The French Retail Generics Market

- Are generics defense strategy effective? -

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Discussion document

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1. Introduction

So far, the substitution right in retail pharmacies does not apply to essentially similar and biosimilar drugs in France

The three status of "copies" in France

	Generics	Essentially similar drugs	Biosimilar drugs
Description	• **Copies of synthetic drugs** • **Bioequivalence has been proven**	• **Copies of synthetic drugs** • **Bioequivalence** (has not or) **cannot be proven**	• **Copies of biotech products** • **Bioequivalence cannot be proven**
Market approval requirements	• **Abridged procedure with simplified dossier reproducing original brand's clinical outcome**	• **Minimal clinical development to document safety/efficacy profile** (e.g. with specific device used)	• **Complete clinical development**
Substitution²	Allowed	Not allowed	Not allowed
Examples	Tablets and capsules (e.g. TAREG)	Inhaled beta$_2$-stimulants (e.g. FORADIL)	Growth hormones (e.g. GENOTONORM)

Source: Smart Pharma Consulting analyses

The wholesaler and pharmacist margins are highly regulated, thus reinforcing direct sales attractiveness for retail pharmacists

Price regulation of reimbursable drugs available on the retail market (2010)

<table>
<tr><th></th><th>Original brand without RPS[1]</th><th>Original brand with RPS[1]</th><th>Generic with RPS[1]</th><th>Generic without RPS[1]</th></tr>
<tr><td>Ex-factory price</td><td colspan="4">▪ Negotiated with / imposed by health authorities (CEPS)
▪ Generics priced -50% below original brands (ex-factory) at the time of their patent expiry</td></tr>
<tr><td>Wholesaler margin</td><td colspan="4">▪ 9.93% of the ex-factory price up to €22.90
▪ 6% from €22.91 to €150
▪ 2% from €150 up to € 400
▪ 0% above € 400
Average margin < 6% considering discounts to pharmacists (-2% on PhP[2]) and ACOSS tax (-2% on PhP[2])</td></tr>
<tr><td>Pharmacist margin</td><td colspan="3">▪ 26.10% of the ex-factory price up to €22.90
▪ 10% from €22.91 to €150
▪ 0% above €150
▪ Fixed fee of €0.53 per pack up to €150</td><td>▪ Same as original brands in nominal value</td></tr>
<tr><td>Pharmacist rebate
Primarily offered through direct sales to pharmacists</td><td>▪ 2.5 % of the ex-factory price
▪ Possibility to add up to 100% of the wholesaler margin</td><td colspan="3">▪ 17% of the ex-factory price
▪ Possibility to add up to 100% of the wholesaler margin</td></tr>
</table>

Source: Smart Pharma Consulting analyses after legal texts and external interviews

[1] Reference price system or TFR = Tarif Forfaitaire de Responsabilité – [2] Pharmacist purchasing price VAT exclusive

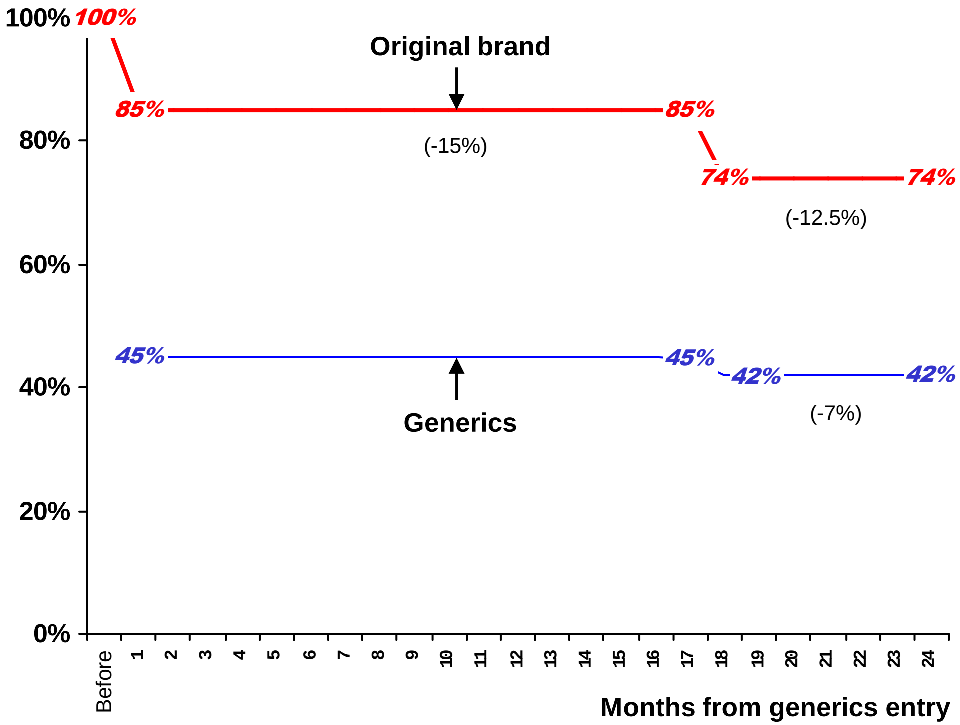
2. Key stakeholders attitudes towards generics

In the absence of reference price, the original brands can preserve only 74% of their ex-factory price after 18 months, due to authoritative price cuts

