Perspective from the Generics Drug Industry (GDI)

9 October 2014

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Overview

1. Generic Drug Industry
    1. Hatch Waxman Act
    2. Generic Utilisation
    3. Future
2. Generic Industry Value
3. Challenges/Opportunities
    1. Generic Marketplace & Supply
    2. Quality
    3. Application review
    4. Improving the value offering of generic drugs

1. Generic Drug – Definition

- A generic drug is comparable to a brand name drug in dosage, safety, strength, how it is taken, quality, performance, and intended use.
- Regulated identity, strength, quality, purity, and potency
- The same rigor applied in regulatory process
- Interchangeable with originator product
- Interchangeable multi-source pharmaceutical products (IMPP)
- Generic Drug Industry (GDI)

http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm

The Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act)

Development of the generic drug industry in the US after the Hatch-Waxman Act of 1984

Garth Boehm, et al

2013

1. Generic Market History - Hatch-Waxman Act

- The modern generic industry – passage of the 1984 **Hatch-Waxman Act**.
- Created an abbreviated regulatory process that facilitated low-cost generic entry (ANDA)
- The purpose of the Act was "to make available more low cost generic drugs by establishing a generic drug approval process for pioneer drugs first approved after 1962."
- The results of the act seek to **balance the interests** of the branded manufacturers with those of generics

H.R. Rep. No. 98-957, Pt. 1, at 14 (June 21, 1984)
Novo Nordisk A/S, et al. v. Caraco Pharmaceutical Laboratories, Ltd., et al., No. 2010- 1001 (Fed. Cir., April 14, 2010)

Drug Efficacy Amendments of 1962

Hatch Waxman Act signed into place

1962

1984

1. GDI vs Innovator Manufacturers

Hatch-Waxman: A Delicate Balance	
Encourage Competition	**Reward Technological Advance**
GENERIC MANUFACTURERS	**BRAND MANUFACTURERS**
• ANDA Process—only "bioequivalence" required • Allows Testing Before the Brand Patent Expires • Creates Incentive 180-Day Exclusivity—for first successful ANDA filer	• Defines the conditions for patent extensions -100% approval time + 50% testing time -up to max extension of 5 years -patent cannot be extended beyond 14 years • Non-Patent Exclusivity -NDA data kept as proprietary by FDA -5 years' data exclusivity for New Chemical Entity -excluding salts or esters -3 years' data exclusivity for improvements to approved brand products via clinical trials (eg, new uses, dosage form, dosage regimens) • Sets forth a process for patent challenges

1. Post Hatch –Waxman Act period

- Opportunity and profits
- Beginning of modern GDI was marked by fraud and other criminality
- The Generic Drug Scandal
- 1984 to 1989
- Late 1990 the public's faith in both the FDA and GDI was shaken

Development of the generic drug industry in the US after the Hatch-Waxman Act of 1984 Garth Boehm, et al, Acta Pharmaceutica Sinica B 2013;3(5):297–311

13 %

84 %

Drug Efficacy
Amendments of 1962

Hatch Waxman Act
signed into place

1962

1984

2012

Only 35 % of top-selling branded drugs with expired patents had generic competition

1. Generic brands vs innovator brands

- Although generic medicines reduce the direct cost of medicine, not all users want a more affordable version of their product
- Those that can afford it, still want the medication that they are used to in terms of branding
- Right of the consumer to be able to make a choice between originator and generic version of products need to be respected
- Place for both innovator and generics in the market place

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Indian Court Rules in Favor of Generic Gleevec

By Jessica Wapner
Posted: April 2, 2013

Yesterday, the Indian Supreme Court ruled against Novartis's claims of patent protection for Gleevec, which would have prevented generic drug makers in India from producing and selling the drug, which is used in the treatment of th otherwise fatal blood cancer chronic myeloid leukemia and other types of cancer.

There are many issues to delve into with this decision. For the moment, in honor of this landmark decision, here is a reposting of my write-up on the case originally posted here last September, which offers some background on the case.

* * *

The Battle Over Generic Drugs in India (and Elsewhere)

A few days ago, in a courtroom in India, a landmark ruling was made that could impact future legal battles over the sale of generic versions of expensive medications in India. When the Delhi High Court rules that Cipla, the country's largest drug maker, could sell its own version of the lung cancer drug, Tarceva (erlotinib), made by Roche. The generic version will reportedly cost about a thir of the proprietary version.

