

The future for Drug and Therapeutics Committees in a changing European market

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APOTEKARE INOM
LÄKEMEDELSKOMMITTÉRNA

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1. Introduction

2. Supply side measures across Europe

3. Rational use initiatives including DTCs

4. Future for DTC activities and members

Reforms will intensify to enhance quality and efficiency to prevent prohibitive tax increases

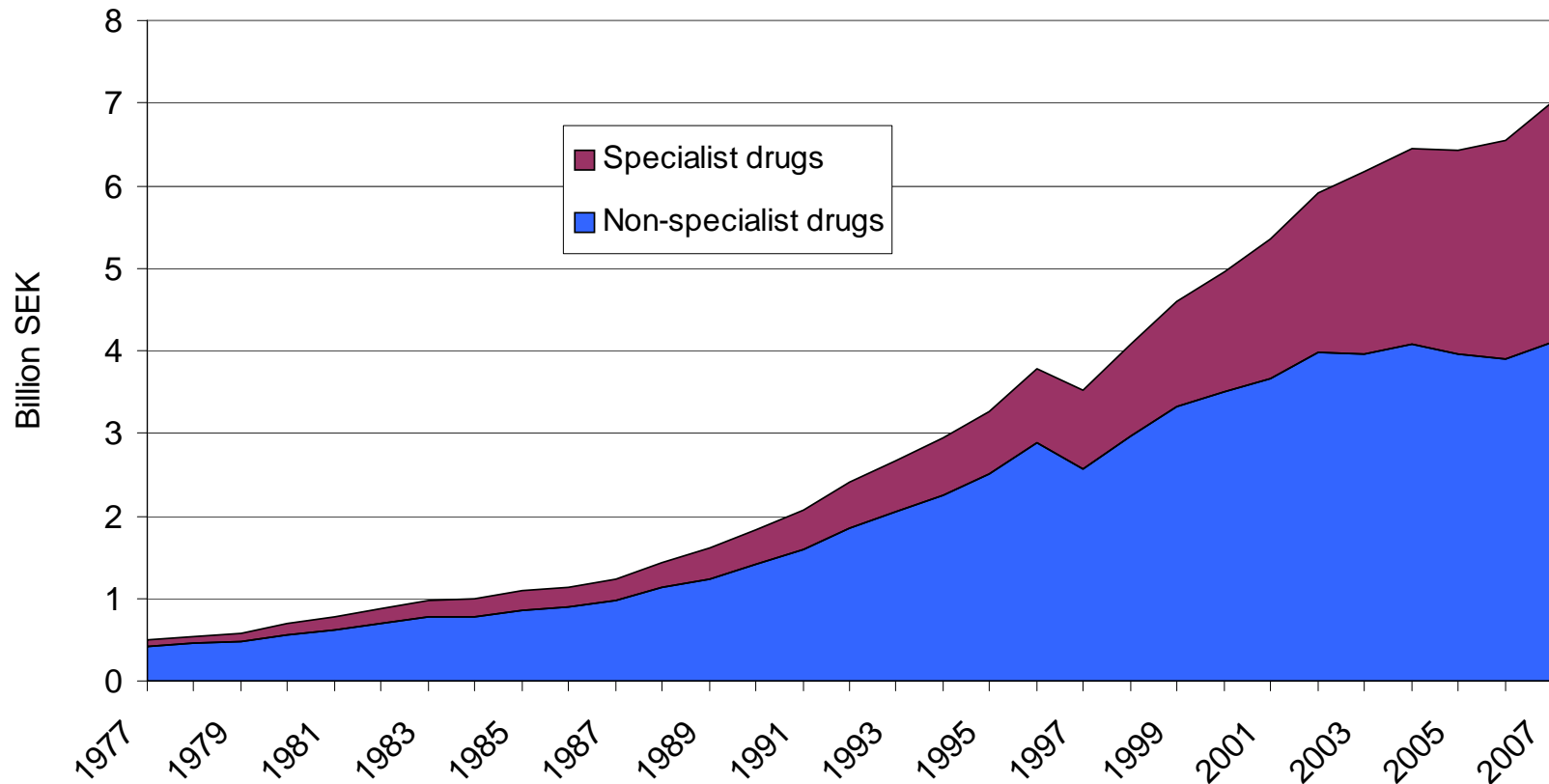
- As you know, healthcare expenditure represents a significant proportion of national expenditure among western countries
- Alongside this, European governments strive to maintain comprehensive and equitable healthcare in the face of greater prevalence of chronic diseases and new expensive drugs
- This will result in further reforms; likely to include:
 - Stricter regulations for granting premiums for new drugs
 - Additional measures to lower prices of interchangeable products in a class as well as generics and originators
 - Greater proactive planning for the introduction of new drugs as well as additional measures to further improve the quality and efficiency of prescribing
 - As a result greater role for DTC activities in the future!

Resource pressures will grow in Europe with the continuing launch of new expensive drugs