Genericized original brands and generics ex-factory price scheme as of 2009

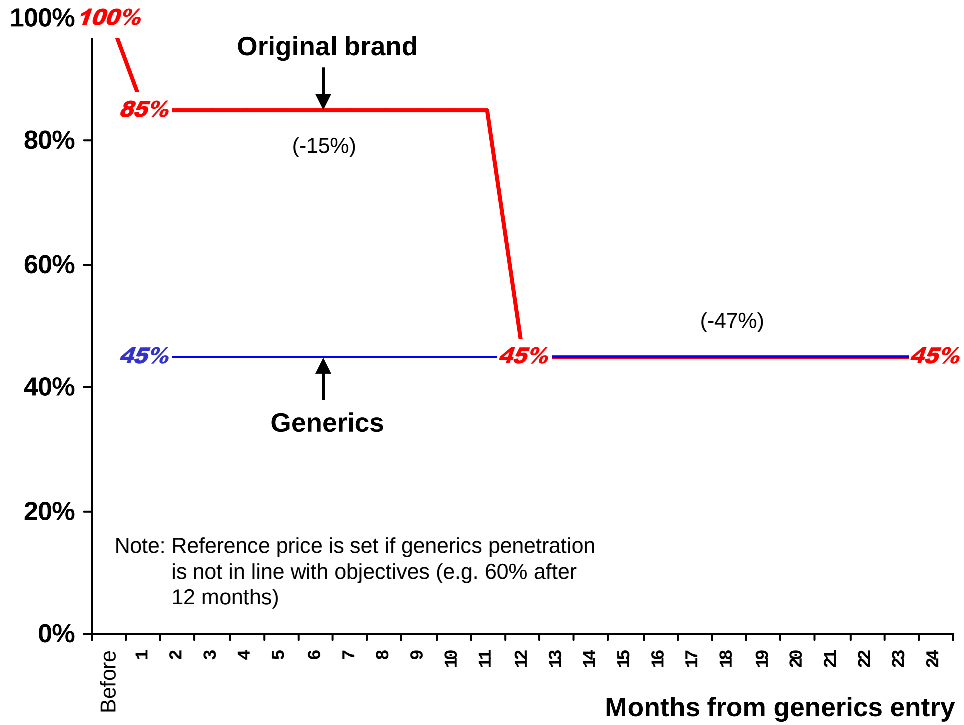
Without reference price

As a % of the original brand ex-factory price before generics entry



With reference price

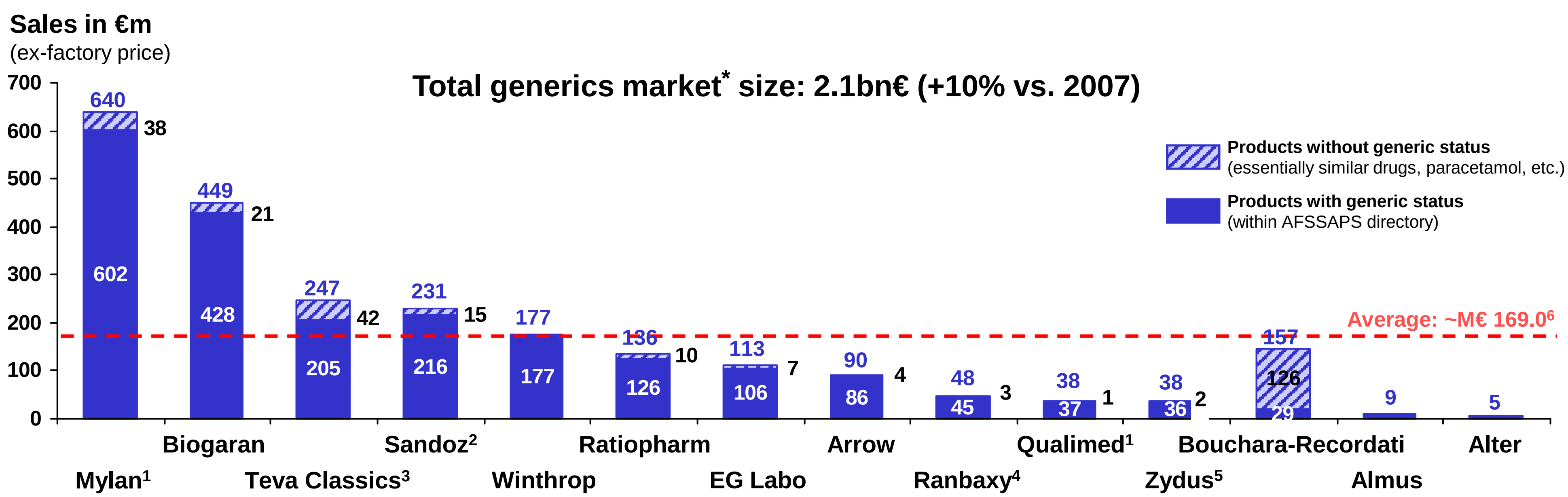
As a % of the original brand ex-factory price before generics entry



Source: Smart Pharma Consulting analyses after legal texts and external interviews

Mylan and Biogaran have both taken a serious advantage over competition in general, they account together for 49% of the generics market

Generics companies in France – Retail market (2008)



Generic business[6]

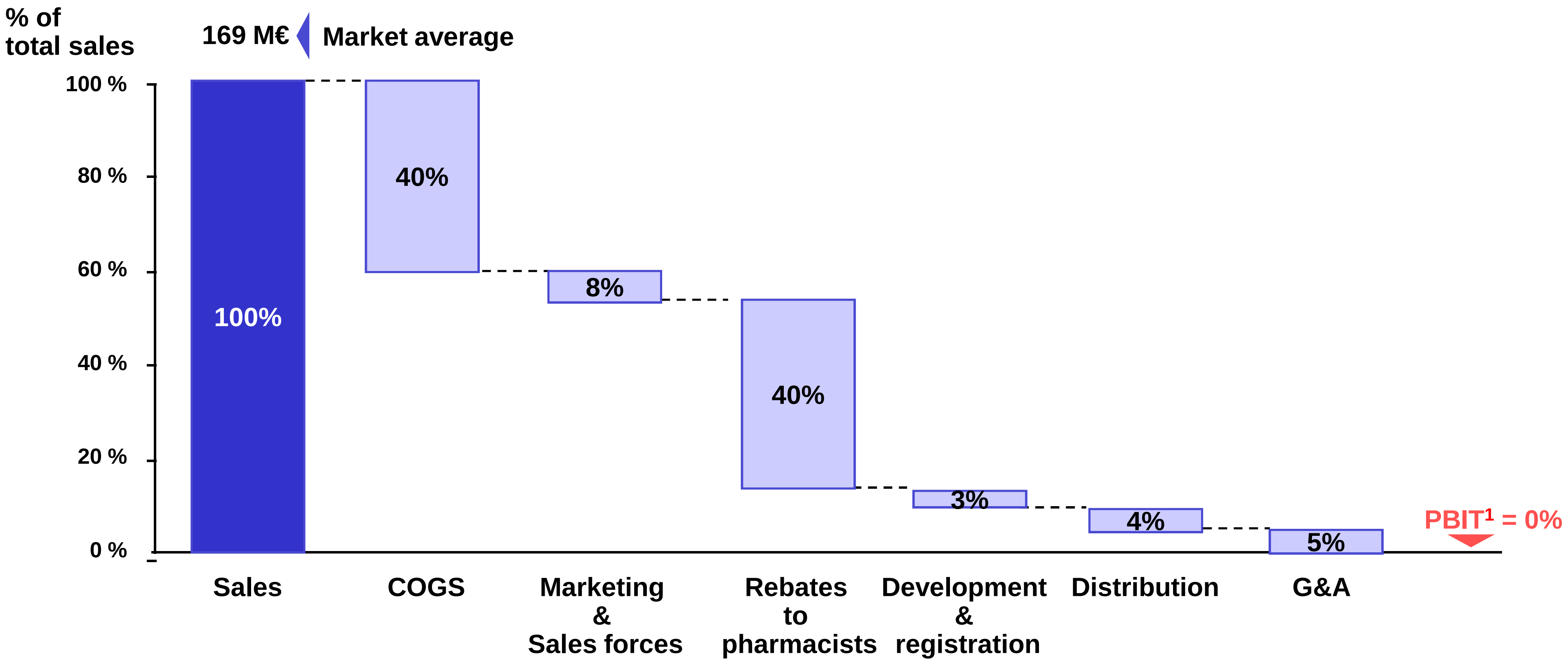
Sales growth 2008/07	+21%	+0%	+31%	-13%	+34%	+6%	+6%	+37%	-8%	+6%	+21%	-31%	+28%	+13%
Market share 08	29%	20%	10%	10%	8%	6%	5%	4%	2%	2%	2%	1%	<1%	<1%

Sources: GERS data – Smart Pharma Consulting analyses

*Open care market only - [1] Both companies belong to Mylan – [2] Acquisition of G.Gam (Hexal) in 2005 – [3] Acquisition of Ivax in 2006 – [4] Acquisition of RPG from Aventis in 2004 - [5] Acquisition of Alpharma in 2003 – [6] Figures only concern sales coming from generics within Afssaps directory

Based on P&L estimates of generics companies operating in France, the top 3 to 4 leading players only are likely to generate operational profits

Cost structure of generics players (2008)