The lawsuit had been brought by Roche against Cipla. Roche accused Cipla of patent infringement, but the judge, Justice Manmohan Singh, sided with Cipla, agreeing that the generic version has a different molecular structure from Roche's original. The ruling upholds Roche's patent on its molecular structure, but allows Cipla to produce its own version, which (presumably) has the same mechanism of action and yields the same outcomes as the Tarceva molecule. Th

http://blogs.plos.org/workinprogress/2013/04/02/indian-court-rules-in-favor-of-generic-gleevec/

Gilead licenses generic hepatitis C drug in India

23 September 2014 Phillip Broadwith

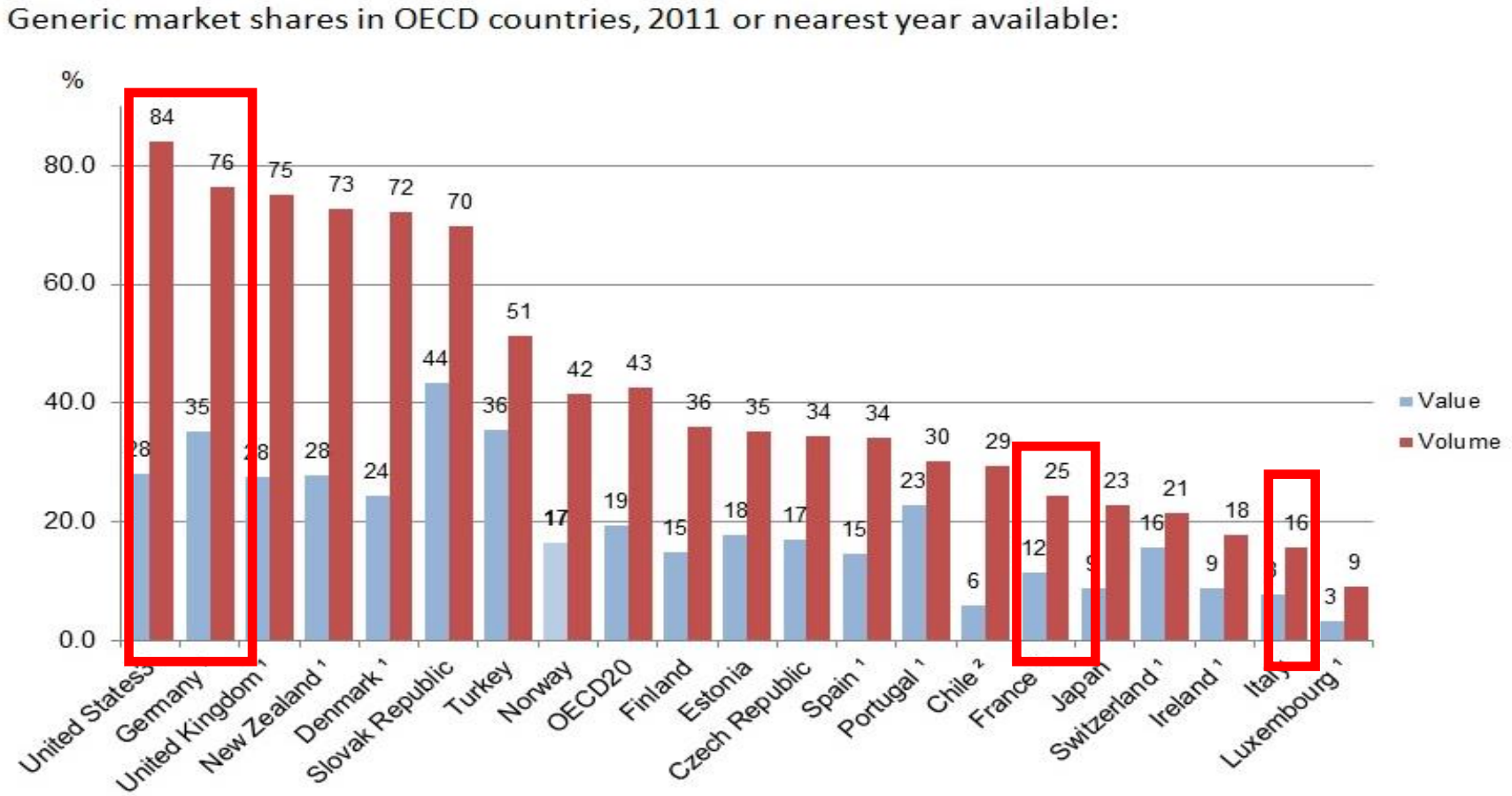
Gilead has granted licenses to seven generic drugmakers to produce its blockbuster hepatitis C drug Sovaldi (sofosbuvir) in India and 90 other developing nations. The company will give each licensee a full technology transfer, in exchange for 7% royalties on all sales.

The move counters several problems Gilead could otherwise face in India. Firstly, there is doubt over whether India would grant a patent for sofosbuvir, since the drug is already approved in the US and EU, and India has a history of refusing patents for molecules 'already in the public domain'. Lack of patent protection would leave Sovaldi open to generic competition. By granting licenses, Gilead at least gets a share of sales.

At the same time, it goes some way towards appeasing activist groups, which have criticised the company for the high prices it has set for Sovaldi. Generic manufacturers will be allowed to set their own prices, which could bring the treatment within the budgets of many more patients.