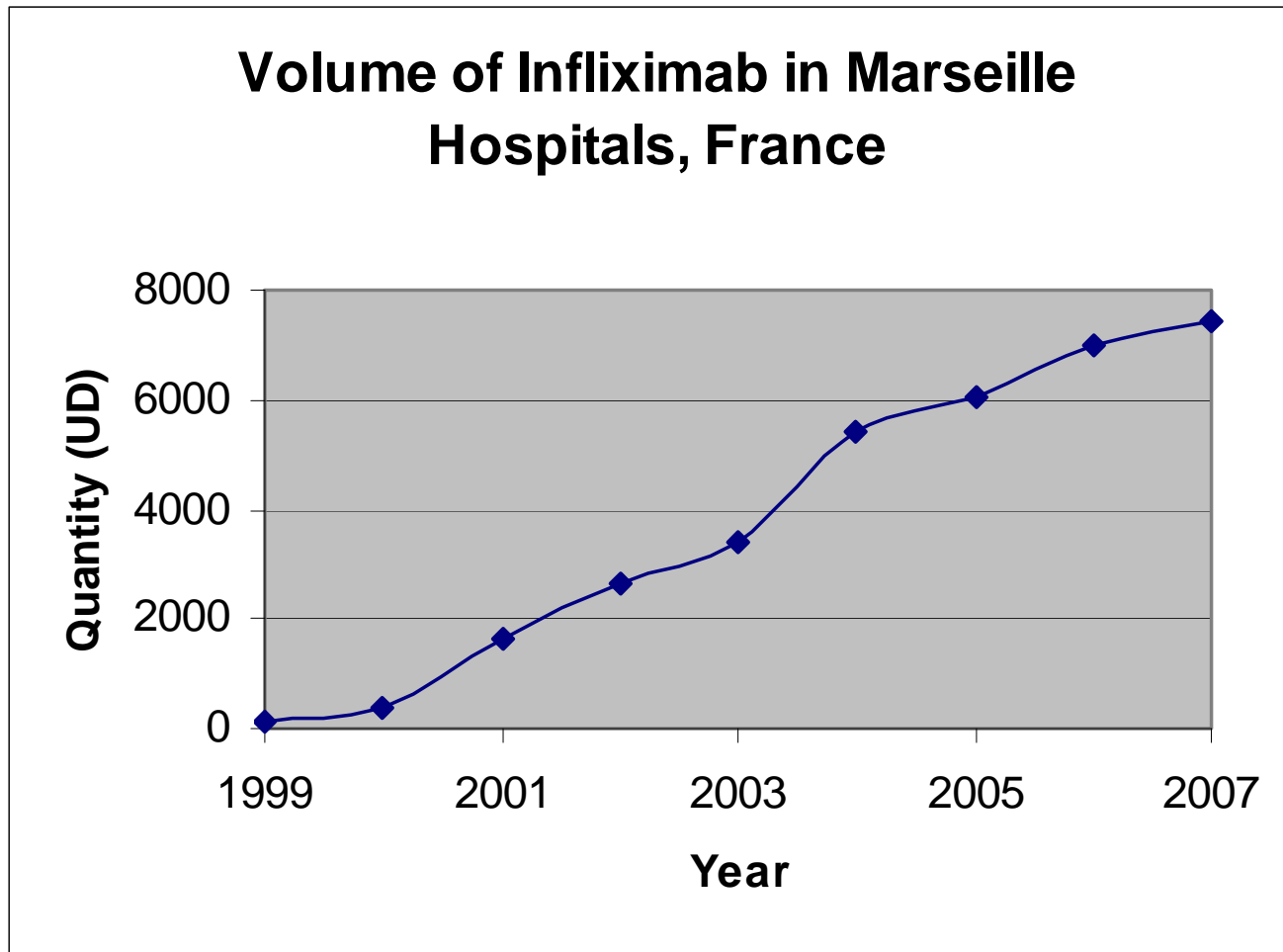
- New biological drugs with acquisition prices over \$50,000 to \$100,000/ patient/ year are adding to resource pressures exacerbated by improving morbidity and reducing mortality
- The pressures will intensify and could crowd out other therapies unless addressed (opportunity costs)
- Additional activities include improved planning for their introduction to optimise utilisation post launch. This involves guidance development, monitoring prescribing, registries as well as other arrangements such as price: volume agreements
- Registries to monitor prescribing against agreed guidance as well as outcomes in practice to modulate future prices and place in care pathways. This requires DTC, database, forecasting and IT skills which Sweden excels at

New expensive specialist drugs are the key drivers of growth in Europe, e.g. Stockholm

Total drug expenditures in Stockholm County
(prescriptions, hospital, OTC) 1977-2007



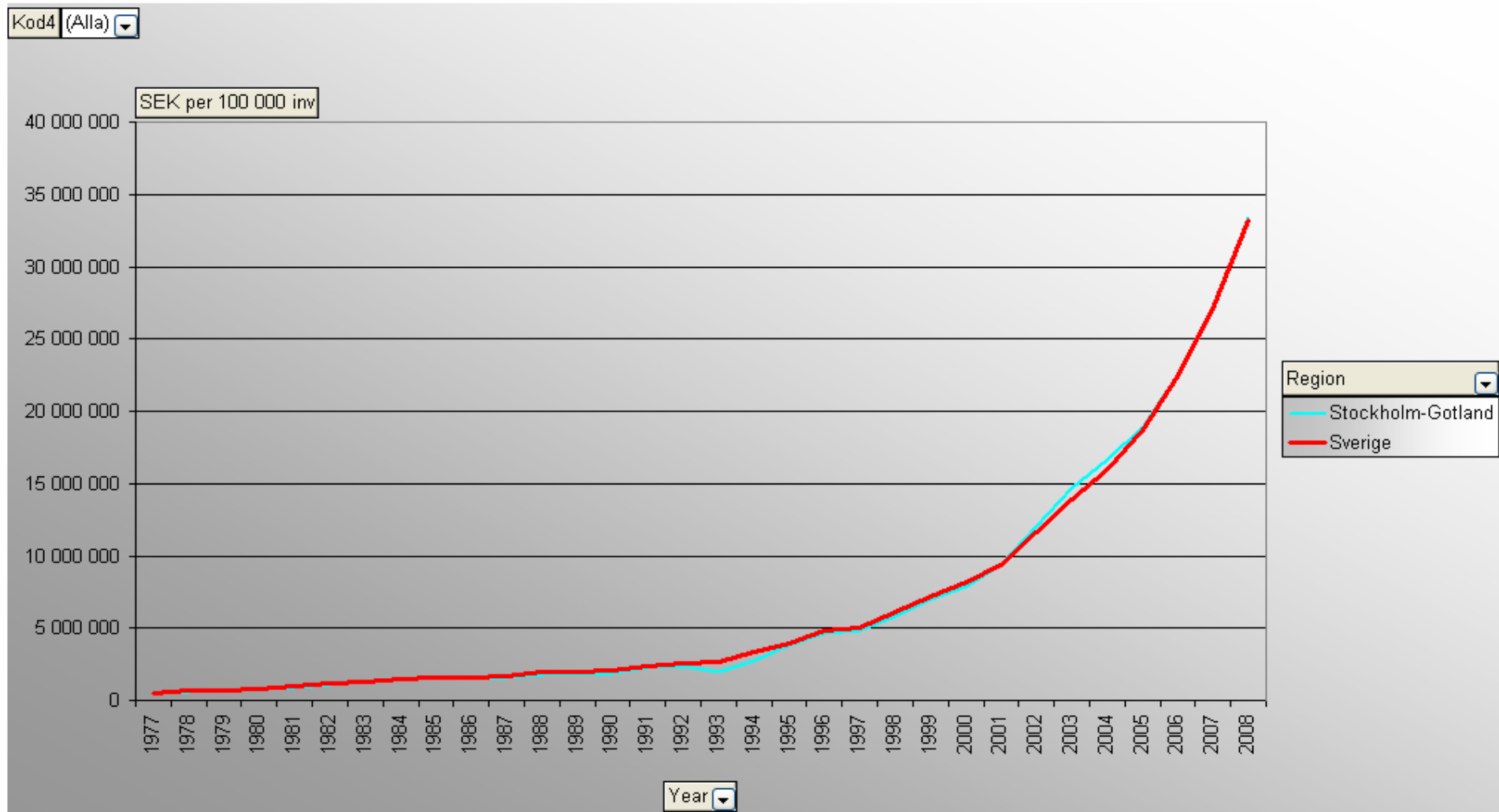
Sales of specialist drugs have also grown in other countries, e.g. TNF alphas in Marseille



HERCEPTIN is crowding out other anti-cancer drugs causing budget pressures in England

- Estimated that HERCEPTIN will cost €2.9mn (£1.9mn)/ year for 75 patients with early breast cancer in one UK hospital
- This will crowd out less expensive treatments unless addressed, e.g. 355 patients can be treated with older drugs at £0.5mn leading to significantly more patients 'cured' (16 overall vs. 3 with a cost/ cure of £650,000 for HERCEPTIN vs. £15,000 for aromatase inhibitors)
- HERCEPTIN also crowds out other palliative treatments, e.g. 4 x cost of taxanes in breast cancer
- These concerns and issues will grow as more high priced cancer drugs are launched requiring proactive DTC activity to ensure equity in cancer care