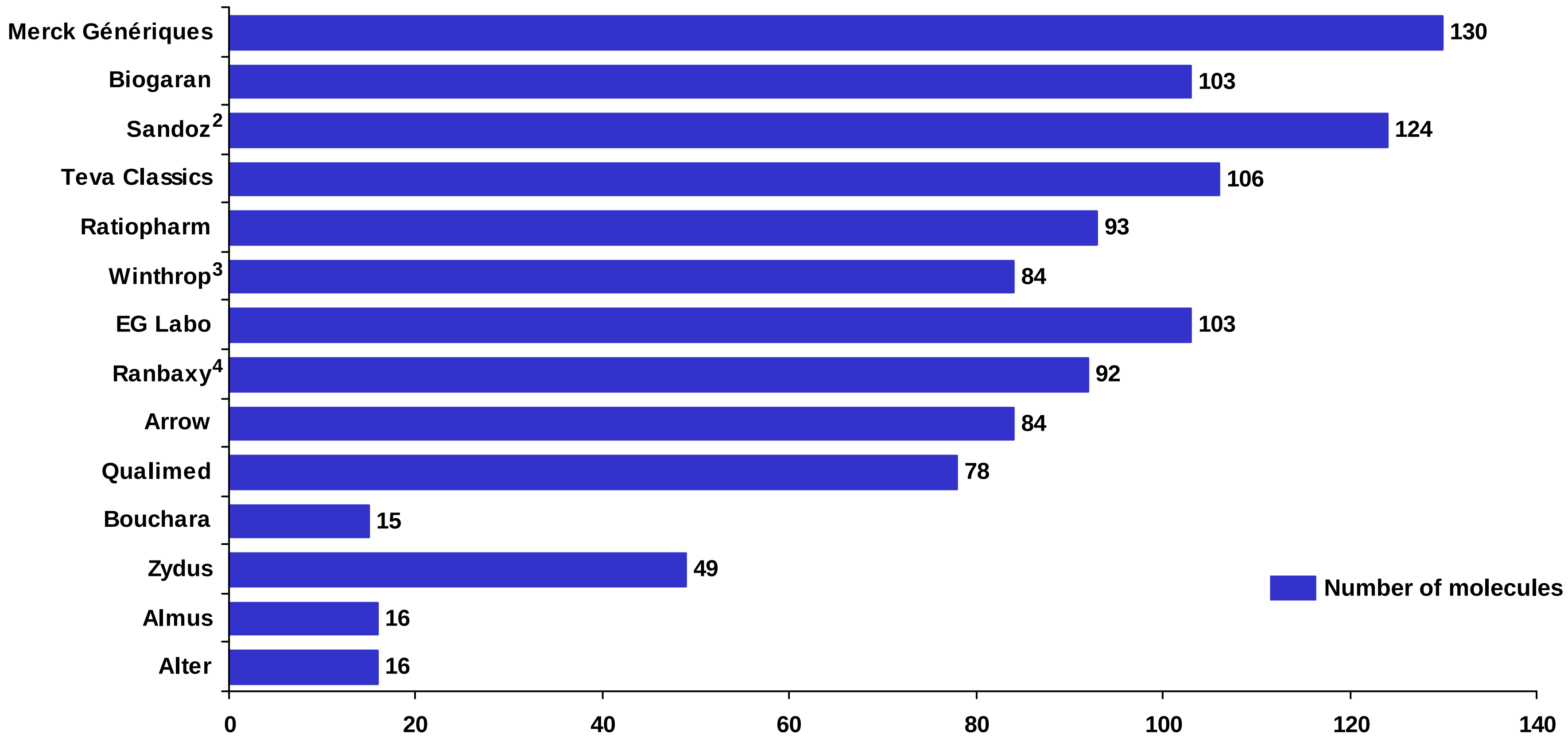


Source : Smart Pharma Consulting analyses

[1] Profit before interest and taxes

The size of generic companies portfolio is one of the key drivers to be listed as the preferred provider, by retail pharmacists

Generic companies' offer[1]



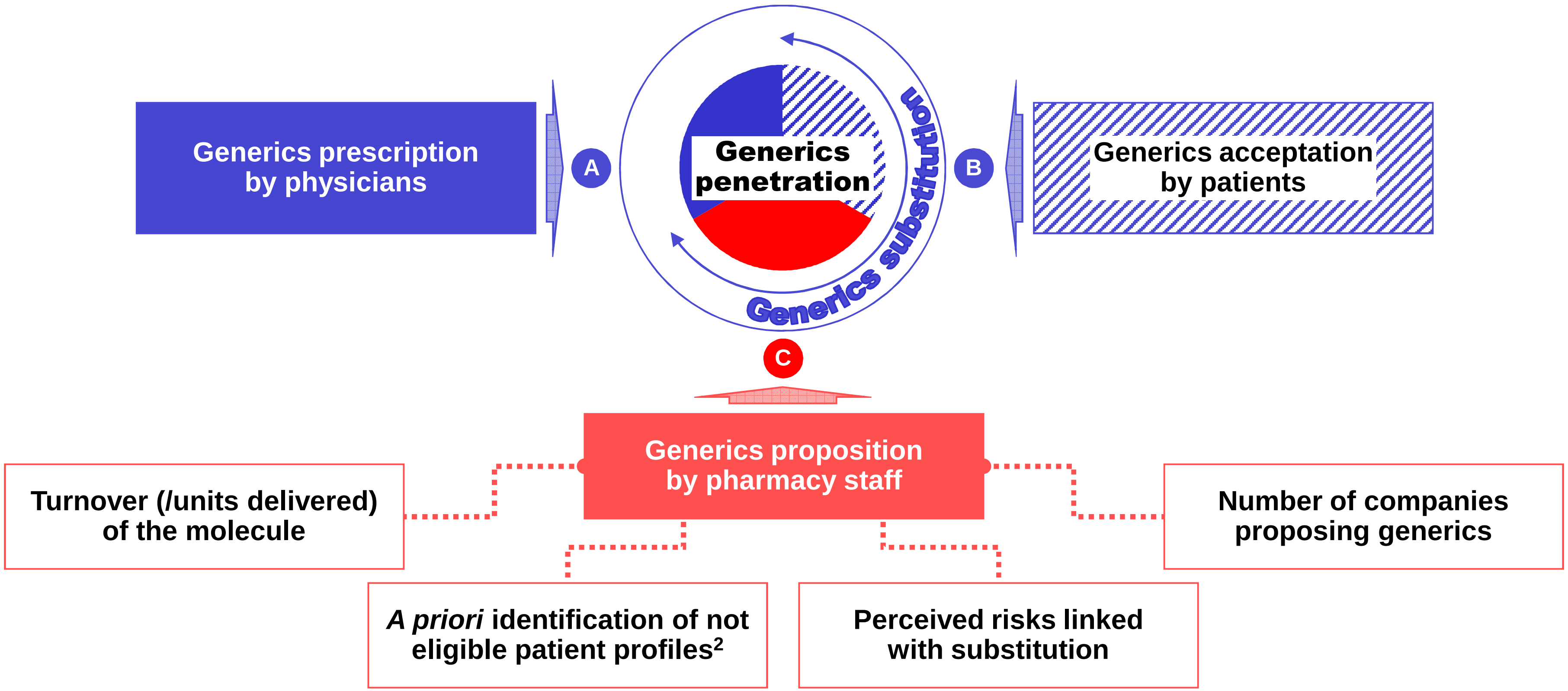
Note: Afssaps Directory includes 199 molecules with generics (and corresponding salts) as of January 2007

Source : GERS Aug. 2006 – Smart Pharma Consulting analyses

[1] Retail market, within and outside Afssaps Directory, generics only – [2] Incl. G.GAM , and GNR molecules – [3] Incl. IREX molecules – [4] Incl. RPG molecules

Generics penetration is facilitated by INN[1] prescription and by substitution which results from the interaction between pharmacy staff and patients

Key drivers of generics penetration



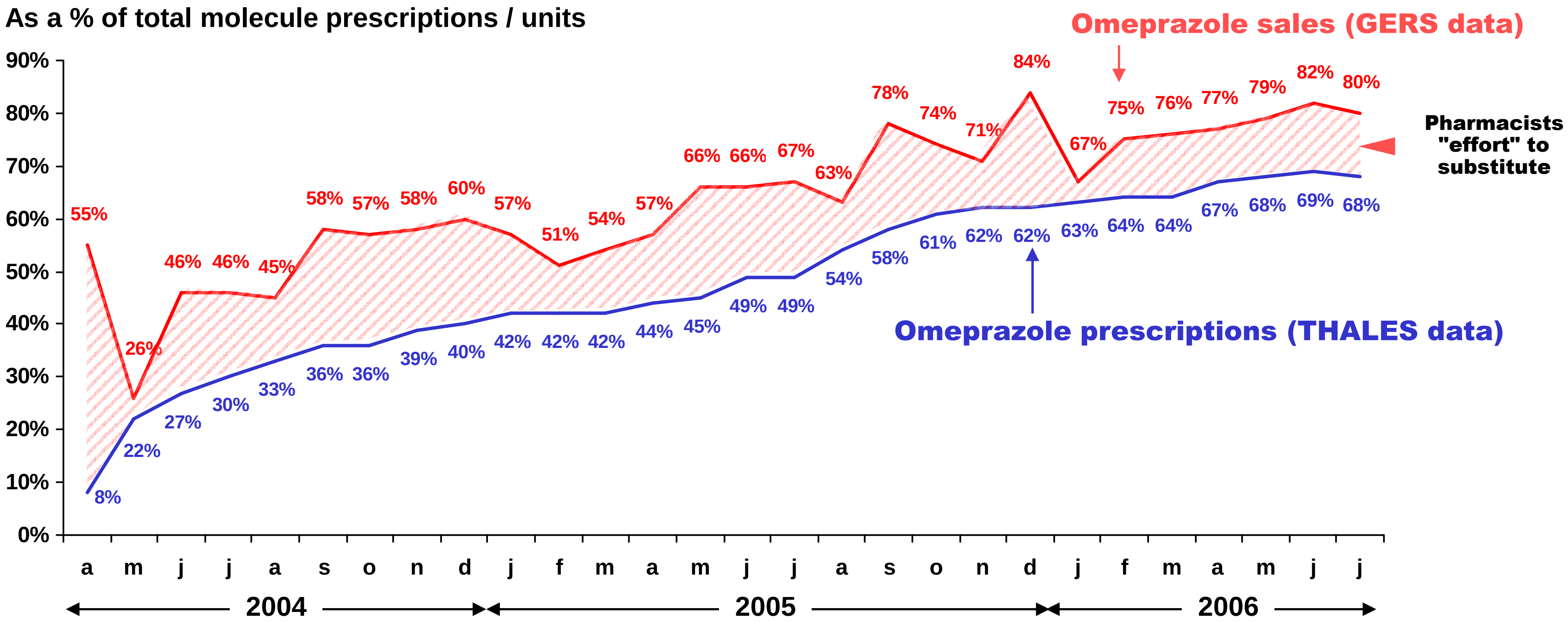
Source: Smart Pharma Consulting analyses