In USA, pool of 3mil patients x $84,000

1. Generic Utilisation in Organisation for Economic Co-operation and Development (OECD) markets

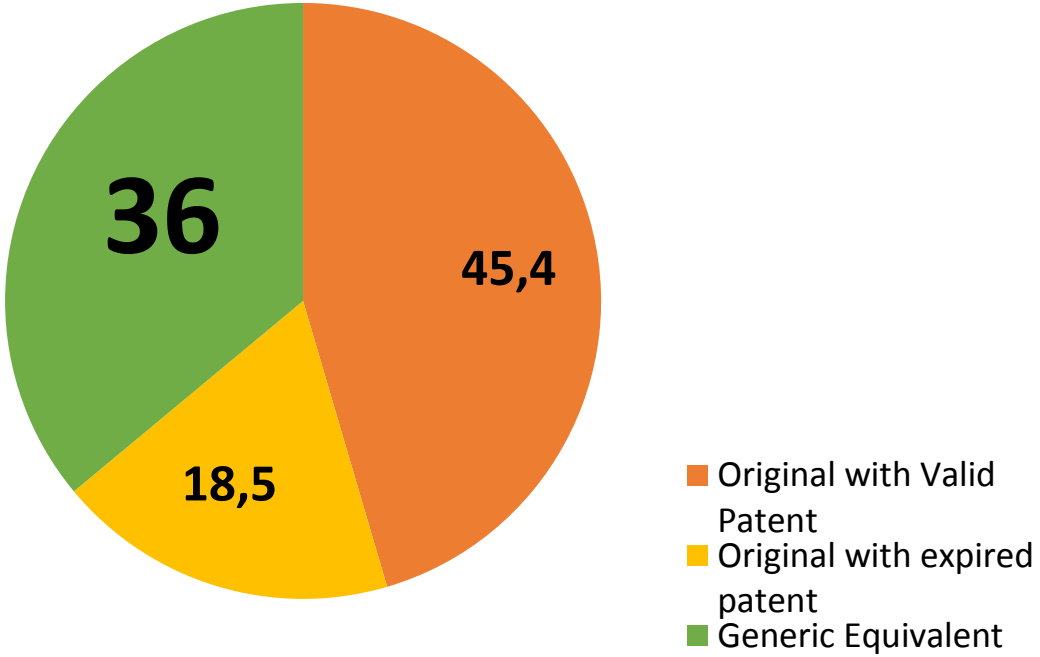


1. Reimbursed pharmaceutical market. 2. Community/retail pharmacy market. 3. For 2012

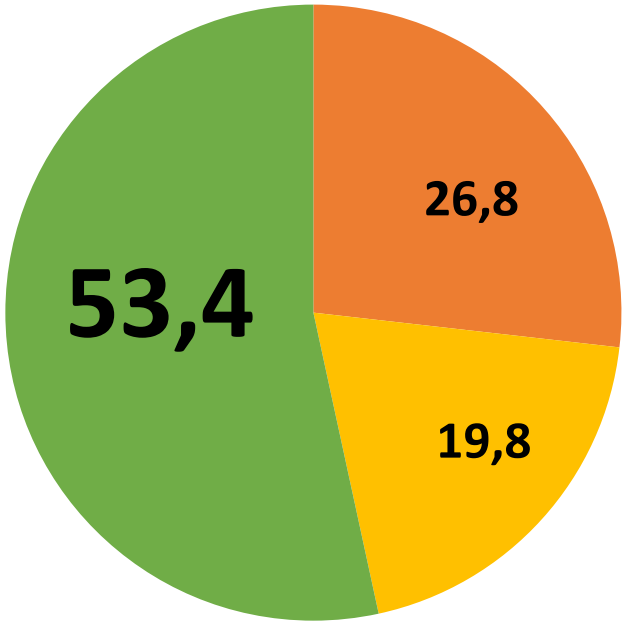
Source: OECD Health Statistics 2013, and IMS, 2013

