2.1 Eligibility criteria

Eligibility criteria for the decision on reimbursement are stated in the Interministerial Committee for Economic Planning (CIPE) Deliberation of 1 February 2001, No. 3, and are also employed for the pricing procedure (cf. 3.2.2).

Criteria to be included in the positive list are:

- product-specific criteria (essential pharmaceuticals policy, medical and therapeutic value, safety, lack of alternative therapies, prescription status, patent status);
- economic criteria (cost-effectiveness, reference price, internal market forecasts);
- disease-specific criteria (severity of illness, special medical needs, number of potential patients).

The Italian Medicines Agency (AIFA) (Technical Scientific Committee (CTS)) is the authority responsible for the decision on the reimbursement category of individual pharmaceuticals.

4.2.2 Reimbursement categories and reimbursement rates

The reimbursement categories have been defined on a legal basis (article 8, paragraph 10 of Law No. 537/1993[51]) since 1994. The methodology for the allocation of a pharmaceutical to a particular class of reimbursement was based on the principle of the homogenous categories.

Initially, three classes (A, B and C) were defined, but at the time of writing pharmaceuticals are grouped in two main reimbursement categories:

- Class A: includes essential pharmaceuticals and pharmaceuticals for serious and chronic diseases. The pharmaceuticals of this group are wholly subsidised (100% of their price) by the National Health Service (NHS). This means that the National Health Service (NHS) bears 100% of the cost of the pharmaceuticals in Class A. Class A contains the subgroup **Class H** which consists of pharmaceuticals which are eligible for reimbursement only when used in hospitals.

Class A with Italian Medicines Agency (AIFA) notes on prescribing pharmaceuticals: within Class A there are pharmaceuticals fully reimbursed by the National Health Service (NHS) for specific diseases only. The pharmaceuticals "with notes" are reimbursable if they are prescribed for diseases included in the AIFA Notes list.

- Class C: comprises pharmaceuticals used for diseases of less importance and for minor ailments (antineuralgic, antipyretic, laxatives, etc); pharmaceuticals whose use is discouraged (e.g. benzodiazepines); and pharmaceuticals not requiring a medical prescription (Non-prescription pharmaceuticals with advertising prohibition (SOP)). The National Health Service (NHS) does not reimburse the pharmaceuticals included in this class, except in the case of patients with specific social diseases.

The Financial Law in 2005 (Law No. 311/2004[52]) also introduced **Class C-*bis*** which comprises pharmaceuticals not requiring a medical prescription and which can be advertised to the public (over-the-counter (OTC) products). The costs of over-the-counter (OTC) products are wholly paid for by users.

Until 1 July 2001 a Class B existed, which included non-essential pharmaceuticals partially reimbursed (at a rate of 50%) by the National Health Service (NHS).

The basis for the reimbursement categories is a legal basis described in the cited Interministerial Committee for Economic Planning (CIPE) deliberation.

Law No. 648/1996[53] provides a procedure according to which patients and/or doctors may apply for reimbursement of individual pharmaceuticals. The procedure is applicable when a valid alternative therapy does not exist. The pharmaceuticals reimbursed by the National Health Ser-

[51] Refer to footnote 41

[52] Law No. 311/2004 (Financial Law 2005) [*Legge 30 dicembre 2004, No. 311"Disposizioni per la formazione del bilancio annuale e pluriennale dello Stato (legge finanziaria 2005)"* G.U. *del 31 dicembre 2004*, *No. 306 S. O. No. 192*]

[53] Cf. footnote 22

vice (NHS) under Law No. 648/96 are specifically listed by the Italian Medicines Agency (AIFA) Technical Scientific Committee (CTS). The list comprises:

- innovative pharmaceuticals, whose marketing is authorised in other European Union (EU) Member States but not in Italy;
- pharmaceuticals not authorised but under development in research trials;
- pharmaceuticals to be used for a therapeutic indication different from the authorised indication.

At present there are 14 molecules (not authorised) for treatment of rare diseases reimbursed by the National Health Service (NHS) under Law No. 648/96.

Table 4.1: Italy – Reimbursement of pharmaceuticals 2005/2006

Reimbursement category	Reimbursement rate (%)	Characteristic of category	% total no. of products
Class A	100	Essential pharmaceuticals, chronic and serious therapies. Reimbursable.	44
Class A with AIFA Notes	100	Fully charged to NHS only if prescribed for specific diseases listed in the AIFA Notes. Reimbursable.	
Subgroup H	100	Pharmaceuticals requiring specialist supervision and reimbursed only when used in hospitals. Reimbursable.	
Class C	0	Pharmaceuticals not reimbursed (pharmaceuticals without proven efficacy and pharmaceuticals with proven efficacy for minor diseases). Non-reimbursable.	56
Class C-*bis*	0	OTC products. Non-reimbursable.	

AIFA = Italian Medicines Agency, NHS = National Health Service, OTC = over-the-counter (pharmaceuticals)

Source: Italian Pharmaceutical Formulary 2005 (PFN 2005– Prontuario Farmaceutico Nazionale)

4.2.3 Reimbursement lists

Italy uses a positive list of all reimbursable pharmaceuticals, named the National Pharmaceutical Formulary (PFN). The list is managed at central level by the Italian Medicines Agency (AIFA).