[1] International non-proprietary name – [2] To whom substitution will not be proposed (e.g. patients have refused substitution several times)

Omeprazole generics penetration in France has been significantly boosted by the increase of physicians INN prescriptions of the molecule

INN[1] prescriptions weight in generics dynamics (1/2)

MOPRAL case study in France



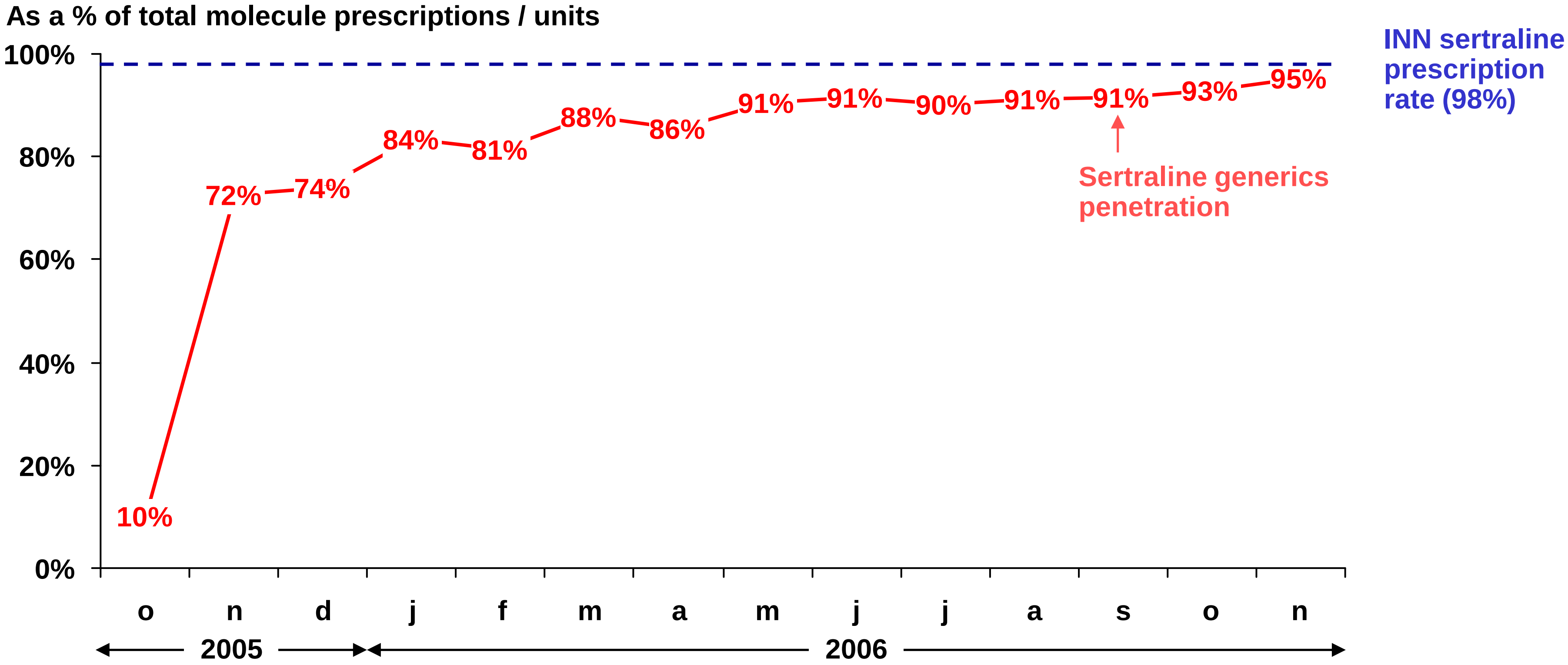
Source: IMS data – THALES data– Smart Pharma Consulting analyses

[1] International non-proprietary name

However without reaching the very high level of INN prescriptions in the UK, which allows generics to gain more than 80% of sales in less than one year

INN[1] prescriptions weight in generics dynamics (2/2)

ZOLOFT / LUSTRAL case study in the UK



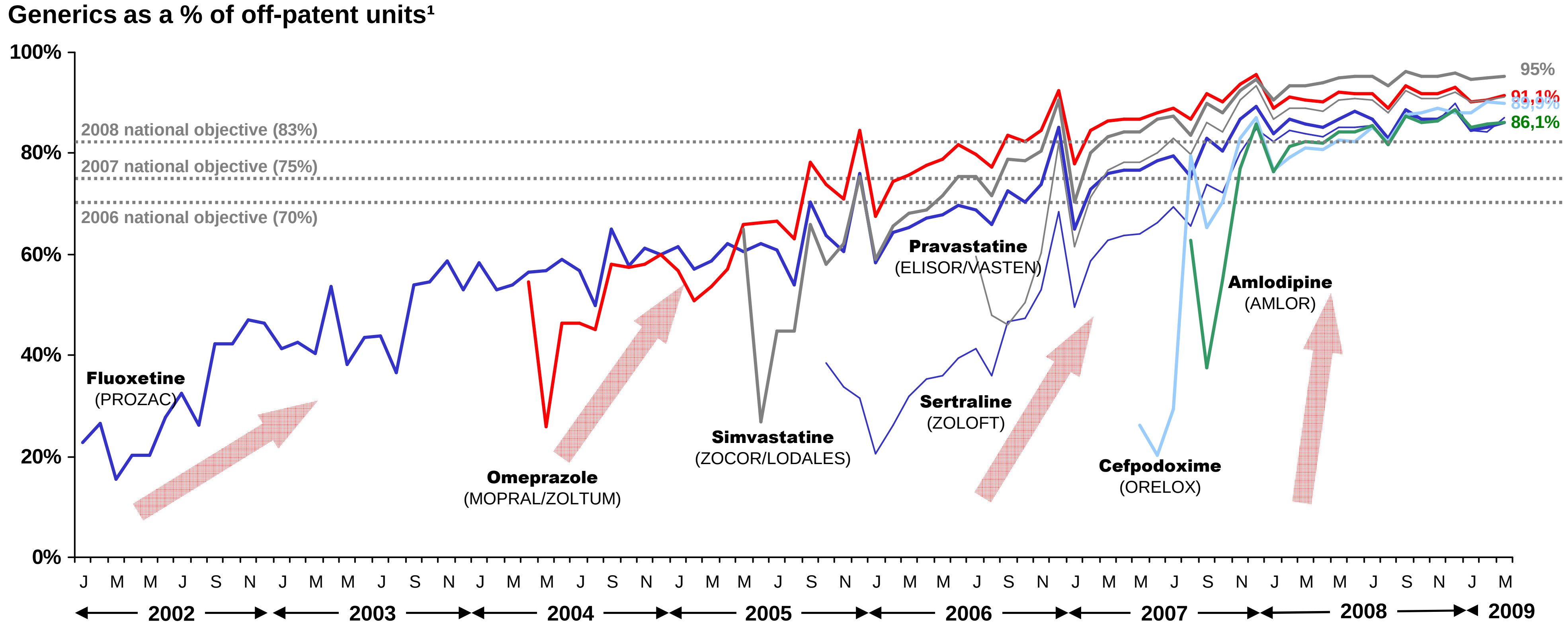
Source: IMS – Smart Pharma Consulting analyses

3. Impact of generics on original brands

Generics penetration accelerated over the years, with scores higher than 85% after 12 months for easy-to-substitute drugs like Amlor