SA generic utilization in private market: 2012

Expenditure %

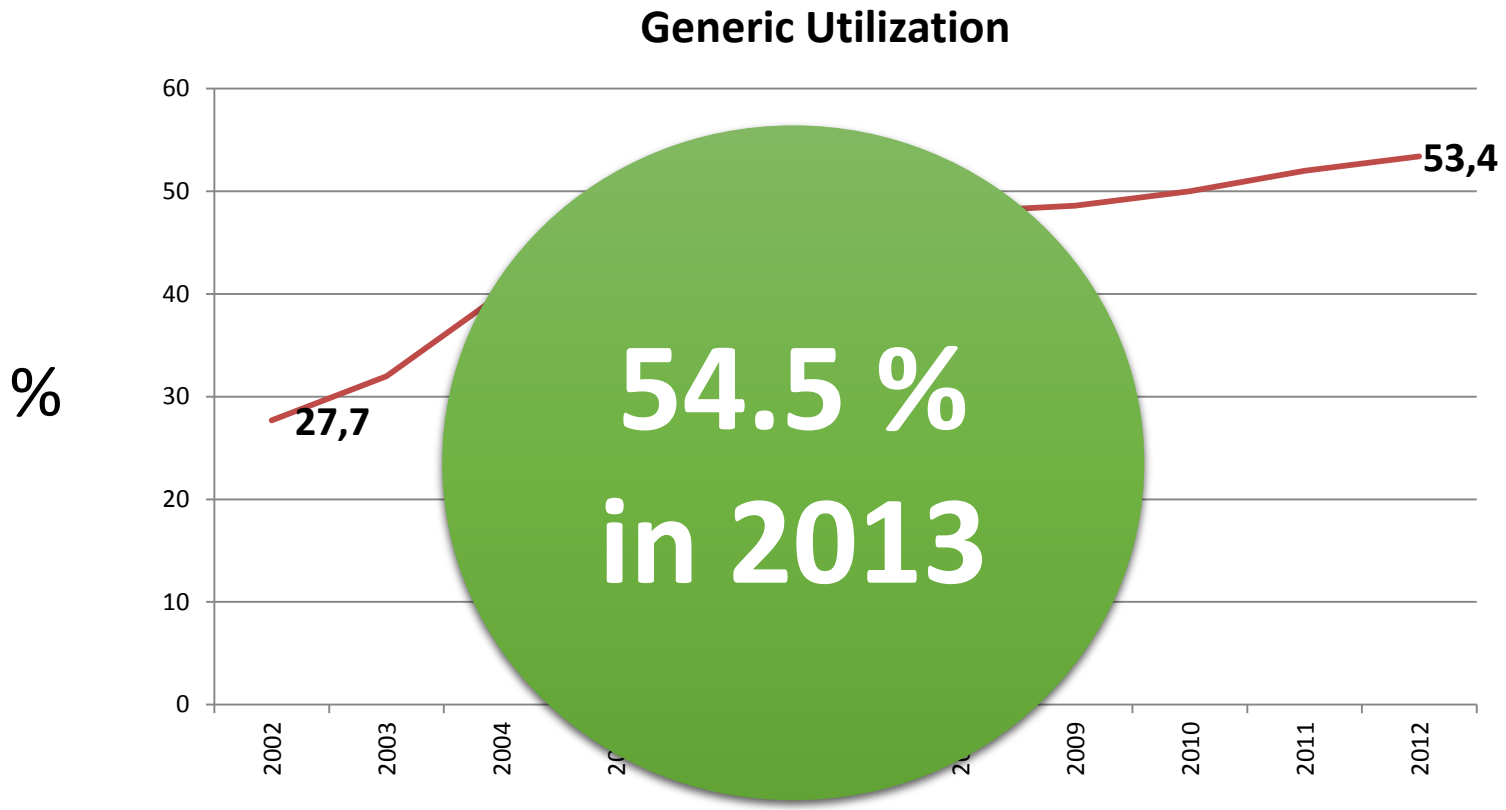


Volume %



Mediscor 2012 Review

SA Volume of generic utilization 2002-2012



Mediscor 2012 Review

1. GDI Overview – Global Factors

1. New players are intensifying competition
2. Downward pressure on prices through tender systems
3. More complex product portfolios
4. Managing a generic company while maintain a lean structure and striving for cost leadership has become more complex
5. Quality control in manufacturing remains a challenge

Generating Value in Generics: Finding the next 5 Years of Growth – Report by McKinsey and Company June 2013