The reimbursement positive list is updated annually, or every six months if public pharmaceutical expenditure (PE) exceeds the 13% ceiling.

Methodological revision of the reimbursement list has been defined by specific laws. The main renewal was established by Law No. 178/2002[54] which provided the restructuring of the list based on cost-effectiveness criteria, in order to contain public pharmaceutical expenditure (PE)

[54] Law No.178/2002 [*Legge 8 agosto 2002, No. 178 - conversione in legge del Decreto-Legge 8 Luglio 2002, No. 138 "Interventi urgenti in materia tributaria, di privatizzazioni, di contenimento della spesa farmaceutica e per il sostegno dell'economia anche nelle aree svantaggiate" GU No. 187 del 10-8-2002]*

planned in financial laws and according to the State-Regions-Trento and Bolzano Autonomous Provinces Agreements of 8 August 2001.[55]

The criteria for inclusion in the lists are the same as those described in the eligibility criteria for reimbursement (cf. 4.2.1).

A copy of the National Pharmaceutical Formulary (PFN) is sent free of charge to every doctor and pharmacist in the country. It is also available on the Italian Medicines Agency (AIFA) web site.

4.3 Reference price system

In 2001 a reference price system was introduced for off-patent pharmaceuticals.[56] The National Health Service (NHS) reimburses the lowest price in a group of interchangeable off-patent pharmaceuticals with the same active ingredients, pharmaceutical form, method of administration, number of units and unit dosage. The reference price system is managed by AIFA, and the reference groups and reference prices are updated monthly.

4.4 Private pharmaceutical expenses

4.4.1 Direct payments

A direct payment by users is required for the purchase of Class C pharmaceuticals (non-reimbursable pharmaceuticals and including all over-the-counter (OTC) products).

4.4.2 Out-of-pocket payments

In Italy the reimbursement system has two main types of out-of-pocket payment (OPP) by patients:

- prescription fees (named “ticket”) – a fixed amount per prescription and/or per pack, (decided at regional level);
- a co-payment for pharmaceuticals in the form of payment of the difference between the price of a more expensive pharmaceutical compared to the cheaper product containing the same active ingredient (reference price) (cf. 4.4.2.2).

Co-payments and prescription charges for pharmaceuticals were introduced in 1978 and were regulated by national legislation until 1 January 2001, when the Italian Government abolished all

[55] [*Accordo tra Governo, regioni e le province autonome di Trento e Bolzano recante integrazioni e modifiche agli accordi sanciti il 3 agosto 2000 (repertorio atti 1004) e il 22 marzo 2001 (repertorio atti 1210) in materia sanitaria. G.U. del 6 settembre 2001, No. 207]*

[56] Cf. footnote 12

types of prescription charges (Law No. 388/2000[57]). As of 2002, in order to contain the expenditure of pharmaceutical care within the planned ceiling of 13% of overall health expenditure (HE) provisioned by Law No. 405/2001,[58] many regional authorities introduced new forms of prescription charges.

4.4.2.1 Fixed co-payments

The prescription fees ("ticket") are only applied in some Regions, in the form of a fixed amount (generally € 1-2) to be paid by patients per prescription and/or per pack. For multi-prescriptions, a top limit per prescription is used, regardless of the number of packs. A monthly or annual out-of pocket maximum (ceiling) is not used.

Specific types of exemptions are applied for particular categories of people: chronically ill patients and people with rare diseases, disabled people and pregnant women. Some regions use criteria for exemption based on income and/or age.

4.4.2.2 Percentage co-payments

In the Italian reimbursement scheme the national regulation no longer requires a percentage co-payment by patients (formerly Class B, cf. 4.2.2). Forms of co-payment are in place, not as percentage payments but in the form of the difference between the price of a more expensive pharmaceutical compared to the cheaper product containing the same active substance (reference price system, cf. 4.3). The co-payment is requested when the price of a pharmaceutical is higher than the reference price.

In Italy there is no minimum co-payment or threshold and there is no annual or monthly out-of pocket maximum (ceiling).

4.4.2.3 Deductibles

There are no deductibles in the Italian pharmaceutical pricing and reimbursement system.

4.5 Reimbursement in the hospital sector

The reimbursement criteria in the in-patient sector do not differ from the out-patient sector. Some pharmaceutical products are classified as hospital-only medicine(s) (HOM) requiring specialist supervision and are grouped in Class H (sub-class of the main Class A).

The pharmaceuticals employed for in-patient care are fully reimbursed and the criteria for reimbursement in the hospital sector are the same as those of the primary care sector (cf. 4.2.1).

[57] Law No. 388/2000 [*Legge 23 dicembre 2000, No. 388 "Disposizioni per la formazione del bilancio annuale e pluriennale dello Stato (legge finanziaria 2001)"* G. U. *No. 302 del 29 dicembre 2000 - S O. No. 219*]
[58] Cf. footnote 47

The main "payer" of pharmaceuticals in hospitals is the National Health Service (NHS), via the Regions. The cost of pharmaceuticals is included in the diagnosis-related group (DRG) reimbursement scheme.