Generics penetration trends on the retail market

Selected high volume drugs



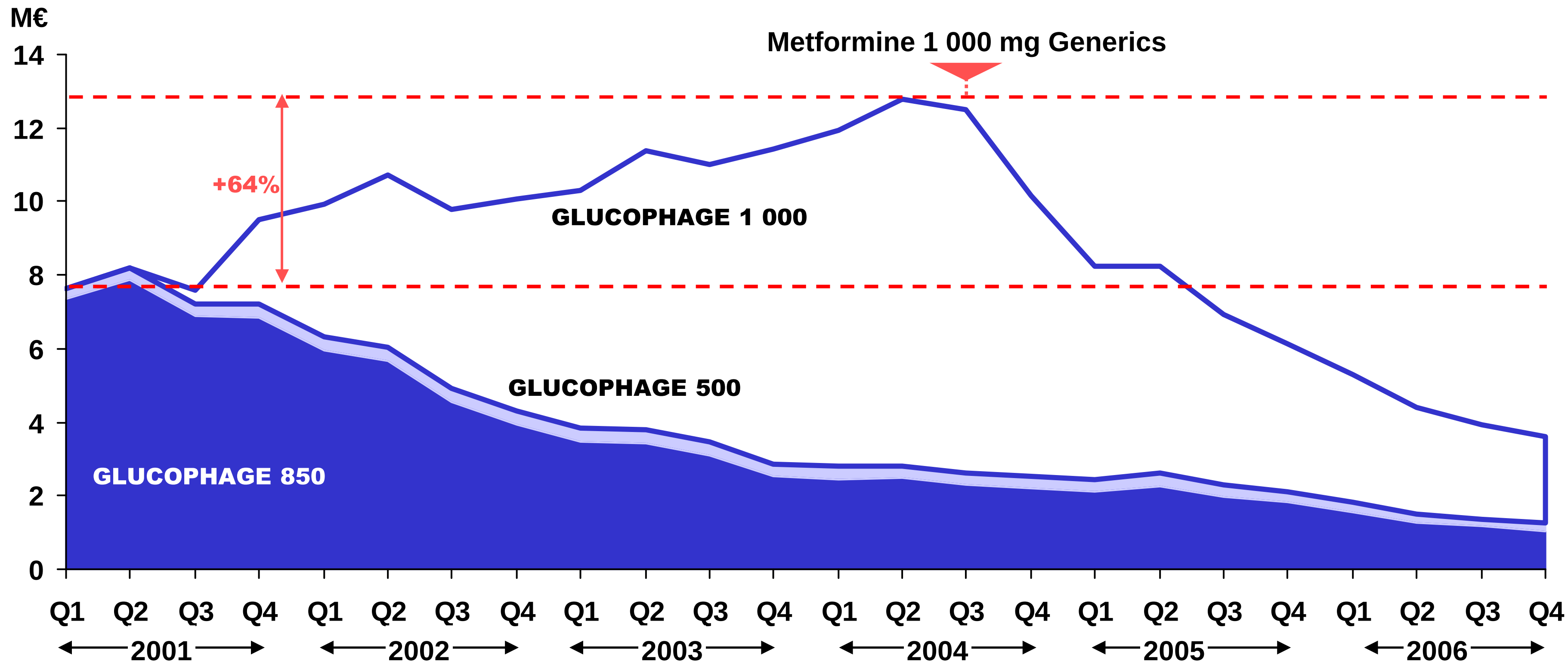
Source: GERS data (month)

¹ Compounded average of the different forms and dosages

GLUCOPHAGE 1000mg launch allowed Merck-Lipha Santé to increase metformine sales by +64% before generics of the 1000mg entered the market

1 New formulation: GLUCOPHAGE 1000mg

GLUCOPHAGE franchise sales evolution – France

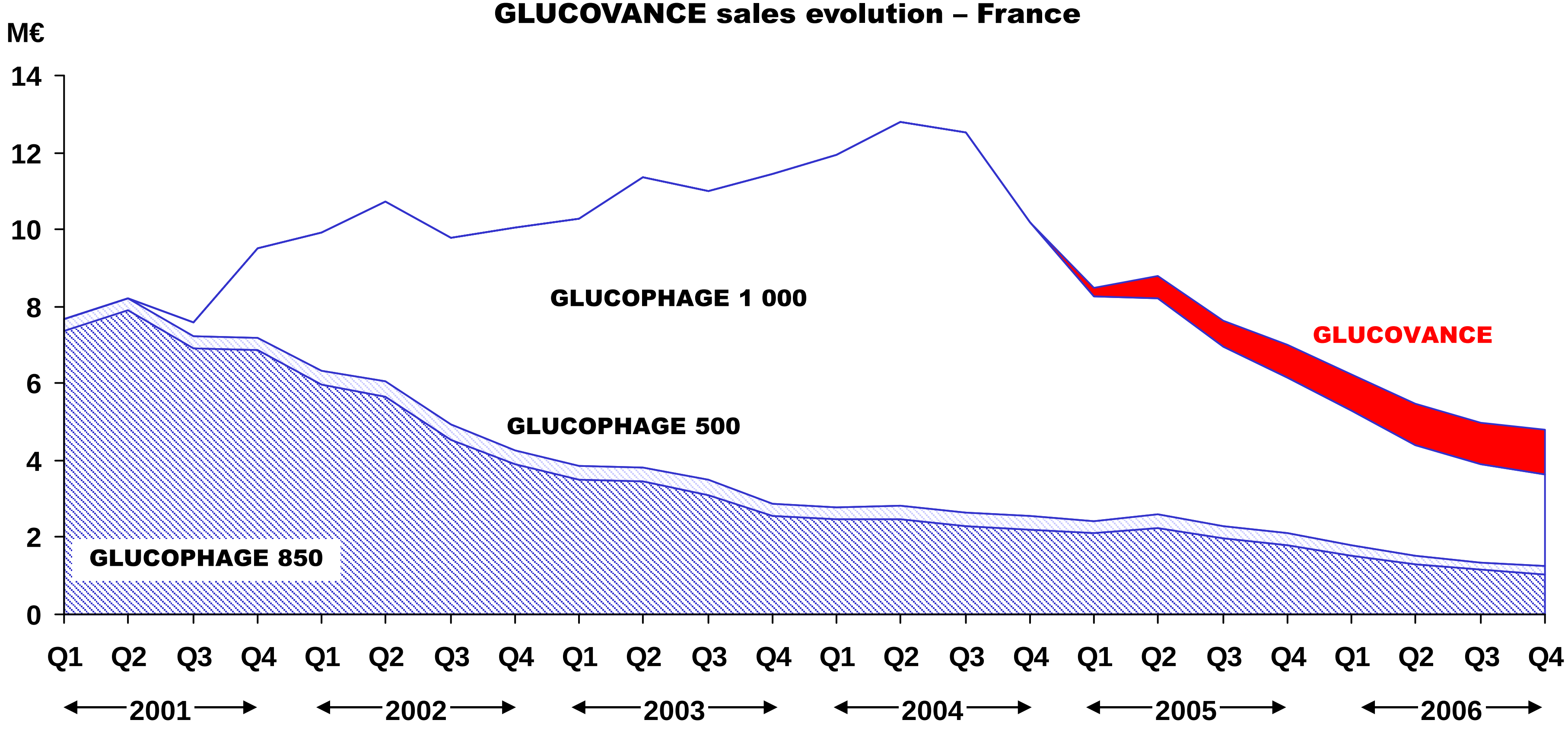


Source: GERS – Smart Pharma Consulting analyses

GLUCOVANCE did not compensate the loss due to generics penetration on other GLUCOPHAGE forms, partially because of its low price