A similar situation could easily arise in Sweden if growth rates for oncology drugs continue



New high priced cancer drugs will continue to cause concern unless addressed

- The next generation of cancer drugs will further improve morbidity and survival in early stage and advanced disease
- However Professor Sikora recently estimated they could cost the UK up to £50billion a year within four years - equivalent to raising the basic tax rate by 15% (15p in the £)
- This will necessarily lead to the following to reduce cost exposure and tax increases:
 - Greater planning pre-launch including true role in practice
 - Greater restrictions on prescribing where concerns
 - Risk sharing and other arrangements building on experiences in countries such as Italy and UK
 - Routine registries post launch to monitor outcomes in practice as well as prescribing against guidance

Risk sharing schemes include new cancer drugs in Italy along with registries and VELCADE in UK

- In Italy, discounts are being negotiated for the reimbursement of new cancer drugs. These include:
 - Tarceva – 50% discount for the first 2 cycles, re-evaluation at 8 weeks
 - Nexavar - 50% discount for first 3 months with re-evaluation at 3 months. Pay back for non-responders
 - Sutent – 50% discount for first 3 months, further discount of 3.4% for patients with metastatic renal cancer
 - Sprycel – 7% discount, 10 – 12 days free treatment
- The VELCADE scheme in the UK whereby J & J refunds non-responders (<50% reduction in serum paraprotein levels by the fourth cycle). NHS continues to fund treatment in responders as cost/ QALY reduced to £20,700
- These schemes provide direction to other countries

Examples of price: volume arrangements include Australia and Europe. These will grow

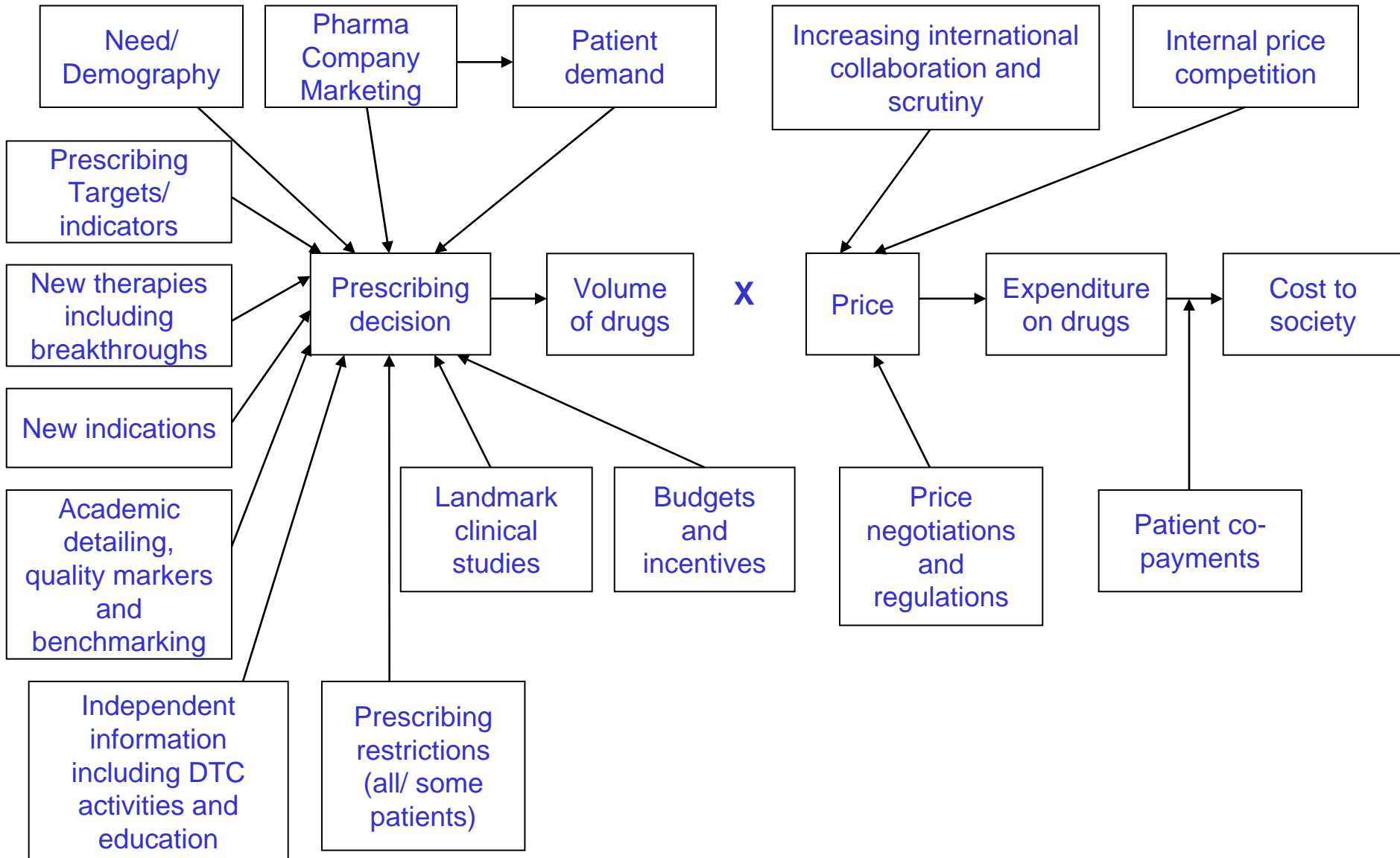
Country	Current arrangements
Australia	<ul style="list-style-type: none">▪ Pharmaceutical companies refund a percentage if expenditure on a new product exceeds agreed limits. This also includes a future price decrease▪ Currently over 14 agreements in place
Estonia	<ul style="list-style-type: none">▪ Annual price: volume agreements are mandatory for all pharmaceuticals in the positive list▪ This includes the rationale supporting the figures▪ Rebates and/ or price reductions if expenditure exceeded
France	<ul style="list-style-type: none">▪ Contracts are signed annually to help keep expenditure within government targets. Innovative, orphan drugs, generics and drugs for children exempt▪ Agreements take into account dosing and utilisation of single drugs as well as classes▪ Rebates in 2004 were €670mn – 3% of total pharmaceutical expenditure

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

Italy currently leads the way in development and utilisation of registries post launch to monitor effectiveness in practice

Medicine	Registered	Concluded
AVASTIN	5252	1702
ELOXATIN	5479	2907
ERBITUX	3534	1599
FASLODEX	5592	2046
HERCEPTIN	5090	1265
NEXAVAR	2148	0
TARCEVA	7415	3389
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Supply and demand (rational use initiatives) impacting on pharmaceutical expenditure



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There are formal P & R systems in most EU countries and growing reference pricing