4.6 Reimbursement-related cost-containment measures

4.6.1 Major changes in reimbursement lists

The new Italian National Pharmaceutical Formulary (PFN)[59] came into effect on 16 January 2003. The National Pharmaceutical Formulary (PFN), updated again in 2005,[60] contains the list of pharmaceuticals reimbursable by the National Health Service (NHS).

The objectives of the 2003 revision were:

- definition of a sustainable price
- narrowing price differentials for similar products
- realignment of pharmaceutical prices.

The revision set out a methodology for setting the reference price. Pharmaceuticals were first clustered into homogeneous categories (i.e. those with the same main indication(s) and with similar clinical efficacy and safety profile). Within each homogeneous category, a reimbursement level (cut-off) was then identified and, accordingly, pharmaceutical companies were asked to adjust their price. Products with prices under the cut-off point are fully reimbursed, while products with higher prices have been de-listed in Class C.

The methodology and related criteria used for the restructuring process were based on the criteria described here.

1) Identification of “homogeneous classes” of substances (active ingredients) based on:

- definition – “substances whose safety and efficacy profile is substantially overlapping in the practice of family medicine”
- Anatomic Therapeutic Chemical (ATC) classification as a starting point, but modifying this where appropriate to meet the above definition.

2) Absolute and relative expenditure in 2001 for each presentation of each individual product and tentative forecast for 2002 expenditure based on 2001 consumption data at 2002 prices.

3) Use of defined daily doses (DDD) to calculate the average daily cost for each active substance.

4) Flexibility clause – case-by-case discussion of cases where the application of the above criteria would affect the availability of pharmaceuticals or distort consumption patterns.

[59] Minister of Health Decree [*Decreto del Ministro della salute del 20 dicembre 2002 “Elenco dei medicinali rimborsabili dal Servizio sanitario nazionale” G. U. No. 4 del 7 gennaio 2003]*

[60] The 2005 update concerned only changes of prices and not the methodology.

The methodology used to calculate the reimbursement level (cut-off point) within each therapeutic category is described here.

1. Within each therapeutic category, the average daily cost of each active substance has been calculated, weighted on the basis of 2001 consumption:

   NHS 2002 price X no. of items 2001 / no. of consumed doses 2001[61]

2. The average daily cost of each active substance within each therapeutic category has been calculated on the basis of the defined daily dose (DDD) (certified by WHO) and has been ranked in ascending order.

3. The reimbursement level (cut-off point) within each therapeutic category has been determined when both the following two conditions have been fulfilled:

   - the number of dispensed doses is at least 60% of the cumulative doses;
   - the cumulative expenditure covered by the National Health Service (NHS) is at least 50% of the market.

4. If an active substance alone covers more than 50% of the expenditure of the individual category, the criteria referred to in point 3 (above) are not applied and the reimbursement value is defined by increasing by 15% the average weighted price of the active substance, which ensures at least the cumulative 5% of the market volume.

The number of groups of pharmaceuticals in the new National Pharmaceutical Formulary (PFN) have been reduced to two: Class A, which lists pharmaceuticals (approximately 4,000) that the State will provide to citizens without asking for co-payment; and Class C, which lists pharmaceuticals that are to be paid in full. Class B, which contained pharmaceuticals that were partially reimbursable, no longer exists. The pharmaceuticals formerly in Class B are free and have been added to Class A; 14 pharmaceuticals have been moved from Class B to Class C.

The new National Pharmaceutical Formulary (PFN) eliminates the bias that arose due to the application of Law No. 405/2001,[62] which had resulted in the introduction of differences in co-payment and delisting (pharmaceuticals paid completely by patients) among the different Regions.

On 1 January 2005 the Italian National Pharmaceutical Formulary (PFN) was revised again.[63] The new National Pharmaceutical Formulary (PFN) 2005 introduced a price reduction applied to 53 selected active substances (equivalent to 296 products), because of an excessive and unjustified increase in consumption higher than the national average of 8.6% on the first semester 2004).

[61] Source: OsMed – National Report 2001
[62] Refer to footnote 11
[63] AIFA Decision 16 December 2004

4.6.2 Introduction / review of reference price system

As previously described in 4.6.1, the reference price system was restructured during the implementation of the new National Pharmaceutical Formulary (PFN).

4.6.3 Introduction of new / other out-of-pocket payments

Not applicable.

4.6.4 Claw-backs

There is no claw-back system in Italy.

In 2007 a further cut of 5% of pharmacy retail price (PRP) has been confirmed, including value-added tax (VAT) on all reimbursable National Health Service (NHS) pharmaceuticals. As an alternative, the pharmaceutical manufacturers may opt for the pay-back mechanism. This consists of delivering the price cut by making a payment to Regions equivalent to the estimated amount deriving from the price reduction in each Region.

4.6.5 Reimbursement reviews

In Italy reimbursement decisions are not made on a regular basis. If evidence changes and a pharmaceutical product is subsequently shown to be more effective than originally assessed, the manufacturer can apply for a variation in the reimbursement classification and indication, as well as for negotiation of a change in the price.