2 New combination: GLUCOVANCE[1]

GLUCOVANCE sales evolution – France



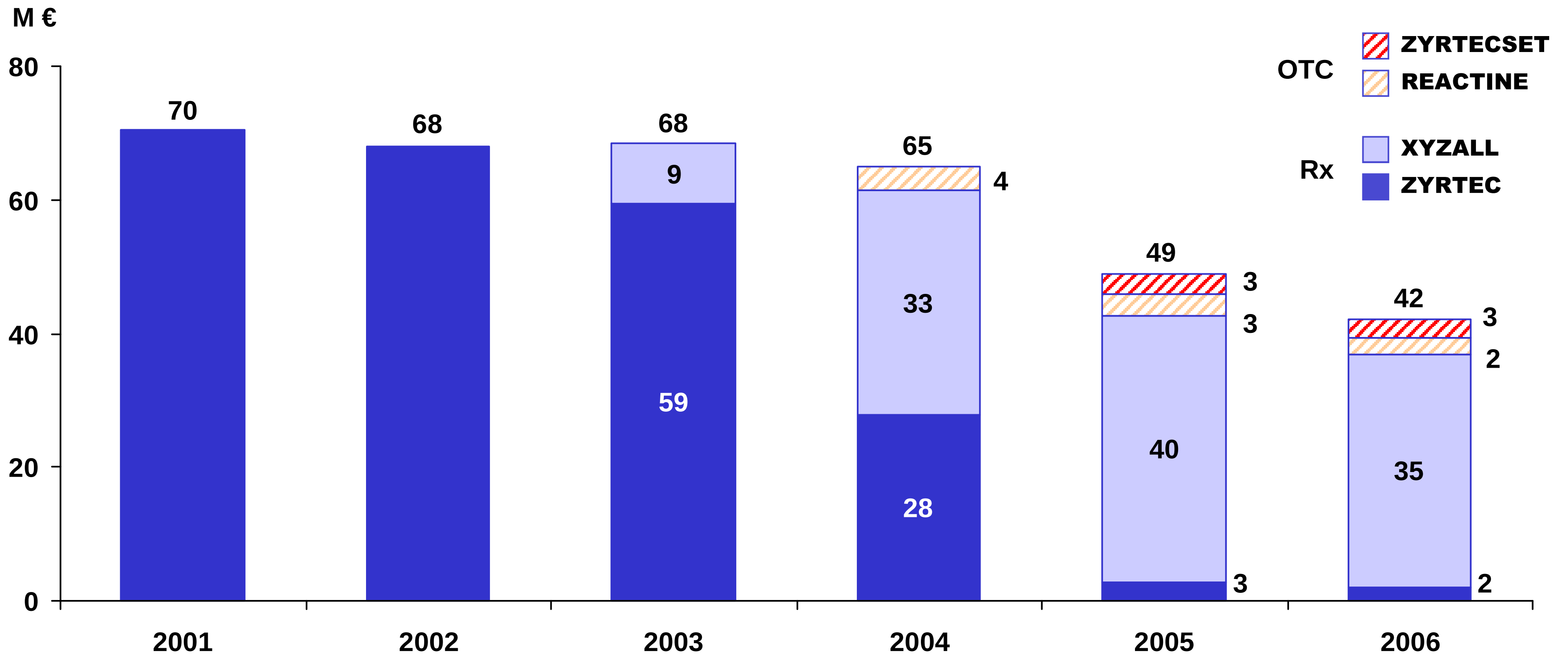
Source: GERS – Smart Pharma Consulting analyses

[1] fixed combination metformine + glibenclamide

ZYRTEC Rx-to-OTC switches, along with the launch of XYZALL, did not allow UCB to compensate for sales losses generated by generics

3 Switches Rx-to-OTC: ZYRTEC – ZYRTECSET

Cetirizine and levocetirizine sales evolution – France[1]

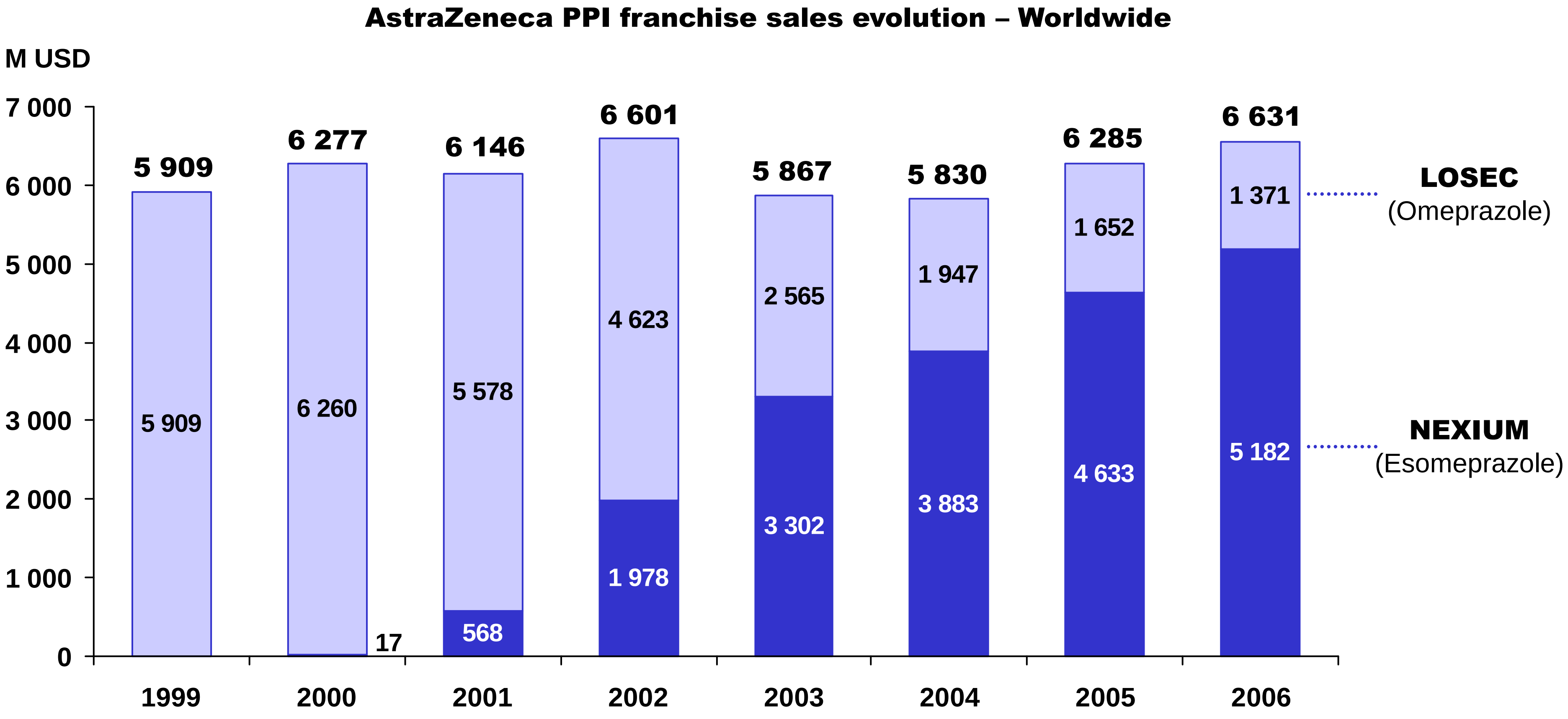


Source : GERS – Smart Pharma Consulting analyses

[1] excl. VIRLIX and cetirizine generics

AstraZeneca succeeded in preserving the G.I. franchise performance by switching prescriptions from LOSEC to NEXIUM