2. Generic Industry Value

Improves affordability and availability

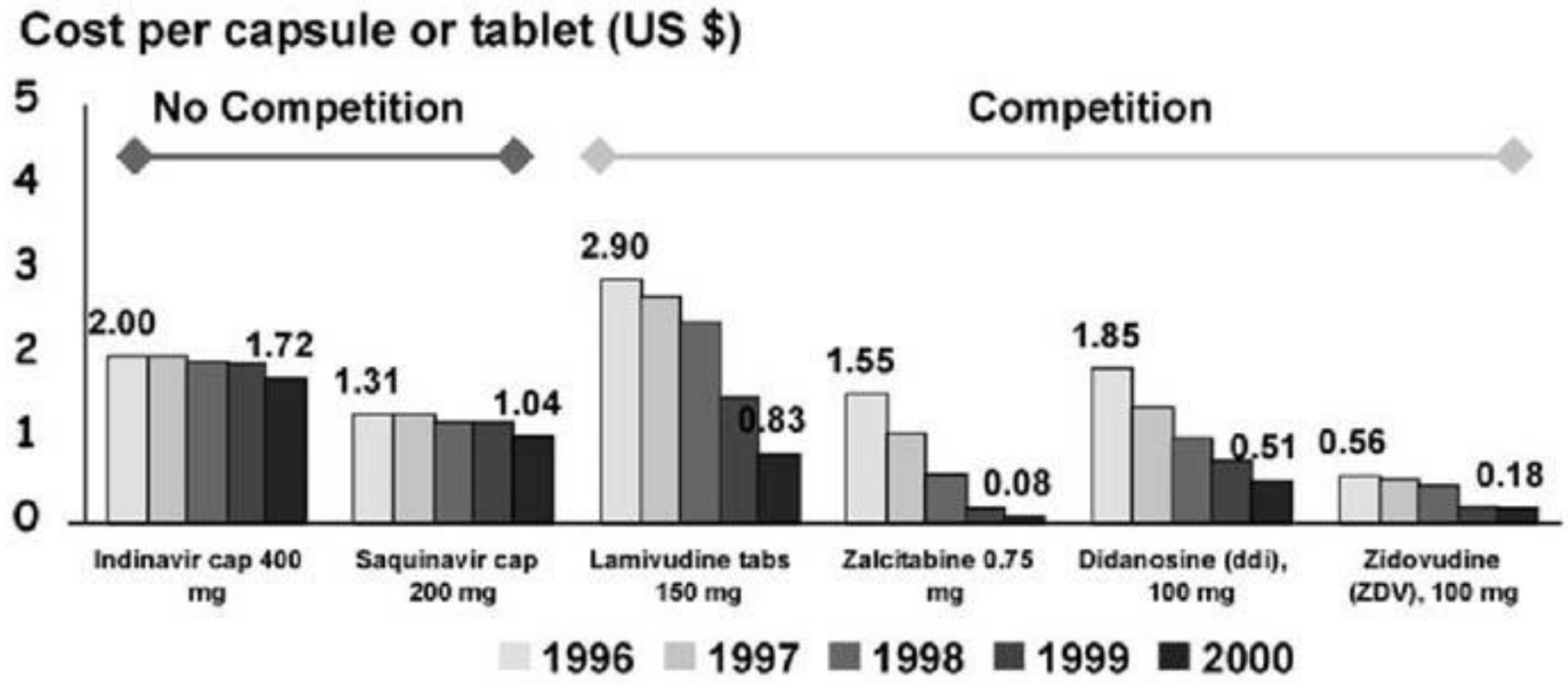
2. Savings due to Generic Drug use

$1.2 trillion in savings

2003 2012

http://blogs.fda.gov/fdavoice/index.php/2014/09/celebrating-30-years-of-easier-access-to-cost-saving-generic-drugs/#sthash.d6mRCron.dpuf

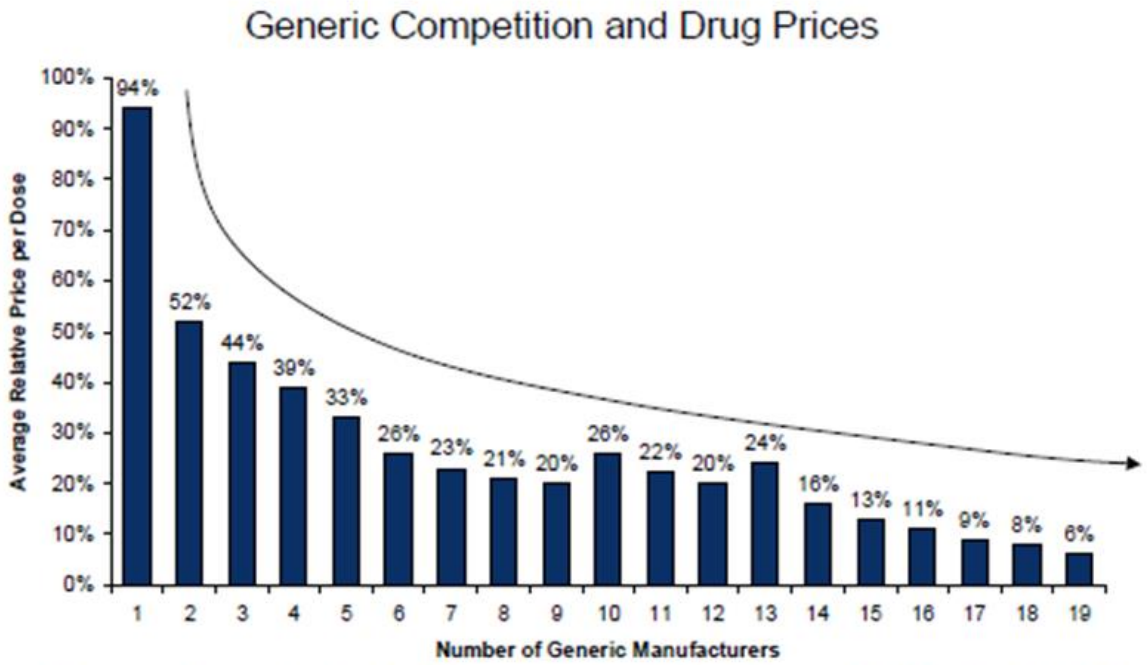
2. Increase availability and affordability



http://apps.who.int/medicinedocs/en/d/Js4912e/3.10.html#Js4912e.3.10

Generic Industry competition

U.S. Prescription Market



Note: Average relative price is defined as the average price / brand price. Data based on an analysis of IMS retail sales data for single-ingredient brand name and generic drug products sold in the U.S. from 1999 through 2004.