5 Rational use of pharmaceuticals

This chapter gives an overview of the current methods used to promote equitable and efficient use of pharmaceuticals.

5.1 Impact of pharmaceutical budgets

In Italy no pharmaceutical budget or prescribing budget is applied nationally to doctors. At local level, many Regions and/or Local Health Units (ASL) monitor the prescribing activities of general practitioners (GP) in terms of expenditure, giving them feedback in order to control and contain public pharmaceutical expenditure (PE) below the expenditure ceiling provided by Law No. 405/2001 (cf. 3.6 and footnote 47).

The system does not have a budgetary connotation but consists only of a monitoring procedure. Sanctions are not applied to general practitioners (GP).

5.2 Prescription guidelines

In Italy a *Piano Nazionale Linee Guida* ((National Guidelines Programme, PNLG) – available at http://www.pnlg.it) promotes efficiency, efficacy and appropriateness of clinical treatments.

The National Guidelines Programme (PNLG) provides tools to health care professionals:

- clinical guidelines
- clinical organisational guidelines
- technical documents for the implementation and evaluation of health care services.

The National Guidelines Programme (PNLG) also offers a database collecting both national and international guidelines and elaborates recommendations based on evidence-based medicine.

5.2.1 Notes on prescribing pharmaceuticals

Notes on limitations (named “AIFA Notes”) are applied in prescribing pharmaceuticals in order to increase the appropriateness of the use of pharmaceutical classes proven to be effective in the treatment of specific diseases and of those associated with frequent severe adverse events. The pharmaceuticals in this category (Class A with Notes) are fully reimbursed by the National Health Service (NHS) for specific diseases only. If pharmaceuticals are prescribed for a disease not included in the list of Class A with AIFA Notes they will not be reimbursed.

The aim of the system is to limit both expenditure and inappropriate utilisation. A full list of AIFA notes is available on the Italian Medicines Agency (AIFA) web site: http://www.agenziafarmaco.it/.

The most recent update of the AIFA Notes was performed by the end of 2006. For this revision a dedicated working group has been created with the aim of analysing all critical aspects in the application of the Notes and providing recommendations to the Technical Scientific Committee (CTS) for the revising phase.

5.3 Information to patients / doctors

5.3.1 Information promoted by AIFA

The issue of safe and effective provision of information to patients has been always of great importance to Italy, which is active in the Working Group on Information to Patients of the Pharmaceutical Forum.

At the Italian Medicines Agency (AIFA), information is provided as described here.

a) Statutory information: a pharmaceuticals database provides electronic consultation on the web site. The National Pharmaceutical Formulary (PFN) is available on the Italian Medicines Agency (AIFA) web site and is sent, free of charge, to all Italian health care professionals. Furthermore, the updated list of generic pharmaceuticals with their marketing price is published on the web site every month.

b) Non-statutory information: the Italian Medicines Agency (AIFA) engages in wide-ranging editorial activities involving free-of-charge publications, a number of which are available in full on the web site and are mainly targeted at health care professionals. These include books, guidelines (e.g. use of pharmaceuticals for children and for pregnant women), national annual and periodical reports on the use of pharmaceuticals in Italy, a bulletin on clinical trials and important information such as newsletters to doctors, which are known as “Dear Doctor Letters”.

Patients have access to information on the web site, with frequently asked questions (FAQ) about “hot topics” and information sheets. Monographic issues (i.e. use of herbal pharmaceuticals/hormone replacement therapy) are dealt with in publications sent to health care professionals with the aim of informing patients.

The Italian Medicines Agency (AIFA) web site is at the time of writing chiefly targeted at health care professionals, and work to include more patient-oriented information is ongoing. All published information/materials are first submitted to experts for review and are successively approved by the Director General.

The Italian Medicines Agency (AIFA) responds to the requirement to provide quality information, as well as to patients’ needs through an online service (*Farmaci-line*) open to citizens and health care professionals. Experienced staff are available to answer questions on safety, efficacy and availability of pharmaceuticals through a free-of-charge telephone number (800-571661), by mail, fax and e-mail. This service represents an important tool for daily information on pharmaceuticals and feedback on states of emergency (i.e. problems related to the safety of various pharmaceuticals containing cerivastatine, sibutramine or coxibs, as well as availability of pharmaceuticals).

5.3.2 Advertising

All advertising for pharmaceuticals in Italy is subject to the requirements of the European Community (EC) Medicine Code (implemented by the Legislative Decree No. 219/2006)[64] codified as Title VIII of Directive 2001/83/EC. The Ministry of Health and the Italian Medicines Agency (AIFA) are respectively the competent institutions in charge of authorising, monitoring and controlling the industry activities of advertising to the general public and to health care professionals.

Advertising of pharmaceuticals on the Internet is not allowed.

5.3.2.1 Advertising to the general public

In Italy the only pharmaceuticals that are allowed to be advertised to the public are pharmaceuticals that are legally classified as over-the-counter (OTC) products. The current regulations prohibit the promotion of prescription-only medicines (POM) to the general public. The group of SOP products, which do not require a prescription, is not allowed to be advertised to the public (see section 3.2).

