Agenzia Italiana del Farm AIFA

Central and Eastern European Society of Technology Assessment in Health Care EESTAHC

# Pharmaceutical Risk-sharing and Conditional Reimbursement in Italy

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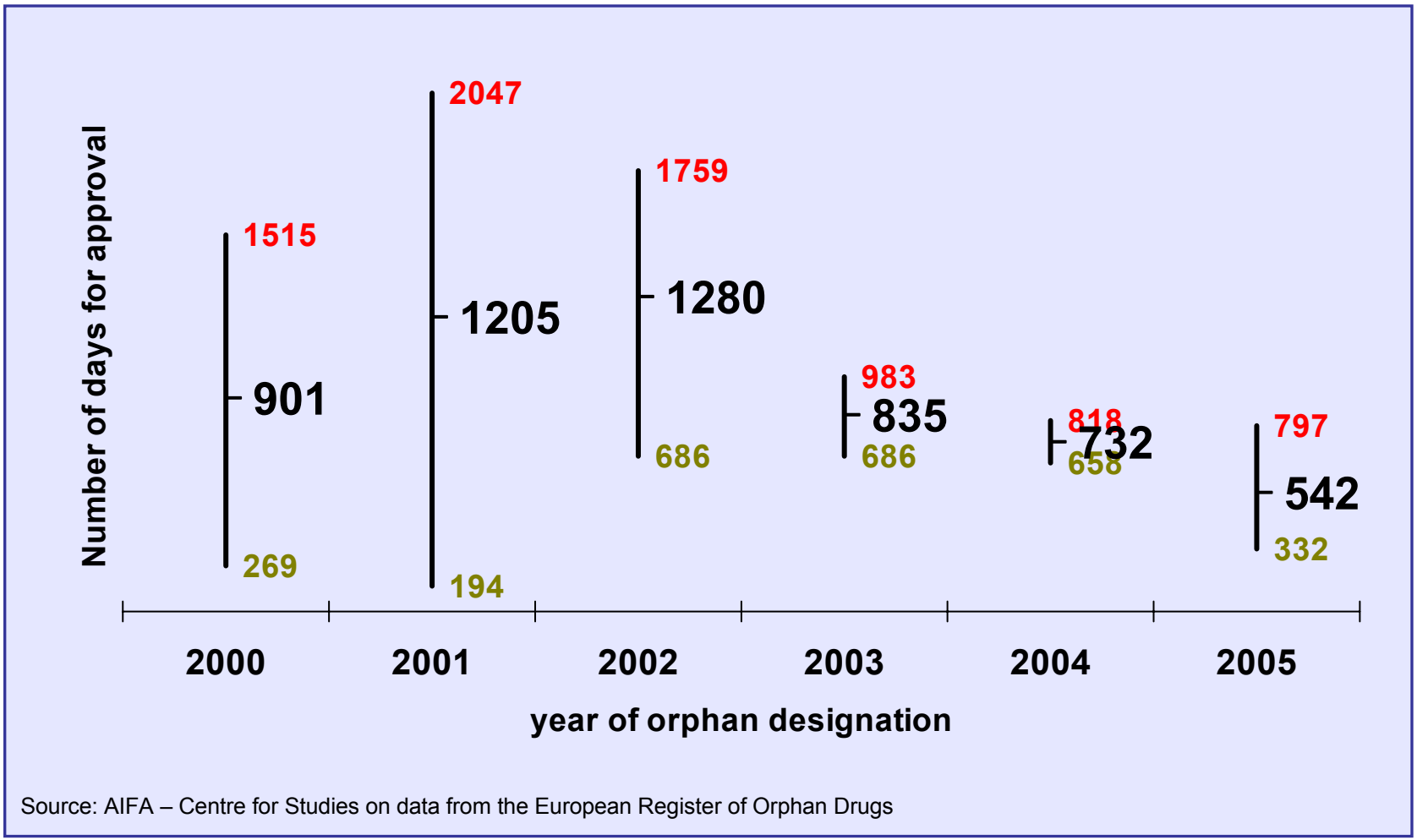
# Outline