Source: FDA website, FDA Analysis of Retail Sales Data from IMS Health, IMS National Sales

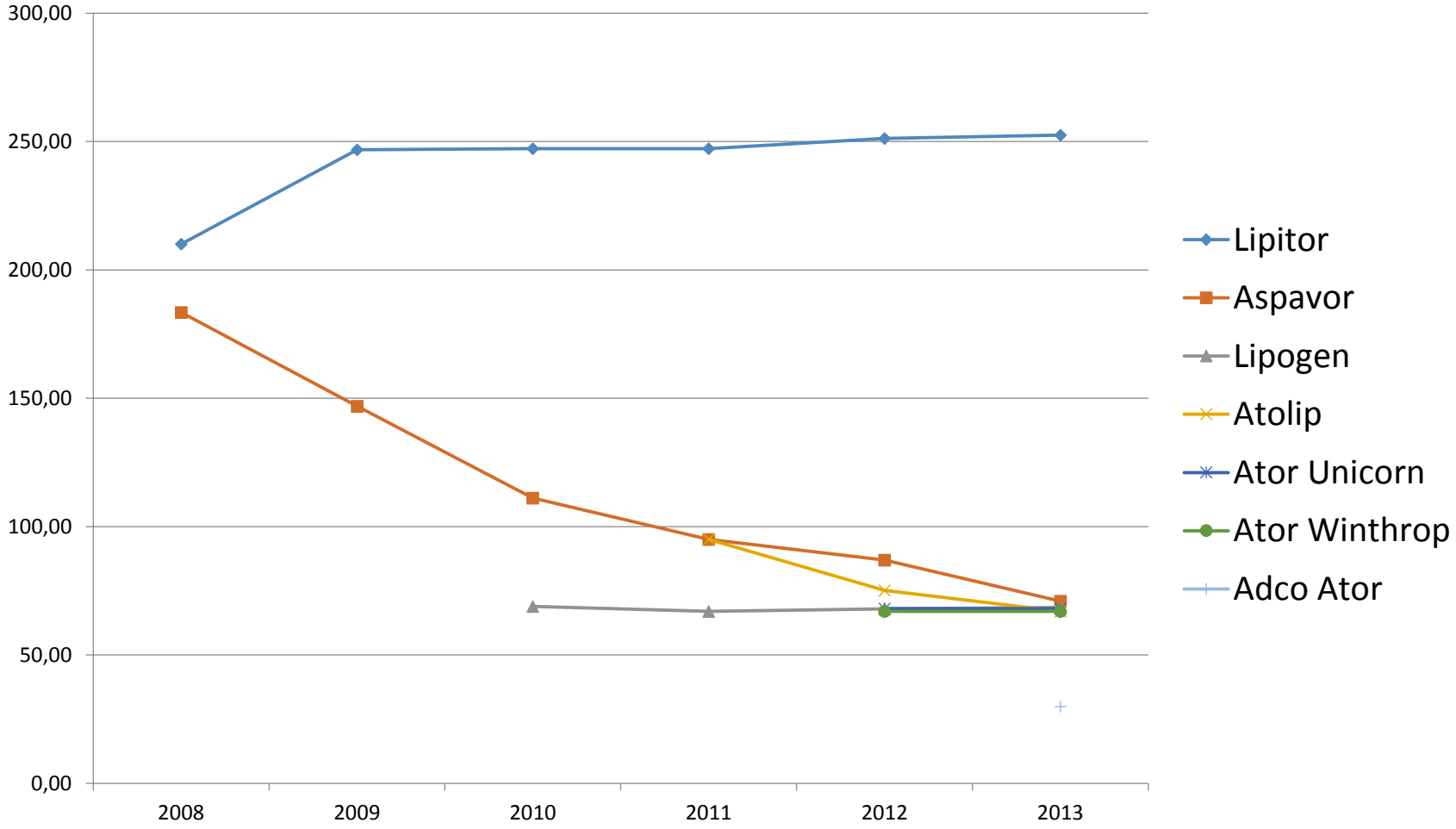
When there is only one generic competitor, the cost of a medication to a buyer drops only slightly below that of the branded equivalent. These days, most generics start with two suppliers: the first-to-file manufacturer and the one selling an "authorized" version, which is the branded product being sold through the generic distribution channel. When that is the case, the price drops almost immediately to about 50% of the brand. At the end of the 180 days of exclusivity, additional manufacturers usually enter the market, and the price continues to drop.

2. GDI Value – Sri Lanka

- The difference in price between originator brands and the lowest price generics ranged from 5 x to 100 x more expensive
- Salary of the **lowest paid unskilled government worker** in Sri Lanka can buy more than **67 % of essential medicines with** less than a single day's wages (month's supply)
- Generic meds was more available than originator brands
- Most of the medicines were affordable to Sri Lanka's lowest income earners.
- Many generic brands and generics available for most of the medicines which in turn has led to **increased availability and affordability**

Dabare PR, Wanigatunge CA, Beneragama BH. A national survey on availability, price and affordability of selected essential medicines for non communicable diseases in Sri Lanka. BMC Public Health. 2014;14:817.