Public advertising must be authorised by the Ministry of Health, after consulting with the Advertising Committee. All advertising is required to be in accordance with the Summary of Product Characteristics (SPC) approved by the Italian Medicines Agency (AIFA) after an evaluation of the safety, quality and efficacy of the pharmaceutical.

The advertising must also encourage the rational use of the product by presenting it objectively, without being misleading and without exaggeration as to its safety, quality and efficacy.

The nature of the advertising must be clear in the message and the product must be identified expressly as a “medicinal product”. The advertisement must also contain:

1. the name of the pharmaceutical and the International Non-proprietary Name (INN) of the active ingredient, if the product contains only one active ingredient;
2. information necessary for the correct use of the pharmaceutical;
3. an explicit, legible invitation to read carefully the instructions on the internal leaflet or on the outer packaging.

5.3.2.2 Advertising to health care professionals

Advertising to health care professionals is permitted exclusively for pharmacists and doctors.

The advertising must contain all relevant information of the Summary of Product Characteristics, the reimbursement classification, the pharmacy retail price (PRP) and the dispensing conditions. The promotional material must be registered and approved by the Italian Medicines Agency (AIFA) before the beginning of the promotional event.

[64] Cf. footnote 14

The Italian Medicines Agency (AIFA) routinely monitors advertisements, investigates complaints received, and provides advice to the industry, health professionals and other regulatory bodies. If the advertising is conducted illicitly, the Italian Medicines Agency (AIFA):

- immediately interrupts or suspends the promotional action;
- suspends the dissemination of promotional material;
- issues a public communication, paid for by the violator, disseminated by the mainstream print media, and published on the advertiser web site and on the Italian Medicines Agency (AIFA) web site.

In the case of prescription-only medicine(s) (POM) the advertising for community pharmacists is limited to the information on the Supplementary Protection Certificate (SPC). This limitation is not applied to hospital pharmacists. In the case of pharmaceuticals dispensable without prescription the advertising to pharmacists may contain other information useful to patients for the correct use of the product.

Company sponsored meetings

Informative and promotional events sponsored by pharmaceutical companies that take place in Italy or in another country must obtain the Italian Medicines Agency's (AIFA) approval 45 days before the beginning of the promotional event. During the meeting it is prohibited to show or distribute samples and promotional material related to the pharmaceutical, except for the Summary of Product Characteristics, procedures and scientific articles.

Samples of a product – always accompanied by the Supplementary Protection Certificate (SPC) – may only be provided to a health care professional qualified to prescribe that product. They must only be provided by medical advisors and may only be supplied in response to written requests which have been signed and dated. No more than 10 samples may be provided to an individual health professional in one year.

Gifts – The provision of gifts or donations to medical practitioners and pharmacists must be inexpensive and relevant to the practice of the professional.

5.4 Pharmacoeconomics

In Italy, the use of health economic analysis for regulatory purposes is limited. At the time of writing, health economic analyses are mainly commissioned by pharmaceutical companies and are addressed to regulators, in order to support the pricing and reimbursement process; they are also used to influence doctors in pharmaceutical prescription.

At regional and local levels, health economic analyses are also developed to make decisions about the selection of better cost-effective options in specific disease management contexts. However, the frequency and the real impact of these analyses remain restricted.

A legal national source of health economic analysis is available at the time of writing.

Pharmacoeconomic analysis in the specific Italian context started to come to light in publications at the end of the 1970s. Later, in 1997, the cost-effectiveness ratio was identified as one of the

key pricing criteria for pharmaceuticals reimbursed by the National Health Service (NHS).[65] Subsequently, the regulation of pharmaceutical pricing has been improved, including a request to producers for methodological details and the main results of pharmacoeconomic analysis evaluating the proposed pharmaceutical, as well as a request for impact analysis on the pharmaceutical budget of the National Health Service (NHS).[66] However, the inclusion of this information in the pricing and reimbursement dossier is not mandatory.

During 2003 the Law Decree regulating the establishment of the Italian Medicines Agency (AIFA) defined the relevance of cost-effectiveness in the assessment of new pharmaceuticals. In particular, the pricing of new chemical entities – for which an added therapeutic value could be expected – should consider the cost-effectiveness of the new pharmaceuticals with respect to already available pharmaceuticals with the same therapeutic indication (or in the same Anatomic Therapeutic Chemical (ATC) category (level 4)). Instead, for the introduction of pharmaceuticals without added therapeutic value, the assessment of pharmacoeconomic data is not necessary, and the pricing generally depends only on the price of already available pharmaceuticals in the same Anatomic Therapeutic Chemical (ATC) group (level 4).

In summary, health economic analysis is not mandatory in Italy for market authorisation or for pricing and reimbursement. Despite this, pharmacoeconomic evaluations are currently solicited to support the regulator's decision-making process, and pricing and reimbursement depend more on aspects related to pharmaceutical impact (on the pharmaceutical budget) and clinical effectiveness than on the magnitude of the pharmaceutical cost-effectiveness ratio. In this respect, no threshold value for the willingness to pay for one quality-adjusted life year (QALY) has been declared, and at the time of writing regulatory guidelines for the production of pharmacoeconomic evaluations have not been implemented.