- Clinical Context
- Economic context
- The Italian Registers
- Rish sharing agreements
- Conditional reimbursement

# Problems to be managed at the time of approval

- Differences between clinical trials and every day practice (external validity of RCTs)
  - *Younger and healthier* population
  - Some populations are under represented
  - Surrogate end-points
  - Few comparative data
  - Few data on long term effects
- Medicines may be approved by faster track or under exceptional circumstances
- Targeted medicines intended for specific subsets of patients

# Number of days from EMEA orphan designation to marketing approval (Oct. 2007) (min,average and max values)




Source: AIFA – Centre for Studies on data from the European Register of Orphan Drugs

# Specificity and Sensitivity

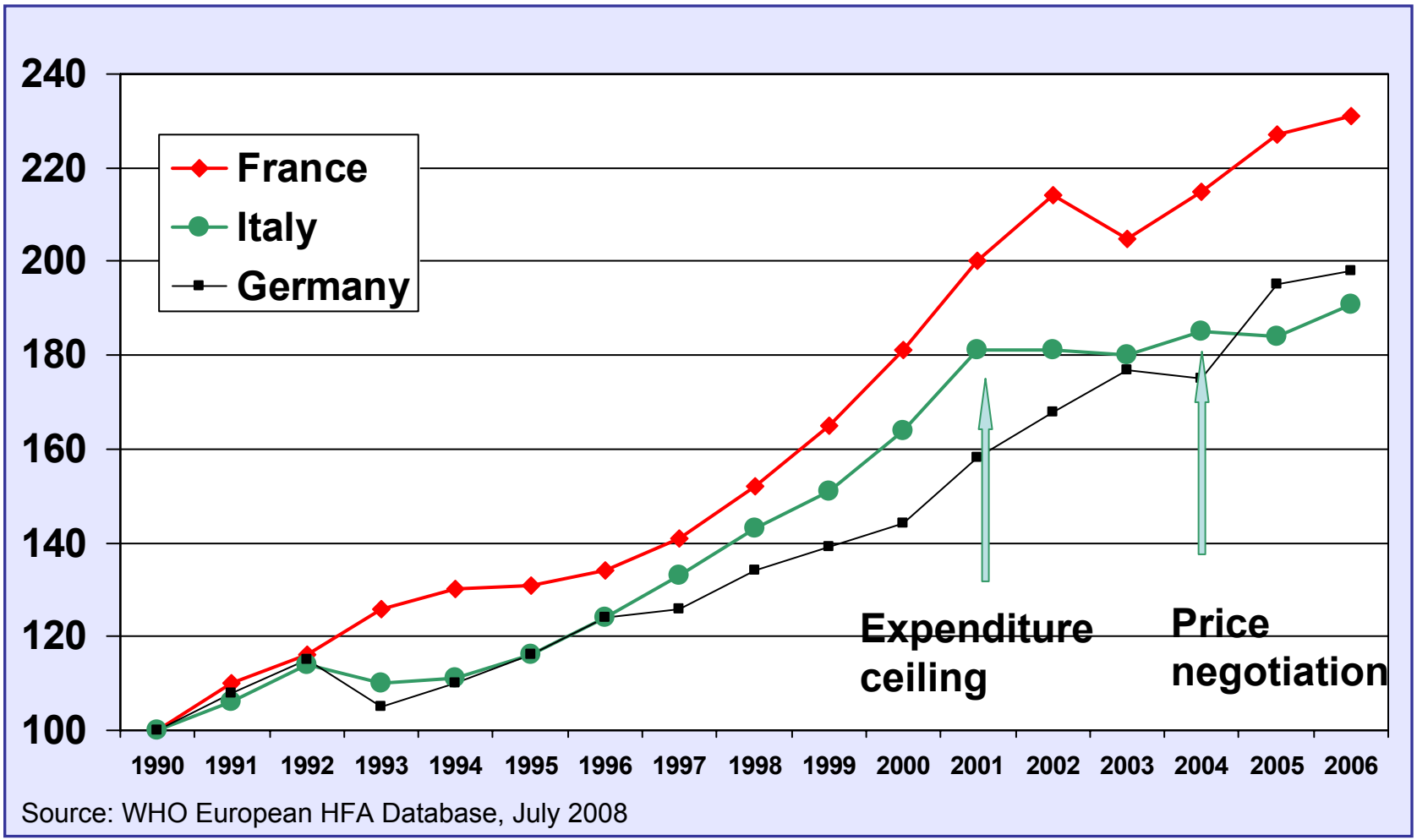
## of some diagnostic tests

| Test | Specificity | Sensitivity | Indication | Reference |
|---|---|---|---|---|
| TPMT *3A, *3C, *2 | 99% | 90% | Acute lymphoblastic leukemia (ALL) | Scheffeler et al., Pharmacogenetics. 2004 Jul;14(7):407-17 |
| HER2 - IHC | 98% | 66% | Breast Cancer | Ainsworth et al., J Clin Pathol. 2005; 58(10):1086-90. |
| UGT1A1*28 | 95% | 22% | Colorectal cancer | www.fda.gov/ohrms/dockets/AC/05/slides/2005-4137S1_08_Venitz.ppt |

- Specificity = proportion of people free of a disease who have a negative test
- Sensitivity = proportion of people with disease who have a positive test

# Time course in pharma expenditure

## (1990-2006; 1990 = 100)




Source: WHO European HFA Database, July 2008

# Price cuttings in Italy 2004-2006

| | |
|---|---|
| 2004 Jun | Generalised price cutting (6.8%) |
| 2004 Dec | Selective price cutting (max 10%) |
| 2005 Jul | Continuation of the 6.8% cut |
| 2005 Dec | Generalised price cutting (4.4%) |
| 2006 Jul | Increase of the cut from 4.4 to 5%<br>Selective cut for all the medicines with an increase higher than the national average |
| 2006 Sep | Price cut 5% |
| 2006 Dec | Prolongation to the 2007 of the cutting |