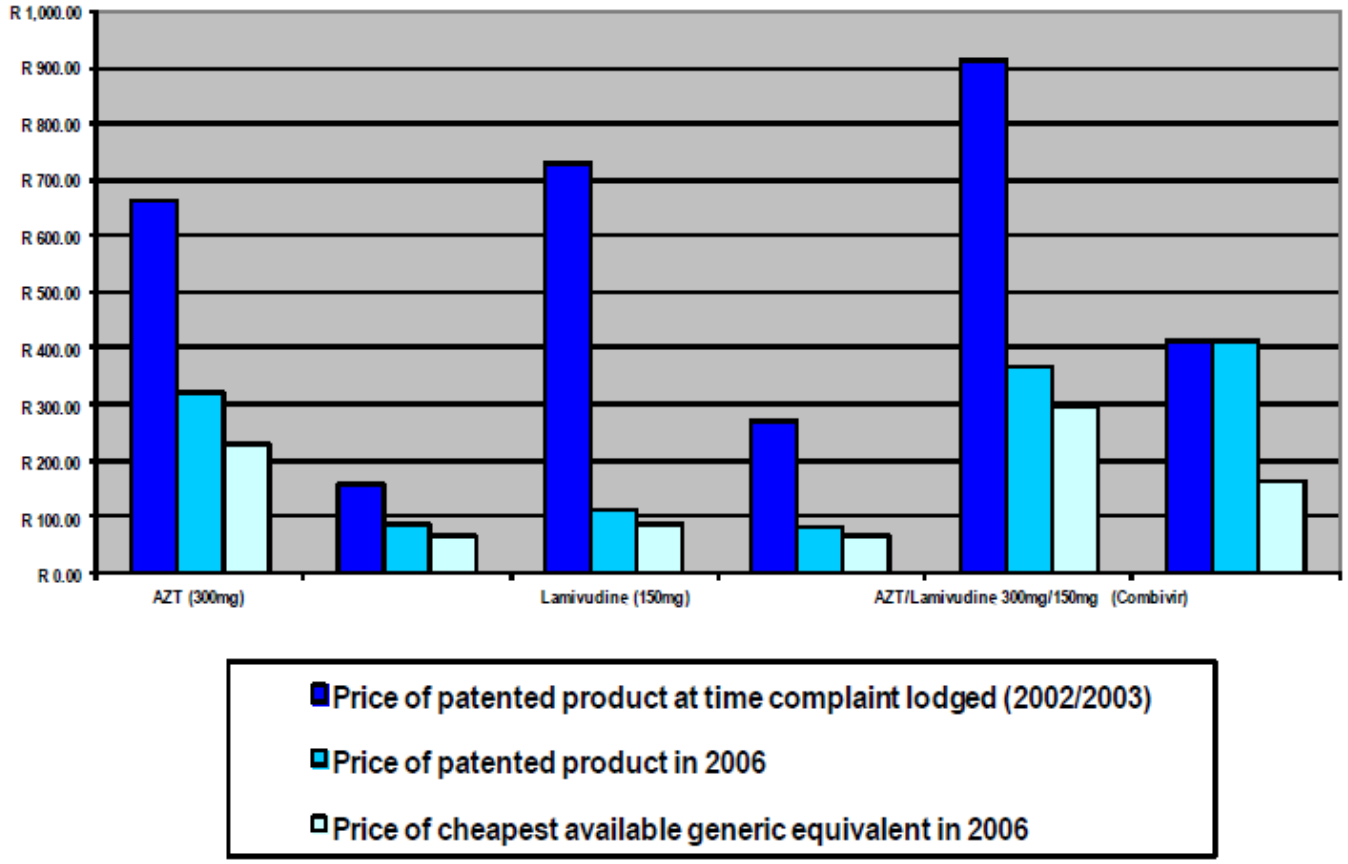
1. GDI value – South Africa



NAPM 2014

2. GDI Value – South Africa

Figure 1: Price comparisons (excluding South Africa's value-added tax)



Source: TAC study on ARV prices, 2006

3. Challenges and Opportunities:

1. Generic Marketplace & Sustainability of supply
2. Quality Issues
3. Review cycle times and number of applications
4. Improving the value offering of generic drugs

1. Generic Market Place and Sustainability of Supply – Generic Oligopolies

- **Large proportion of the generic drug supply** can be in the hands of a few large generic companies.
- In USA in 2009, nearly 50 % of the generic drug supply was produced by the top **4 generic companies**
- Oligopoly is result of major purchasers only wanting to **deal with a few well know and established manufacturers**
- Purchasers essentially **control market** and act as de facto 'kingmakers' in generic market place
- **Fragile drug supply situation** where production problems at one company can rapidly lead to critical drug shortages

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1. Generic Market Place and Sustainability of Supply – Supply problems

FDA review in 2005:

1. Manufacturing problems – Usually due to compliance issues
2. Growth in demand while manufacturing stay constant
3. Supply chain issues: API, final product manufacturers, wholesalers etc.
4. Pricing and reimbursement policies – Price ceilings

Jensen V, Kimzey R, Saliba J. An overview of the FDA's drug shortage program. P T 2005;30:174–7.