5.5 Generics

In Italy, the generics market has been underdeveloped for a long time. Generics were introduced for the first time in 1996, but the main policy measures to promote the generic pharmaceutical market were launched in 2000 and they are:

1) the reference pricing (RP) scheme, under which patients pay part of the cost of high-priced products;

2) the pharmacists' right of substitution.

The share of generic pharmaceuticals in terms of value was 0.7% of the pharmaceutical market and 1.2% in terms of volume in the year 2000. In 2005, these values were 2.5% of the total

[65] CIPE Deliberation No. 5/2001 [*Deliberazione del Comitato Interministeriale per la Programmazione Economica del 30 gennaio 1997, n. 5 "Individuazione dei criteri per la contrattazione del prezzo dei farmaci" G.U. del 13 maggio 1997, No. 109].*

[66] CIPE Deliberation No. 3/2001 [*Deliberazione del Comitato Interministeriale per la Programmazione Economica del 1° febbraio 2001, No. 3 "Individuazione dei criteri per la contrattazione del prezzo dei farmaci" G.U. del 28 marzo 2001, No. 73]*

pharmaceutical market in value terms and 4.5% in volume terms. The consumption in 2005 of the total off-patent market was 24.1% of the total defined daily dose (DDD) and the corresponding expenditure was 13.1% of the net public expenditure. Furthermore, the net expenditure percentage for unbranded generics was 3.0% in 2005.

The pricing procedure for generics is explained more in detail in 3.4.2.

Table 5.1: Italy – Market share of generic pharmaceuticals by value and volume 2000-2004

Generic market share	2000	2001	2002	2003	2004
Market share by volume (%)	1.2	1.7	2.8	3.8	4.5
Market share by value (%)	0.7	0.9	1.7	2.2	2.5

Source: Simoens S and Coster S (2006), Sustaining Generic Markets in Europe - April 2006

Table 5.2: Italy – Consumption of off-patent pharmaceuticals by value and volume 2001-2005

Off-patent consumption and expenditure	2001	2002	2003	2004	2005
Consumption in DDD/1000 per day	n.a.	98.5	148.9	166.8	194.4
Consumption % DDD	2.1	14.0	20.8	21.7	24.1
Expenditure per capita (in €)	n.a.	14.8	19.7	22.0	26.8
Expenditure (net) %	0.5	7.0	9.8	10.1	13.1
Generic unbranded (net expenditure %)	n.a.	n.a.	1.7	1.9	3.0

DDD = defined daily dose, n.a. = not availbale

Source: OsMed – National Reports 2001-2005

5.5.1 Generic substitution

From 2001 generic substitution has been encouraged at pharmacy level in Italy. Pharmacists are allowed to substitute the cheapest generic if the prescription involves off-patent pharmaceuticals. Substitution by pharmacists is subject to patient agreement and the absence of physician prohibition of this. If the patient disagrees the substitution and the price of the branded pharmaceutical is higher than the reference price (price of the cheapest generic available), and the difference in price is paid by the patient (reference price system).

5.5.2 Generic prescription

In Italy doctors may use the brand name or the International Non-proprietary Name (INN) prescription or the name of the generic product. Doctors are also obliged to inform patients about the availability of generic products when the prescription concerns off-patent products.

5.5.3 Generic promotion

In 2001 the Ministry of Health launched an advertising campaign to inform patients of generic pharmaceuticals through a publication posted by mail to each family in the country.

The Italian Medicines Agency (AIFA) conducted pro-generic pharmaceutical media campaigns targeted at patients in 2007.

5.6 Consumption

Data on the utilisation and consumption of pharmaceuticals in the Italian prescription market, by value and volume, are collected by the Italian National Observatory for Pharmaceutical Use (OsMed) since 2000.

Individual consumption data are not monitored. Data on pharmaceutical use in Italy refer both to pharmaceuticals fully reimbursed by the National Health Service (NHS) and pharmaceuticals paid for by patients. Data on reimbursable pharmaceuticals are collected by “Federfarma” (the national federation of private pharmacies) and “AssoFarm” (the association of public pharmacies). Data are received from local offices (provincial) and aggregated by Region. The coverage of data at national level was approximately 90% in 2005. Data on pharmaceuticals not covered by the National Health Service (NHS) are provided by IMS Health (wholesalers to pharmacies).

6 Current challenges and future developments

This chapter covers the most pressing pharmaceutical challenges for the health care system and the future plans to find solutions to these challenges.

6.1 Current challenges

The main challenge that the pharmaceutical system faces at the time of writing is the implementation of a central database named "*Tracciabilità del Farmaco*" (Traceability of Medicines), collecting and recording information about each pharmaceutical marketed in Italy.