# The new Italian system (since Jan. 1, 2008)

- New ceilings
  - 14% of the NHS expenditure in primary care
  - 2.4% of the NHS expenditure in hospital
- Pay back in case of over expenditure in primary care, according to the budget assigned to every company at the beginning of every year
- Savings from patent expiration (generics) transferred to innovative medicines

# Hospital Expenditure for medicines 2006

| | € mill | % |
|---|---|---|
| *Antineoplastic and immunomodulating agents* | *1341* | *32,37* |
| *Antiinfectives for systemic use* | *1066* | *25,73* |
| *Blood and blood forming organs* | *688* | *16,61* |
| *Nervous system* | *332* | *8,01* |
| *Sub - total* | *3427* | *82,72* |
| ... | | |
| *Total* | *4143* | 100 |

# The access to cancer medicines in UK

- Some anticancer medicines are not reimbursed by the NHS
- **But** patients may buy theirselves the medicine and then can receive it in a NHS hospital

- Richards' report - Improving access to medicines for NHS patients (November 2008)

Minimising the number of patients who may want to purchase additional medicines

# THE MAIN QUESTION

- **Clinical or economic problem ?**

- A better knowledge of the place in therapy of the newer medicines is in the interest of patients (obtaining clinical results and avoiding useless risks)
- A sustainable health care system is in the interest of patients (equitable access)

# Italian Registers

# Italian National Registers

- To provide data on
  - medicine and posology prescribed
  - disease state and progression
  - adverse events
  - treatment withdrawals for any reason

**To monitor the appropriate use of given medicines**

**Information on the *therapeutic value* in clinical practice**

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# Farmaci sottoposti a monitoraggio

**Programmi generali:**

- Farmaci antineoplastici
- Farmaci orfani
- Farmaci per la psoriasi
- Farmaci anti HIV
- Farmaci antipsicotici
- Farmaci antidiabetici
- Farmaci cardiovascolari