4 Back-up brands: LOSEC – NEXIUM

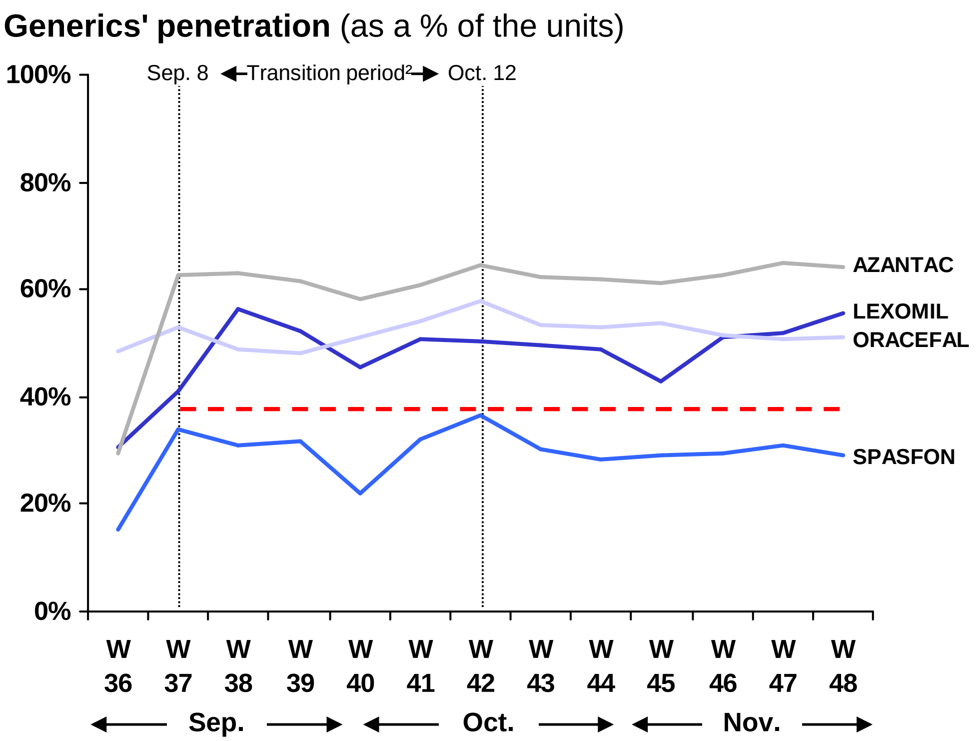


Source : Annual reports – Smart Pharma Consulting analyses

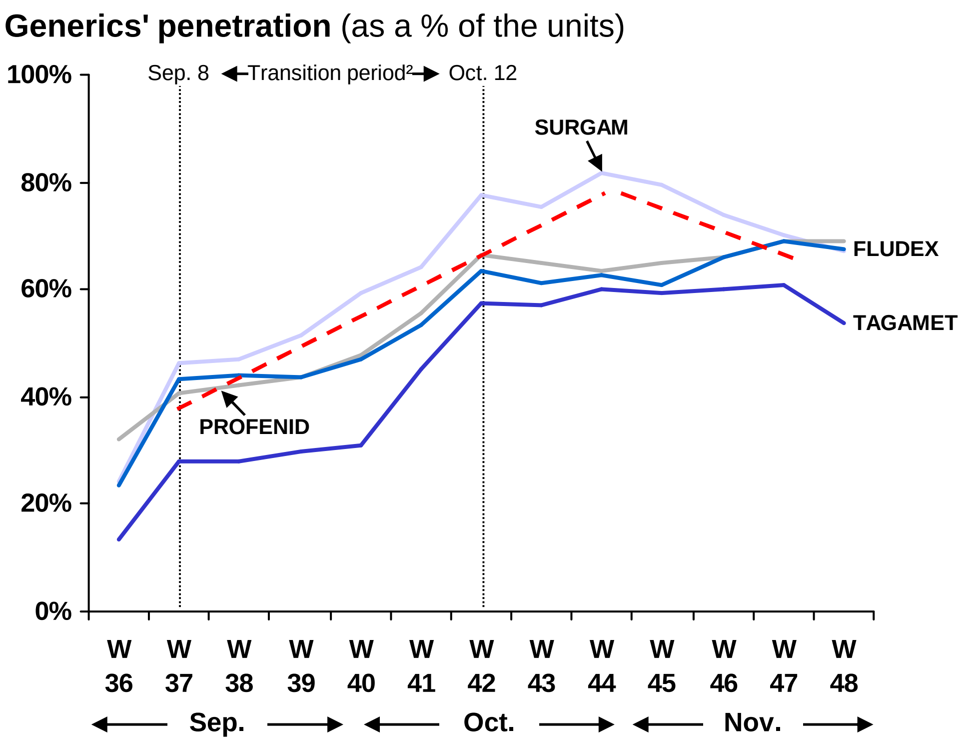
Aligned brands have followed similar trends irrespective of the therapeutic area, and so did not aligned brands

5 Price adjustment

Alignment of reference brands' prices (2003)



No alignment of reference brands' prices (2003)



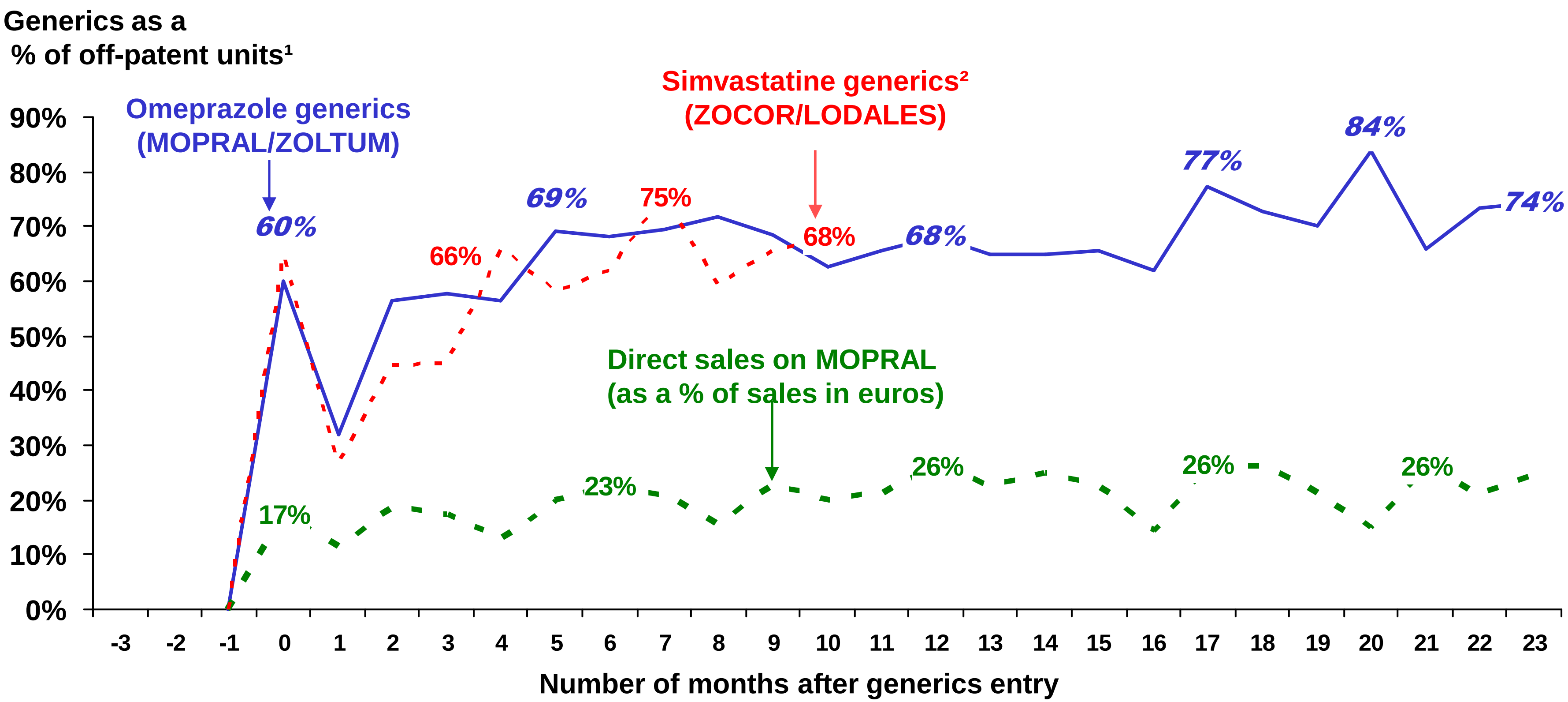
Source: GERS – Smart Pharma Consulting analyses

¹ Reference price – ² To sell out products with former prices with no impact on patient reimbursement

MOPRAL and ZOCOR cases show that direct sales to pharmacists do not slow down generics penetration, unless great stock pressure is imposed