- European countries such as Austria, Belgium, France, Italy, Poland, Spain and Sweden have formal pricing and reimbursement systems for new products. There is 'free' pricing in Germany, Sweden and the UK; however restrictions in Sweden and UK where concerns with the value of new drugs
- The process typically starts with assessment of innovation
- Different approaches across Europe with processes generally not transparent although outcomes important for pricing
- Reforms growing across Europe to lower the price of generics and originator brands as well as interchangeable brands in a class once generics available. These will accelerate

Most European countries have formal P & R

Country	National P & R systems	Regional initiatives
Austria	Formal P & R system with prescriptive pricing	No regional initiatives
England	Free pricing for new products. NICE legally binding	Yes – via PCT initiatives
France	Formal P & R system. Negotiated prices	Some regional initiatives (hospital)
Germany	Free pricing. Reference pricing for some classes and negotiated prices with Sickness Funds	State initiatives (Sickness Funds and Physician Associations)
Italy	Formal P & R system with negotiated prices	Yes via Regions (budgets)
Scotland	SMC for appraising value. Not legally binding	Health Board initiatives
Spain	Formal P & R system with negotiated prices	Yes – via AACCs (budgets)

Austria has a transparent system where the level of innovation for new drugs drives prices

Therapeutic benefit for patients	Number of patients treated	Price (acquisition costs) in comparison with listed products
Substantial added	Majority	Higher prices based on average EU prices - Pharmacoeconomic study required
	Subgroup	Higher prices based on average EU prices - Pharmacoeconomic study required
Added	Majority	Maximum 10% higher
	Subgroup	Maximum 5% higher
Equal/ similar		Lower (minimum 10%)

- Only 10% of new drugs are perceived as innovative – ‘substantial addition’, with 99% of decisions upheld
- These measures combined with aggressive pricing for generics and voluntary price reductions have limited growth in pharmaceutical expenditure in Austria in recent years

The innovation level for new drugs in France is divided into five categories. This drives prices

- New drugs in France are assigned an ASMR (Amelioration du service medical rendu – the additional therapeutic benefit versus current standards) score:

ASMR rating	Explanation (versus current drugs)
I	Major improvement (new therapeutic area, reduction of mortality)
II	Significant improvement in efficacy and/or reduction of side-effects
III	Modest improvement in efficacy and/or reduction of side-effects
IV	Minor improvement
V	No improvement

- Approximately 13% of new drugs in recent years granted ASMR I or II (21 – 22% including ASMR III) with majority ASMR IV or V (78%)
- There is now Pan-EU pricing for ASMR I to III to accelerate availability. Price and volume negotiations for others with price reductions expected for ASMR V

Prescrire in France uses a different approach to categorizing innovation of new drugs

7 Point system used by Prescrire in France to assess the level of innovation of new drugs and new indications

Category	Description
Bravo	A major therapeutic advance where previously no treatment
A real advance	Important therapeutic innovation but certain limitations
Offers an advantage	Some value but does not fundamentally change the present therapeutic practice
Possibly helpful	Minimal additional value and should not change prescribing habits except in rare circumstance
Nothing new	May be a new substance but superfluous as it does not really add to the current possibilities – most cases a me-too
Judgement reserved	Judgement reserved until better data and/ or a more thorough evaluation of the drug is available
Not acceptable	Product without benefit but with the potential for real disadvantages, e.g. patient safety

Prescrire believed no major advances in 2005. TC scrutiny likely to grow to conserve resources

Category	Description
Bravo – Major advance	No drug
A real advance – but limitations	One drug – VARIVAX (chickenpox vaccine) in defined sub-group only
Offers an advantage	Four new drugs including Premetrexed (plural mesothelioma) and Trastuzumab (breast cancer)
Possibly helpful	20 new drugs or indications
Judgement reserved	2 new drugs
Not acceptable	7 new drugs, 9 new indications, 3 line extensions including Efalizumab for psoriasis and Duloxetine for stress incontinence

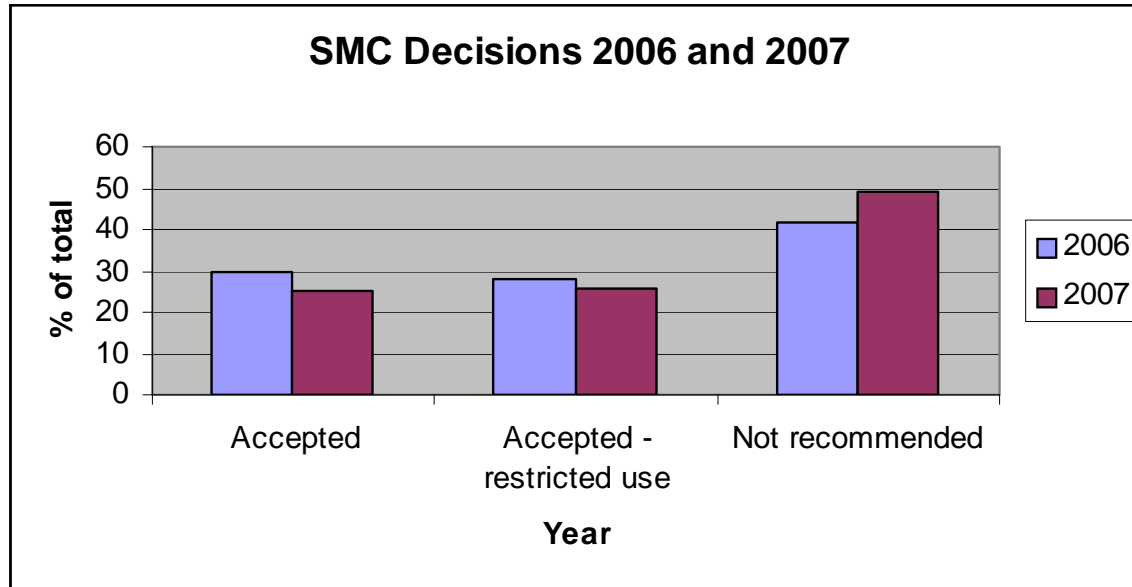
Economic criteria used for new drugs in Canada, Ireland, Sweden, UK and US. Cut-off levels in UK

Country	Current decision making criteria
Canada (CDR)	<ul style="list-style-type: none">▪ Strict assessment of the clinical and economic benefits of new drugs▪ Recommended that manufacturers use clinically relevant outcome measures in robust studies to strengthen the review (clinically focused)▪ No formal cost/ QALY cut-off level
Ireland (HSE)	<ul style="list-style-type: none">▪ Selected products assessed against cost/ QALY cut off of €45,000▪ Some flexibility depending on disease area
Sweden	<ul style="list-style-type: none">▪ Cost-effectiveness and cost-utility analyses are used by TLV to determine reimbursement for new drugs (no, limited or total population)▪ However no formal cost/QALY and no budget impact consideration puts pressure on Counties

Economic criteria used for new drugs in Canada, Ireland, Sweden, UK and US. Cut-off levels in UK