**Progetti specifici:**

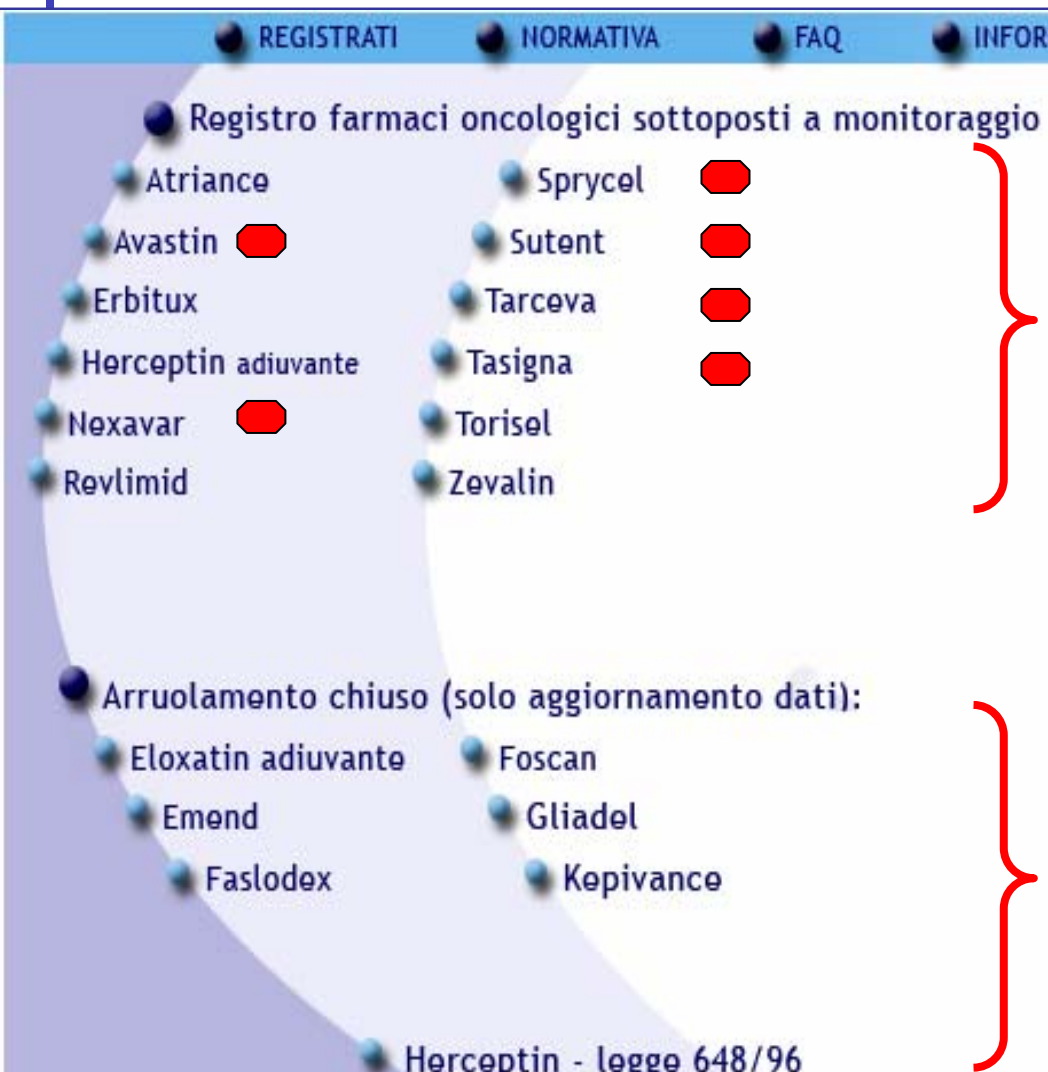
- Tysabri
- ADHD
- Xolair
- Xagrid
- Xigris

Con il Registro dei farmaci a monitoraggio l'agenzia Italiana del Farmaco AIFA, intende mettere a disposizione degli operatori sanitari un punto di accesso unificato ai progetti di monitoraggio che sono richiesti, laddove necessario, a complemento delle determinazioni di immissione in commercio delle singole specialità medicinali (in luogo delle precedenti schede di rilevazione dati cartacee).