The project is included among the European Community (EC) obligations (Directive 2001/81/EC) and Italy has been one of the first countries to implement this with Law No. 39/2002.[67] The aim of the project is:

- to check if the so-called Essential Levels of Care (LEA) are delivered, which define a minimum of health care services provided by the State;
- to improve the pharmacovigilance activities;
- to reduce the adverse events in hospitals, where the traceability system is also a useful tool to guarantee the supply cycle and to assure the administration to the patient of the proper pharmaceutical in the correct dose;
- to monitor the packs of pharmaceuticals to prevent any kind of fraud against the National Health Service (NHS);
- to prevent and avoid possible illegal activities (counterfeiting) harmful to public health.

The "Traceability of Medicines" offers the opportunity to monitor each individual pharmaceutical pack itinerary among several subjects, from the manufacturer to the individual patient, in order to know step by step all information about that pharmaceutical.

The project was carried out in two stages: in stage 1, begun in 2005 and almost finished at the time of writing, the aim was to monitor output data for manufacturers, depositaries and wholesalers, while in stage 2, recently begun, the aim is to monitor output data and incoming data for each stakeholder, including hospitals and pharmacies.

In order to obtain the data, the subjects involved in the project have to send information about:

- the product name and the market authorisation holder;
- the identifying number code present on the pack;
- the initial and final progressive number for each market authorisation number (*Autorizzazione all'Immissione in Commercio*, AIC) reported in that batch;
- the identifying number (code) of the sender and of the receiver;

[67] Cf. footnote 34

- the batch and the expiration date;
- the price reimbursed by the National Health Service (NHS);
- the number of control package stamps they received and the number of those that will be destroyed.

The following data will be included in the central database:

- supply of the control package stamps which will have to be reported on the pharmaceutical pack;
- each individual package pathway from the manufacturer to the individual patient;
- information about the medicinal supplying value distributed to the National Health Service (NHS), according to the homogenous therapeutic category;
- consumption expressed as defined daily dose (DDD).

The advantages of the project are:

- the possibility to gain epidemiological information on the use of pharmaceuticals from both hospitals and the Region, along with their impact on health;
- analysis of prescription and use appropriateness through the availability of high-quality data;
- careful monitoring and cost estimate of pharmaceutical expenditure (PE) at national and regional levels in relation to the pharmaceutical expenditure (PE) ceiling;
- availability of more detailed information for decision-makers.

6.2 Future developments

At the time of writing the (AIFA) is implementing a structural revision of the pharmaceutical pricing method and expenditure monitoring. A further aim of the new system is better monitoring and control of the public pharmaceutical expenditure (PE).

The new pricing method will be based on the following principles:

1. the ceiling expenditure will be based at national level and at regional level (corresponding to a fixed amount of the total health expenditure (THE));
2. in the period 2007-2009 the pharmaceutical expenditure (PE) is forecast to increase by 12.8% (approximately 4% per year) with respect to the total health expenditure (THE) of year 2006, analogously to the total health expenditure (THE);
3. an expenditure ceiling will be defined for each active ingredient and for each manufacturer, with incentive mechanisms for innovative products;
4. in the event that the expenditure ceiling is exceeded, the manufactures should refund the National Health Service (NHS) through a pay-back mechanism.

7 Appendixes

7.1 References

ADF (2006) - Associazione Distributori Farmaceutici – La struttura della distribuzione intermedia farmaceutica – March 2006 available at http://www.adfsalute.it/distribuzione/struttura.asp

AIFA (2007) *Scadenza dei diritti di brevetto sui farmaci* – Centre for Studies - January 2007

Corte dei Conti (2005) (Court of Auditors) - Sezione delle autonomie (2005). *Relazione sulla gestione finanziaria delle Regioni. Esercizi 2003 – 2004*. Deliberazione n. 7/2005. Rome, 2005

EUROSTAT (2003*) General and regional statistics* (2003 data), available at (last access 02 October 2006): http://epp.eurostat.ec.europa.eu.

Farmindustria (2006) *Indicatori farmaceutici 2006* – Centro Studi. Roma. Available at: http://www.farmindustria.it/Farmindustria/html/indicatori_farmace.asp?anno=2007&menu2expand=elTwo.

ISTAT (2005) – Istituto Nazionale di Statistica – Health for All database - available at http://www.istat.it/dati/dataset/

ISTAT (2007) – Istituto Nazionale di Statistica – Health for All database - available at http://www.istat.it/dati/dataset/

Ministero della Salute (2005). Direzione generale del Sistema Informativo. Ufficio di Direzione Statistica: Attività gestionali ed economiche delle ASL ed aziende ospedaliere. Annuario statistico del Servizio Sanitario Nazionale. Anno 2004. Rome, May 2005

OECD (2006) *Health Data 2006 – Statistics and Indicators for 30 Countries* – June 2006

OECD (2006b) *Factbook 2006: Economic, Environmental and Social Statistics* (2003 data), http://stats.oecd.org/WBOS/ViewHTML.aspx?QueryName=187&QueryType=View&Lang=en, last access 2 October 2006.