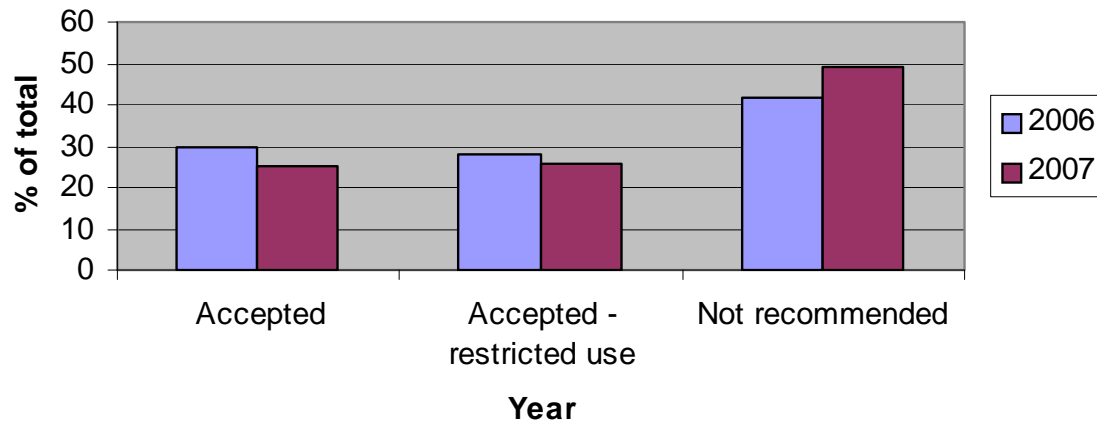
Country	Current decision making criteria
UK – Scotland (SMC)	<ul style="list-style-type: none">▪ New drugs typically funded if ICER is below cost/QALY of £20,000; above £20,000/QALY, decisions incorporate issues such as degree of uncertainty and innovative nature of new drug▪ Above an ICER of £30,000/QALY, the case has to be strong even in priority disease areas
UK - England	<ul style="list-style-type: none">▪ No formal cost/QALY cut-off levels▪ In reality with few exceptions, NICE approves funding for new technologies with a cost/QALY less than £20,000 - £30,000
US (MCOs)	<ul style="list-style-type: none">▪ Typically MCOs in the US place new products on Tier 3 or 4 (highest co-payment) until they can assess their value in practice▪ CEAs generally used rather than CUAs with no formal cost/ QALY cut-off levels

SMC transparency and not legally binding increases the aggressiveness of decision making



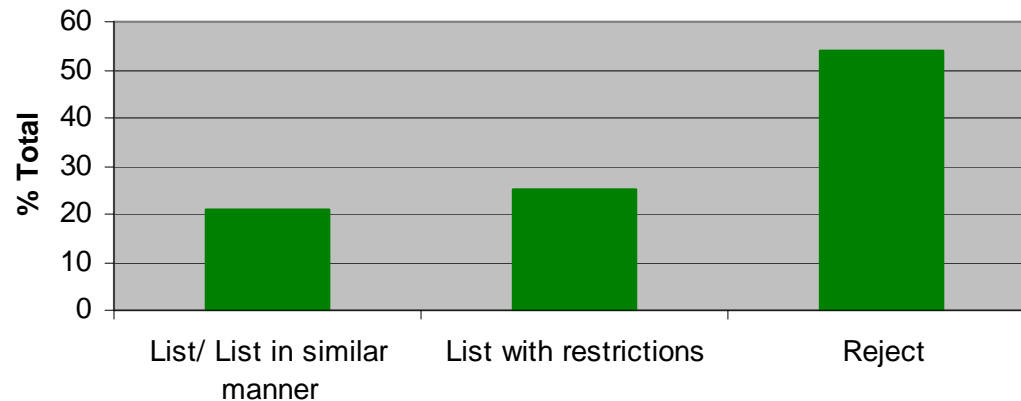
Year	TLV decisions
October 2002 to March 2005	<ul style="list-style-type: none"> The TLV denied reimbursement for 13 drugs in 107 cases of 'principal importance' (12%) and gave limited or conditional reimbursement to 12 drugs (11%) due to concerns with their cost-effectiveness
2006	<ul style="list-style-type: none"> 10% of New Chemical Entity (NCE) applications (4 out of 40) were not approved for reimbursement Over 20% of new NCEs only received restricted reimbursement due to concerns with their value. Examples included rimonabant and rosuvastatin
2007	<ul style="list-style-type: none"> 5 new applications (10%) were denied reimbursement, with restricted reimbursement assigned to 11 applications Delisting of cough medicines

SMC Decisions 2006 and 2007



Interestingly the % of submissions accepted or rejected similar between Canada and SMC despite different emphasis on data scrutiny

CDR decisions (Initiation up to April 2007)