6 Commercial offers to distributors

MOPRAL (2004-2006) and ZOCOR (2005-2006) case studies – France



Source: GERS – Smart Pharma Consulting analyses

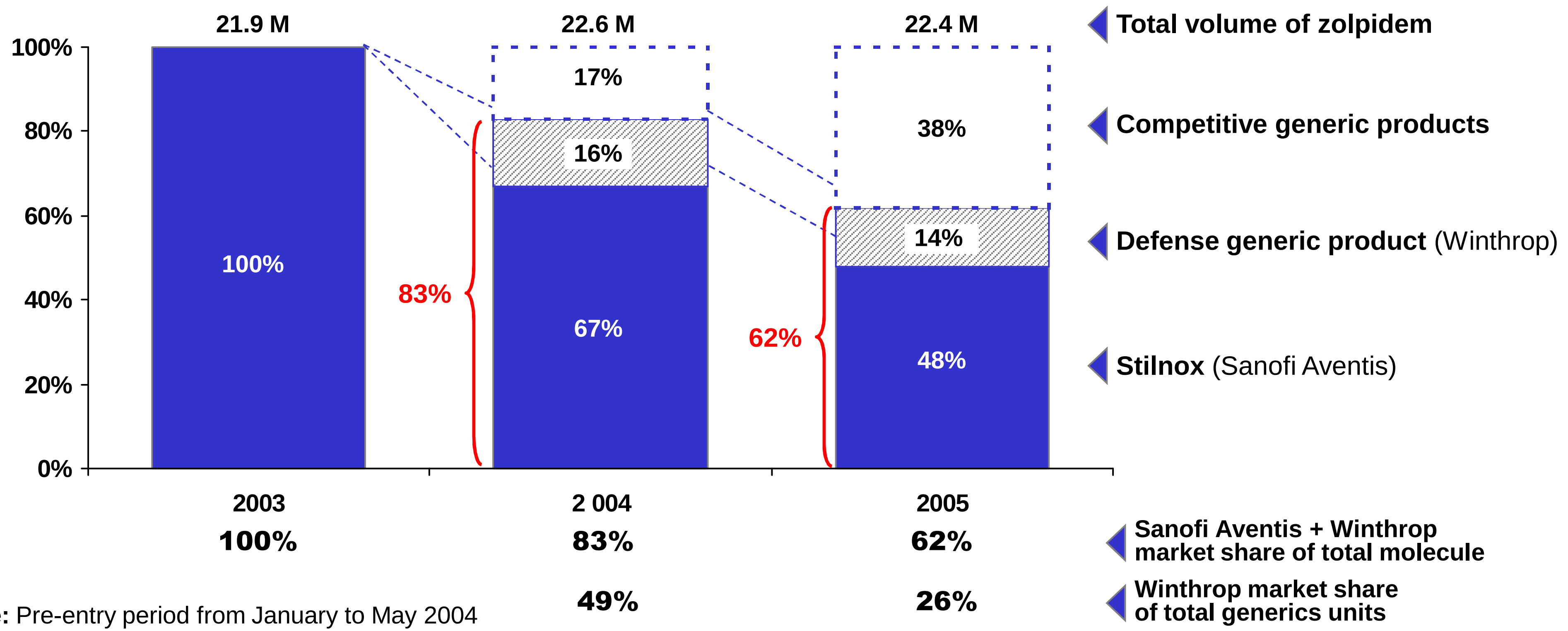
[1] Including brand and generics units – [2] No direct sales on ZOCOR and LODALES

5. Offensive strategy

By introducing its own generic, 5 months before patent expiry, S-A managed to secure 83% of zolpidem volumes after one year and 62% after two years

7 Flanking generics: Stilnox case study (1/2)

% of the total in M units



Note: Pre-entry period from January to May 2004

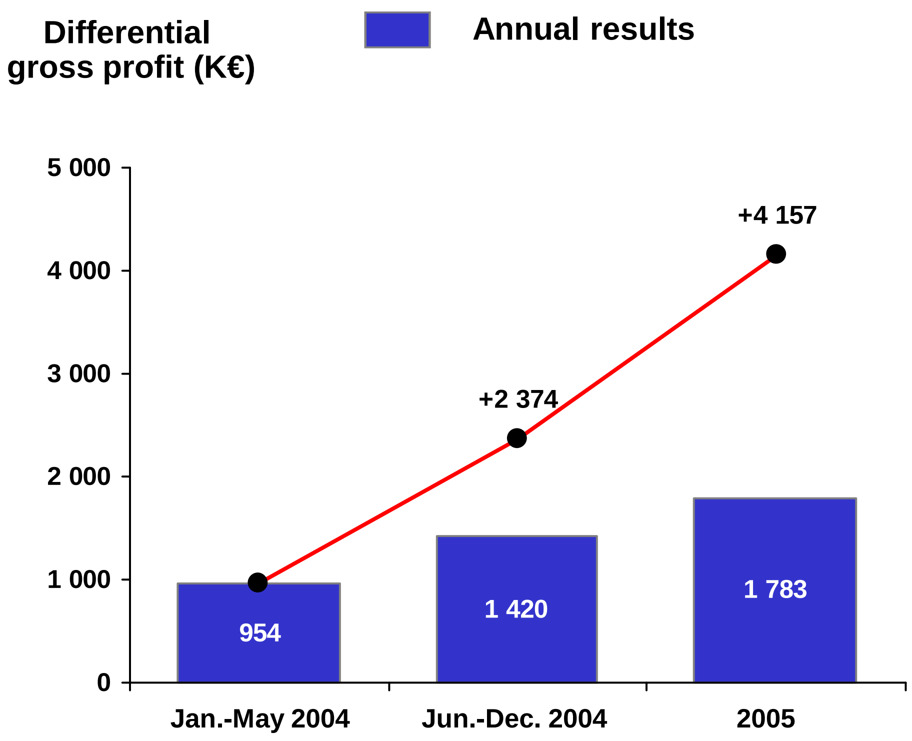
Source: Smart Pharma Consulting analyses and estimates after GERS market data

5. Offensive strategy

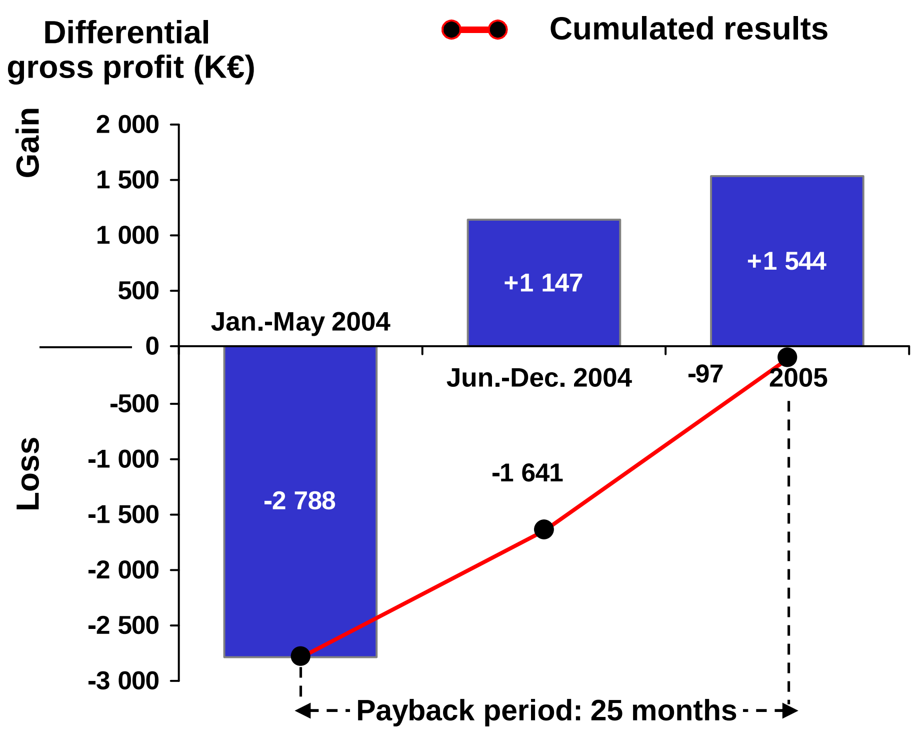
The payback period for Stilnox, resulting from the zolpidem authorized generic deal, which has been granted to Winthrop, exceeded two years

7 Flanking generics: Stilnox case study (2/2)

Zolpidem Winthrop profit gain/loss Vs. base case



Stilnox profit gain/loss Vs. base case



Source: Smart Pharma Consulting analyses and estimates after GERS market data

6. Conclusion

Few strategies have shown to be effective in defending original brands against generics competition and most of them required anticipation

Key points

- The French generics market is likely to growth at a pace of +11% p.a. by 2009
- To curve the cost of genericable molecules, Health Authorities have developed measures to favour generics substitution and have applied price cuts
- In an attempt to defend their original brands, R&D-based companies have carried out various strategies, the efficacy of which are most often limited:

Reduce genericable sales	Efficacy
1 **New formulation** (e.g. Glucophage)	
2 **New combination** (e.g. Glucovance)	
3 **Switches Rx-to-OTC** (e.g. Zyrtec)	
4 **Back-up brands** (e.g. Losec / Nexium)	

Limit generics penetration	Efficacy
5 **Price adjustment** (e.g. Lexomil)	
6 **Discounts to distributors** (e.g. Mopral)	

Offensive strategy	Efficacy
7 **Flanking generics**	

High Low

Source: Smart Pharma Consulting analyses