Il Registro unificato intende porsi come strumento innovativo di comunicazione con l'Autorità regolatoria, per una efficace semplificazione degli iter burocratici richiesti dalle procedure e per l'avvio di un processo virtuoso in grado di supportare una sempre migliore pratica clinica a tutela del paziente.

***http://monitoraggio-farmaci.agenziafarmaco.it***

http://monitoraggio-farmaci.agenziafarmaco.it




- Open registers

- Registers closed (only update for the ongoing patients)

# Number of patients registered in the Italian Register of Oncological Medicines (>43,000 pts)

| Medicine | Registered | Concluded |
|---|---|---|
| AVASTIN | 5252 | 1702 |
| ELOXATIN | 5479 | 2907 |
| ERBITUX | 3534 | 1599 |
| FASLODEX | 5592 | 2046 |
| HERCEPTIN | 5090 | 1265 |
| NEXAVAR | 2148 | 0 |
| TARCEVA | 7415 | 3389 |
| …….. | …… | …… |

# Risk-sharing agreements

# Risk sharing

**Ex-post evaluation and reimbursement:**

- **If the medicine is effective is paid by the NHS**
- **If it is ineffective company reimburses the amount**

- **Advantages**
  - **Avoiding to exclude from reimbursement some medicines which could be of some help to some patients**
  - **Facilitating a quicker access after the medicine has received EMEA approval**
  - **Possibility to collect data on real use**
  - **Avoiding useless expenses to the NHS (sustainability)**

# Legal framework

- No specific legal framework for risk-sharing agreements
- According to the legislation for pricing and reimbursement decisions (negotiation procedure)
- A risk-sharing agreement, as suggested by the AIFA Oncologic Working Group, is agreed between AIFA (P&R Committee) and Markeying Authorisation Holder during the negotiation procedure

# Medicines on a Risk-sharing agreement

**Erlotinib (Tarceva®, Roche)**
NSCLC after failure of at least one prior chemotherapy regimen

**Sunitinib (Sutent®, Pfizer)**
Metastatic renal cell carcinoma (first and second line treatment)

**Sorafenib (Nexavar®, Bayer)**
Renal cell carcinoma (second line treatment)
Hepatocellular carcinoma

**Dasatinib (Sprycel®, BMS)**
Chronic myeloid leukaemia and Acute lymphoblastic leukaemia

**Bevacizumab (Avastin®, Roche)**
metastatic carcinoma of the colon or rectum
breast cancer
NSCLC
advanced and/or metastatic renal cell cancer