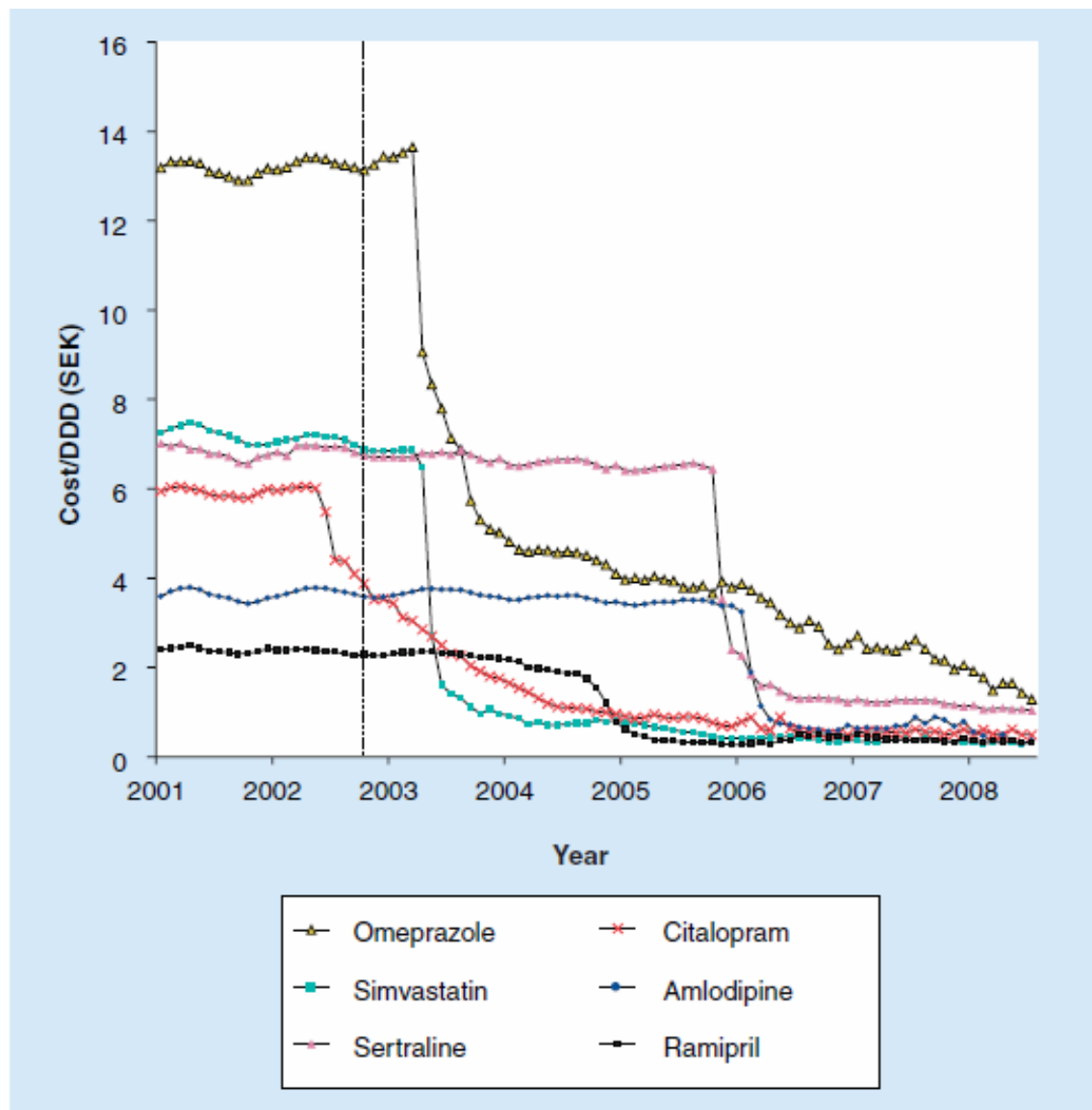


Generic prices vary considerably across Europe. Likely to see greater convergence in the future

- **Austria** – Generic and originator prices 60% below originator prices (once 3 launched). Subsequent generics lower prices
- **France** – Generics must be 55% below originator price. In addition, pharmacists typically receive discounts
- **Germany** – Reference price scheme (similar to class schemes). Competition coupled with patient and physician incentives helps drive down prices
- **Italy** – Generics must be at least 20% below originator prices
- **Spain** – Currently reference pricing for generics with the cheapest product dispensed
- **Poland** – Prices for generic atypicals 44 to 77% below originator prices
- **Sweden** – Mandatory generic substitution coupled with regular review of prices, demand side measures and patient acceptance of generics has helped to obtain low prices
- **UK** – New transparent regulations has led to low prices, e.g. 28 x 20mg simvastatin less than €1 (98% below originator)

Generic prices have fallen in Sweden with reforms. This impacts on overall class prices

Cost/DDD
for 6
products in
top 25
prescribed
ambulatory
care
products in
Sweden on a
DDD basis



Reference pricing for products in a class is releasing considerable resources, e.g. Germany

- Considerable savings in Germany through reference pricing for drugs grouped by comparable pharmacological and therapeutic activities (Level 2), e.g. statins and PPIs

Proton Pump Inhibitors	1998	2003	2006	2007	% difference vs. 2007 vs. 2003
Utilisation (DDDmn)	180.6	570.7	888.0	1157.5	102.8
Expenditure (€mn)	486.7	990.1	968.7	974.8	-1.5
Cost/ DDD PPIs (€)	2.69	1.73	1.09	0.84	-51.4

Statins	1998	2003	2006	2007	% difference vs. 2007 vs. 2003
Utilisation (DDDmn)	468.3	1168.1	1736.8	2065.0	76.8
Expenditure (€mn)	642.9	1108.9	572.5	480.5	-56.7
Cost/ DDD statins (€)	1.37	0.95	0.33	0.23	-75.5

Value-based pricing is growing in Sweden providing examples to other EU countries

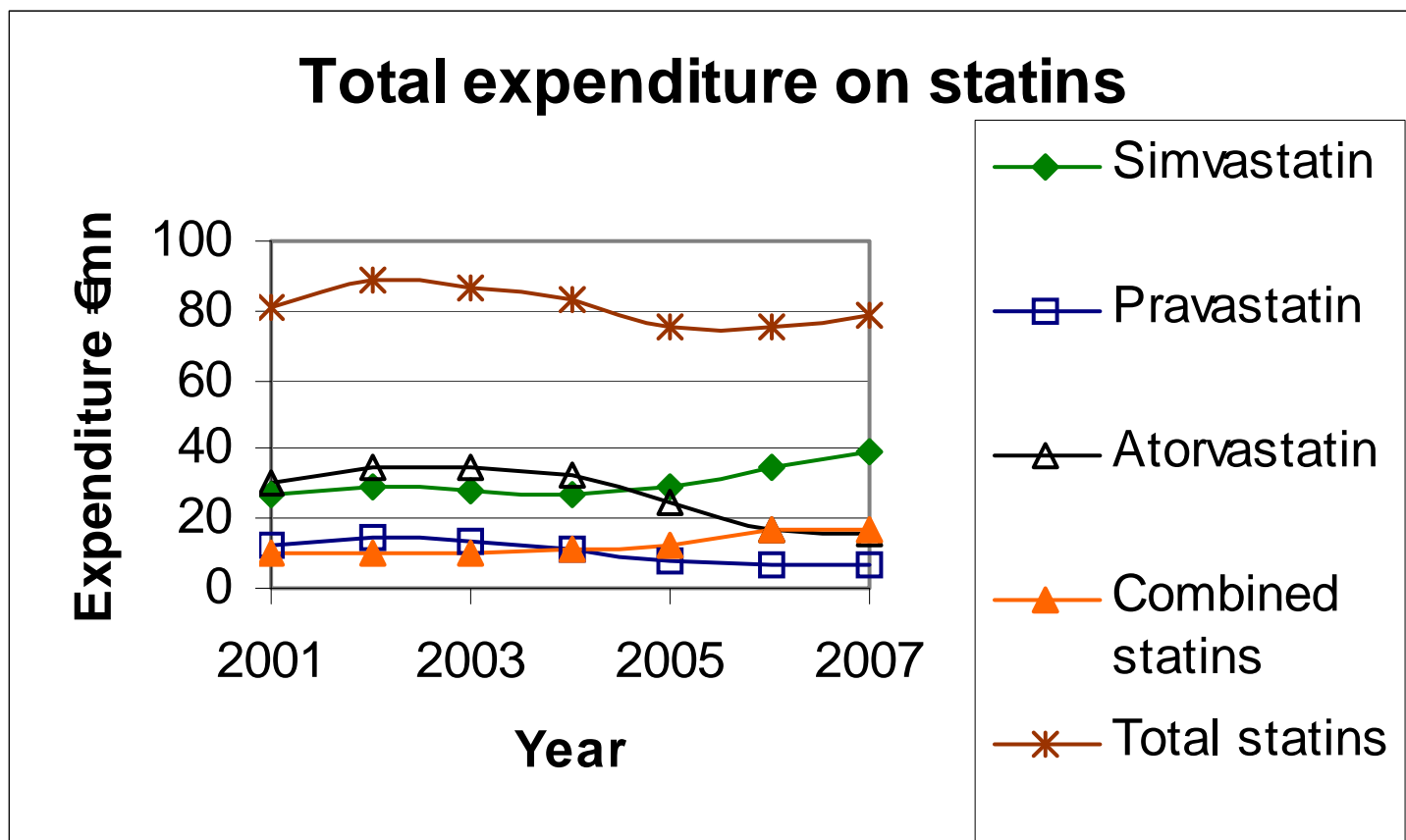
- Prescriptive pricing for PPIs in Sweden (maximum 25% above generic prices) set an example to other countries, e.g. UK. Less prescriptive pricing for other classes
- Estimated savings from full implementation are:
 - SEK42mn/ year for the triptans
 - SEK175mn/ year from the review of PPI prices
 - SEK40mn/year from respiratory products
 - SEK400mn/ year from the review of anti-hypertensives including restricting ARB use
 - SEK40million/ year from the review of antidepressants
 - SEK170mn/ year from the review of lipid lowering drugs
- Instigation of VBP principles for all 49 therapeutic will release further resources and provide examples to other European countries considering such initiatives