2. Quality Issues

FDA review in 2005:

- Primary reasons for drug shortages include quality and manufacturing issues
- Fundamental problem identified is the inability of the market to observe and reward quality
- This lack of reward for quality encourage manufacturers to keep costs down by minimizing quality investments.
- These dynamics may have produced a market situation in which quality problems have become sufficiently common and severe to result in drug shortages

2. Quality Issues:

How can quality be ensured?

2. How can quality be ensured?

Punishment

Reward

2. Quality Issues

- Pharmaceutical companies that produce substandard regulatory work should be dealt with on an individual basis
- It might also be the case that substandard/non-compliant dossiers might also be an indicator of a companywide philosophy of noncompliance and poor quality

3. Review cycle times and number of applications

- Prior to Hatch-Waxman Act FDA warned re shortage of reviewers
- Over the past several years approval time for generic submission (ANDA) has nearly doubled
- 2700 ANDAs waiting review
- Reviewing time was 32 months

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3. Review cycle times and number of applications

Dual registrations:

- Should be allowed but need to explain the need for more than one registration
- A reduction of dual registrations will assist in reducing the load on the regulator

4. Improve the value offering of generic drugs

Supply Side	Demand Side
Improve market approvals of generics	Improve doctor attitudes towards generics
Intellectual property policies	Remove financial disincentives for pharmacists to dispense generic medicines
Generic pricing policy	Incentives for patients to demand generic medicines
Reducing information asymmetry on pricing through education	Co-pays on originators
Generic competition (free market system)	

4.Generic drug prices and policy in Australia: room for improvement. A comparative analysis with England

OBJECTIVE: To assess the degree to which reimbursement prices in Australia and England differ for a range of generic drugs, and to analyse the supply- and demand-side factors that may contribute to these differences.

RESULTS: Analysis of drug reimbursement prices for 15 generic molecules (representing 45 different drug presentations) demonstrated that Australian prices were on average over 7-fold higher than in England

VS

x 7

SJ Mansfield in the Australian Health Review – 2014 Feb;38(1):6-15

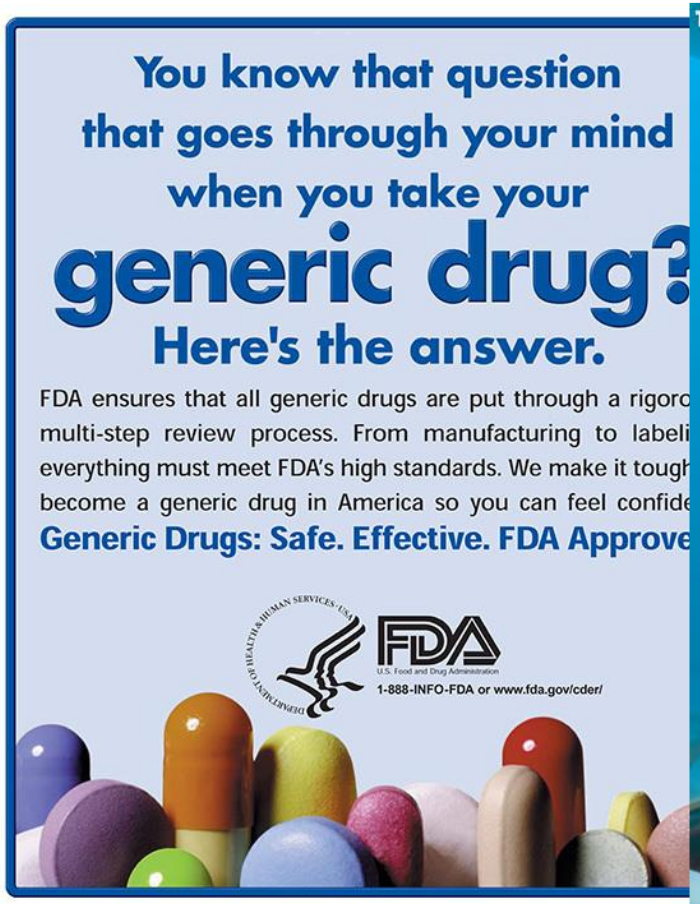
4.1 Generic drug prices and policy in Australia: room for improvement: a comparative analysis with England

The results suggest that particular policy areas may benefit from review in Australia, including

1. The length of the price-setting process
2. The frequency of subsequent price adjustments
3. The extent of price competition between originators and generics
4. Medical professionals' knowledge about generic medicines
5. Incentives for generic prescribing

VS

Education Material



In Summary:

- Generic medicine offers a lot of value - Affordability and access
- Generic medicine utilisation in markets differs
- An improvement in generic medicine utilisation will increase the value offering
- The value offered by generic medicine can be increased by industry and regulator actions

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