**Nilotinib (Tasigna®, Novartis)**
Chronic myeloid leukaemia

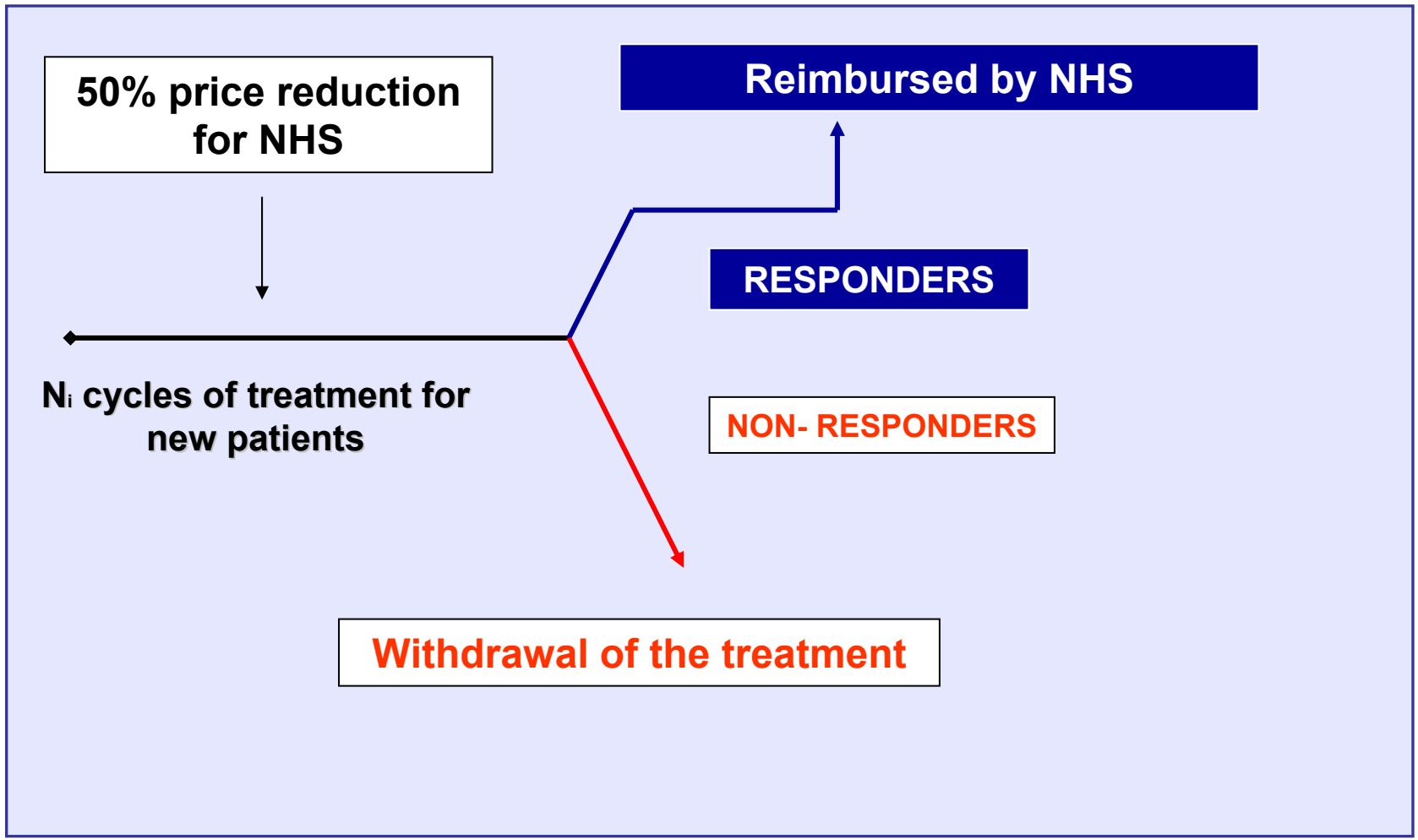
# How a new medicine is included in a negotiation for Risk-sharing agreement