Austria has implemented voluntary price reductions in a class once generics available

- Austria has implemented voluntary price reductions for existing brands in a class once generics are available
- Prescribing restricted if Companies reluctant to lower prices, e.g. atorvastatin restricted to second line (similar to Sweden) leading to lower utilisation and savings in practice

Year	Annual savings from price reductions	Cumulative savings from price reductions
2002	€20.9mn	€20.9mn
2003	€39.3mn	€60.2mn
2004	€50.8mn	€111.0mn
2005	€27.8mn	€138.8mn
2006	€70.4mn	€209.2mn

Generics plus restricting atorvastatin moderating statin costs in Austria despite increased volumes



Combined statins include cerivastatin, fluvastatin, lovastatin and rosuvastatin

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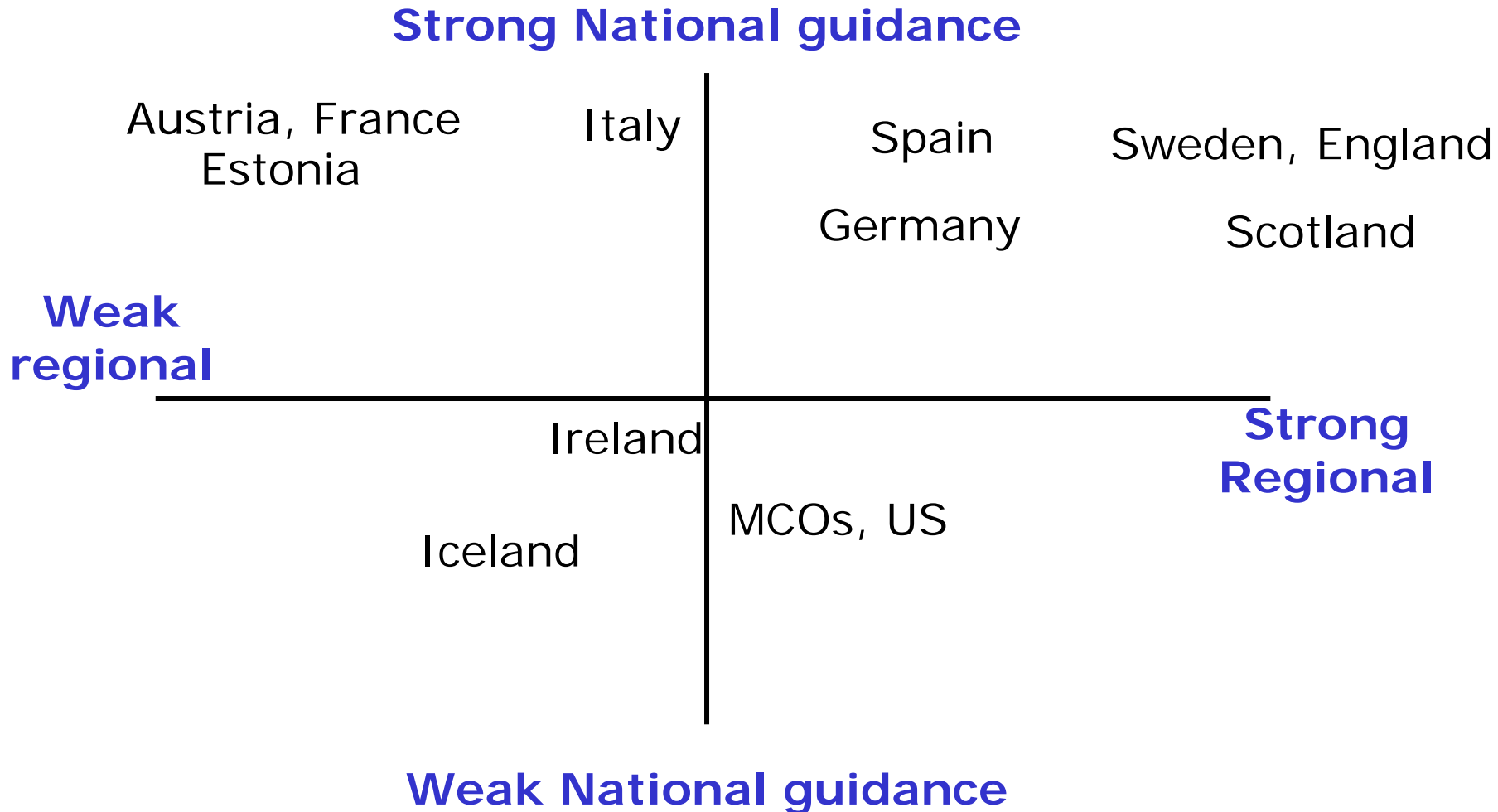
A range of measures implemented across Europe to enhance rational use. These will grow

- A range of combined measures have been instigated across Europe to improve the quality and efficiency of prescribing. These vary depending on:
 - Whether national or regional budgetary responsibility
 - Extent of DTC activity including pharmaceutical advisers
 - Physician characteristics and likely motivators
 - Current barriers to rational prescribing
 - Extent of non-medical influencers including pharmaceutical companies, the media and patient groups
- Counties such as Stockholm and Östergötland, as well as countries such as Austria and France, are successfully using patients and patient groups to enhance rational prescribing
- DTC activities will necessarily grow becoming a future target for pharmaceutical company marketing activities

The measures can be divided into national and regional initiatives; alternatively 4 'E's

- The initiatives across Europe can be divided into a number of categories; these include:
 - Pan-European approaches
 - Predominantly national initiatives to improve the quality and efficiency of prescribing
 - Predominantly regional initiatives including DTCs
- Alternatively around the 4 'E's:
 - **Economics** - financial incentives, budget devolution
 - **Education** - Academic detailing, guidelines, audits, benchmarking and formularies
 - **Engineering** - structural changes, prescribing targets, limiting pharmaceutical company activities
 - **Enforcement** – legally binding arrangements, restricted lists, rebates