OsMed (2000-05) Osservatorio Nazionale sull'Impiego dei Medicinali / Italian National Observatory for Pharmaceutical Use - *The use of pharmaceuticals in Italy* – National Reports years 2000-2005

Simoens S and Coster S (2006), Katholieke Universiteit Leuven – Research Center for pharmaceutical care and Pharma-economics – *Sustaining Generic Markets in Europe* – Belgium, April 2006

7.2 Further reading

Annessi Pessina E., Cantù E. Whither managerialism in the Italian National Health Service? Int J Health Plann Manage 2006; 21(4): p. 327-55

France G. Taroni F. The evolution of health policy-making in Italy. J Health Polit. Policy Law 2005; 30(1-2): p. 169-87

Garattini L, Ghislandi S., Off-patent drugs in Italy: a short-sighted view? Eur J Health Econ 2006; 7 (1): p. 79-83

Ghislandi S, Krulichova I, Garattini L. Pharmaceutical policy in Italy: towards a structural change? Health Policy 2005; 72 (1): p. 53-63

Health Care System in transition – Italy Profile - European Observatory on Health Care Systems, 2001 available on http://www.euro.who.int/observatory/Hits/TopPage
Health Report 2005 – Seven Keywords of NHS – CEIS Health Report 2005 available on: http://www.ceistorvergata.it/sanita/index.asp

Highlights on health in Italy, WHO Regional Office for Europe, Copenhagen 1998 (http://www.who.dk/country/ita01.pdf)

Jommi C, Fattore G. Regionalisation and drugs cost-sharing in the Italian NHS, Euro Observer 2003; 3: p. 1-4

Jommi C., Paruzzolo S., Public Administration and R&D localisation by pharmaceutical and biotech companies: a theoretical framework and the Italian case study. Health Policy 2007; 81: p. 117-130

Management of the Italian National Health System: Complexity and Perspectives of the New Institutional Set-Up - CEIS Health Report 2006 Donia Sofio A. Meneguzzo M. Mennini F.S. Spandonaro F. - CEIS - Sanità, Faculty of Economics, University of Rome "Tor Vergata
able on: http://www.ceistorvergata.it/sanita/index.asp

Mapelli V, Lucioni C. Spending on pharmaceuticals in Italy: macro constraints with local autonomy. Value Health 2003; 6 (Suppl 1): p. 31-45

Pharmaceutical Pricing and Reimbursement - Italy profile - Jommi C. *University Luigi Bocconi, Milano* available on: http://ec.europa.eu/enterprise/phabiocom/docs/tse/italy.pdf

Rapporto OASI – Osservatorio sulle Aziende Sanitarie Italiane, CERGAS, Università Bocconi (2006), now available on-line (www.unibocconi.cergas.it)

Rapporto Osservasalute 2006 – Stato di salute e qualità dell'assistenza nelle regioni italiane – Osservatorio Nazionale sulla salute delle regioni italiane, Italy available on http://www.osservasalute.it/

7.3 Web links

The Italian Medicines Agency (AIFA)	http://www.agenziafarmaco.it
Ministero della Salute	http://www.ministerosalute.it
Ministero dell'Economia e delle Finanze	http://www.tesoro.it
Federfarma	http://www.federfarma.it
ADF/ Wholesalers	http://www..adfsalute.it
Farmindustria	http://www.farmaindustria.it
Assogenerici	http://www.assogenerici.org
Cittadinanza attiva	http://www.cittadinanzattiva.it
Eurostat	http://epp.eurostat.ec.europa.eu/portal/page?pageid=1090,30070682,1090_33076576&_dad=portal&_schema=PORTAL

7.4 Detailed description of authors

Editors

Dr. Nello Martini – General Director – Italian Medicines Agency (AIFA)

Dr. Pietro Folino Gallo – Head of Centre for Studies – Italian Medicines Agency (AIFA)

Dr. Simona Montilla - Centre for Studies – Italian Medicines Agency (AIFA)

Contributors

Prof .Eugenio Anessi Pessina – Chatolic University of Rome "Sacro Cuore"– *Chapter 1 Background (excepted Sec.1.1)*

Prof. Giuseppe Gesano – Istituto di ricerca sulla popolazione e le politiche sociali – Consiglio Nazionale delle Ricerche (CNR), Rome – Italy– *Section 1.1 - Demography*

Dr. Luisa Muscolo – OsMed Co-ordination Unit – Italian Medicines Agency (AIFA) – *Section 2.1.3.4 Hospitals*

Dr. Pier Luigi Russo – OsMed Co-ordination Unit - Italian Medicines Agency (AIFA) – *Section 5.4 Pharmaco-economics*

Dr. Daniela Settesoldi – Centre for Studies – Italian Medicines Agency (AIFA) – *Section 6.1 Current Challenges*

Acknowledgements

Dr. Mario Bruzzone – Head of Pricing and Reimbursement Unit – Italian Medicines Agency (AIFA)

Dr. Silvia Fabiani – Head of Quality Assurance Unit – Italian Medicines Agency (AIFA)

Dr. Domenico Nicola Caiazza – Pricing and Reimbursement Unit – Italian Medicines Agency (AIFA)

The figure on page 4 was kindly provided by Dr. Frank Heins – Istituto di ricerca sulla popolazione e le politiche sociali – Consiglio Nazionale delle Ricerche (CNR), Italy