## Proposal

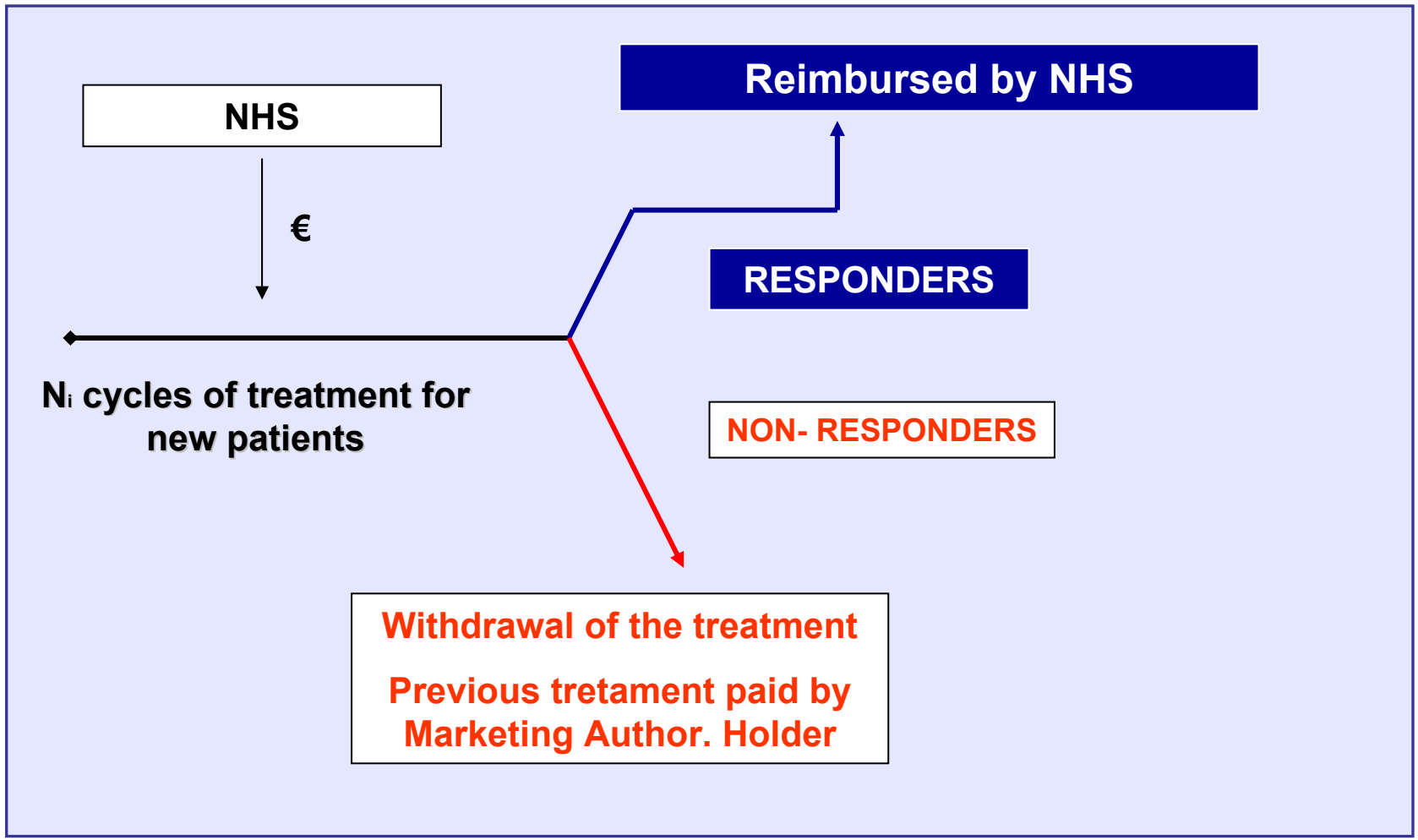
**suggested by the AIFA Oncologic Working Group on the following criteria:**

- **Epidemiological data of the disease**
- **Possibility to clearly define a subset of population responsive to the treatment**
- **Results from clinical trials**

# Risk sharing procedure (i)



# Risk sharing procedure (ii)



# Conditional reimbursement

# Conditional reimbursement

***NEW MEDICINES* with:**

- **A new mechanism of action**
- **Marketing Authorisation based on non-inferiority trials**

***Potential innovative medicine***

***CONDITIONAL REIMBURSEMENT MECHANISM***

**The medicine is reimbursed for a limited period of time, under specific conditions, waiting to be re-evaluated**

# Conditional reimbursement

***MAIN OBJECTIVES***

- **to evaluate the utilisation in clinical practice**
- **to collect epidemiologic data**
- **to get additional information on the efficacy / safety profile for the re-evaluation**

***DESCRIPTION***

Period of time in which AIFA **reimburses** and **monitors** the drug considered as **potential innovation**

Treatments will be initiated only by specialist centres selected by the Italian Regions

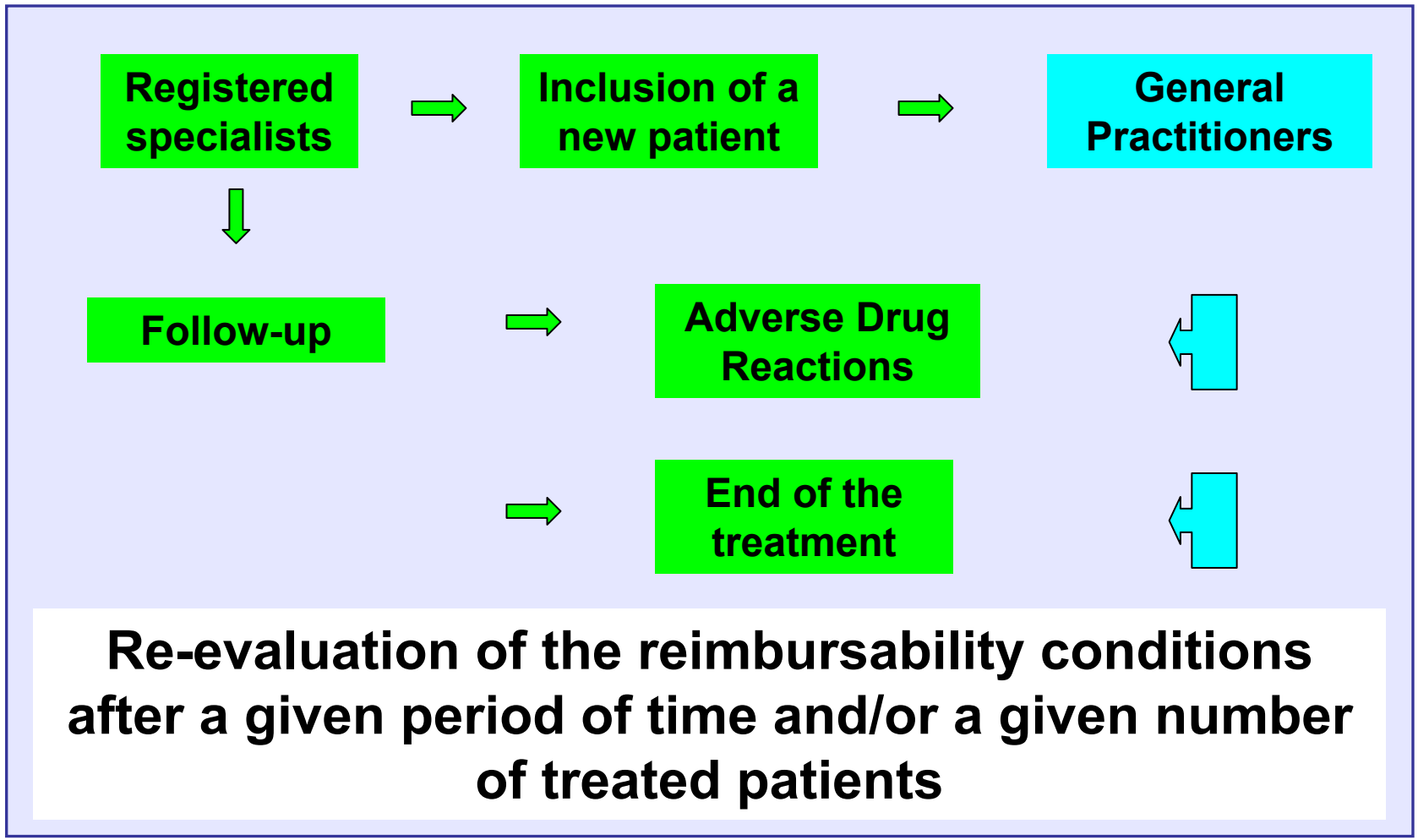
# Conditional reimbursement

**Medicines on conditional reimbursement from January 2008:**

- **Ivabradine** — **for chronic angina pectoris**
- **Exenatide**
- **Sitagliptin**
- **Vildagliptin**

} **for type 2 diabetes mellitus (in pts. resistant to oral antidiabetic treatments)**

# Flow of conditional reimbursement



# New antidiabetics (Oct. 2008)

- Number of centers 1,495
- Number of specialists 3,981
- Number of patients 16,750
- 3.41 x 10,000

- 126 withdrawals for ADRs
- 1,161 (7%) withdrawal for therapeutic failure

# Conclusions

- Italy is trying to develop new strategies for conciliating equal access and sustainability for newer medicines
- Risk sharing seems promising but further evaluation of its health and budget impact is needed