European countries divided into predominantly national, regional or combined initiatives



National measures incorporating the 4 'E's include educational initiatives and guidance

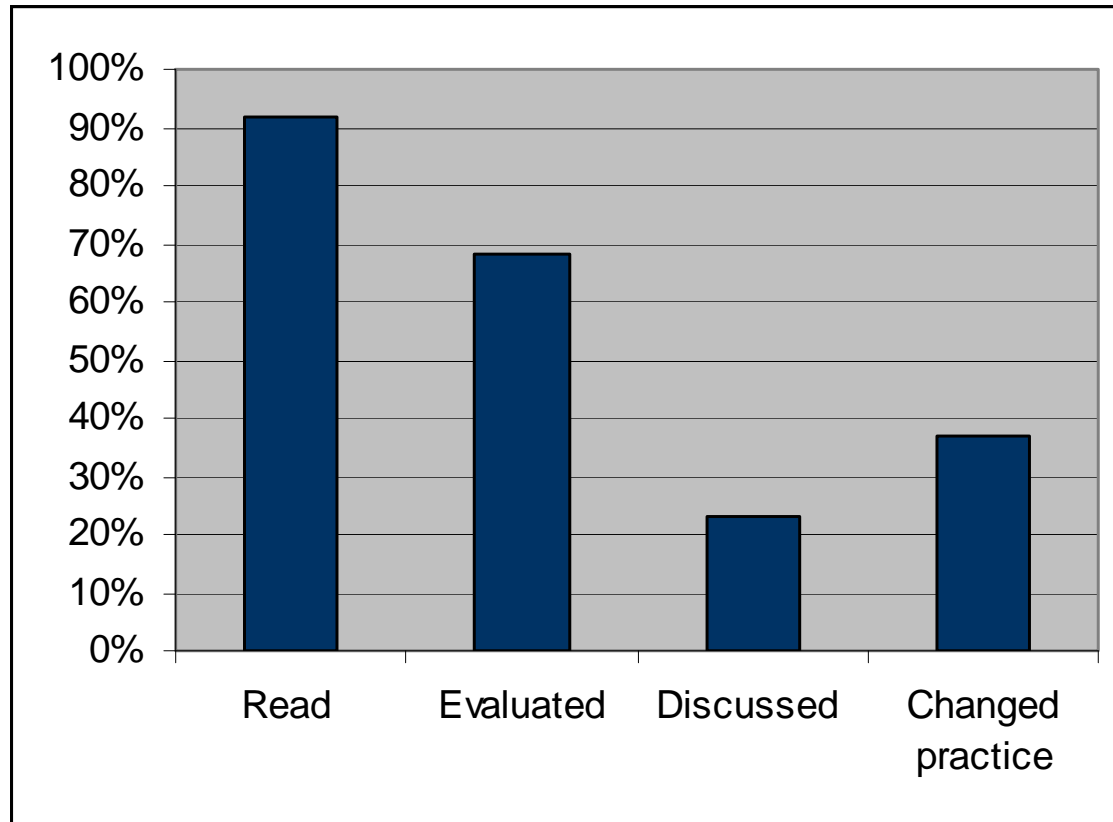
- National initiatives incorporating the 4 'E's include:
 - Guidance, e.g. 'Medicines and Reasons' initiative in Austria, NICE guidance and MeReC Bulletins in UK
 - Prescribing auditing and benchmarking activities in Austria and growing in France (EPP)
 - Targeted educational activities among physicians and patients, e.g. France for antibiotics and generics
 - Disease management programmes, e.g. Germany, as well as Quality and Outcomes Framework (QoF) in UK
 - Prescribing restrictions – all or sub-populations, e.g. Austria, Italy (AIFA notes) and Sweden
 - Rebate schemes (Price: Volume agreements) for excessive prescribing, e.g. Belgium, France, Estonia, Hungary and Italy
 - Alongside this, growing pre launch/ Horizon Scanning activities, e.g. Italy, Sweden and UK

Austria has recently introduced 'Medicines and Reason' initiative to enhance rational drug use

- The 'Medicines & Reason' initiative has recently been introduced in Austria to enhance rational use of drugs
- Implementation helped by:
 - **Focus** - only one guideline per year
 - **Involvement** - all key stakeholders involved in their development including physicians and industry
 - **Finance** - dedicated budget
 - **Dissemination** - Guidelines produced for physicians and patients. Insurance companies organise meetings with physicians to discuss implementation
- Generally good acceptance by physicians as seen in recent surveys. Implementation enhanced by active dissemination and the production of patient booklets

Austrian physicians typically read guidelines for GI diseases and changing behaviour

Action taken by 405 physicians following guidelines on the management of acid-related upper gastrointestinal disease



Multifaceted initiatives in France have helped to increase generic prescribing and dispensing

- Generic prescribing rates have risen in France where multiple sources exist - 74.5% by volume in 2007 vs. 55% in 2004
- Increase helped by comprehensive campaigns with physicians, pharmacists and patients
 - Patients educated about the quality of generics and higher co-payments if wish a more expensive brand
 - Physicians received salary increases for increasing their INN/ generic prescribing rates
 - Pharmacists set targets for generic substitution rates coupled with financial incentives
- Estimated that measures to lower generic prices and increase generic prescribing rates saved €1bn/ year in 2007

Instigating prescribing restrictions for new ambulatory drugs in Austria helps limit impact

- New premium priced ambulatory care products in Austria assigned to a 'red' or 'yellow' box requiring prior authorisation by CMO of insurance company for reimbursement
- Restrictions can be reduced by lowering prices

Box	Total costs (€1000)	Average cost/ prescription (€)
Green	1560681	15.99
Light yellow	181428	86.46
Dark yellow	232740	155.26
Red	11573	111.68
Average		19.45

Regional activities incorporating the 4 'E's are similar including education and monitoring

- Regional initiatives incorporating the 4 'E's include:
 - Italy (especially Northern Regions)**
 - Prescribing guidance, benchmarking and financial incentives along with Horizon Scanning activities
 - Spain (e.g. Catalonia)**
 - Prescribing guidance for common diseases, benchmarking and financial incentives
 - Sweden**
 - Active DTC activities, prescribing guidance, prescribing targets, monitoring of prescribing/ benchmarking, educational interventions, incentive schemes, and patient involvement along with Horizon Scanning activities
 - UK**
 - Prescribing guidance including local adaptation of national guidance, prescribing targets, incentive schemes, benchmarking and educational interventions

Sweden provides direction to other countries when enhancing their demand side measures

DTC activities to improve quality and efficiency include:

- Specific DTC law with defined activities
- Regional guidance on optimal drugs to prescribe for given indications based on evidence and input from experts, e.g. Wise Drug List in Stockholm as well as therapeutic ladders
- Computerised tools for analysis and benchmarking of prescribing patterns, e.g. DU90% methodology. Alongside this national prescribing register to monitor changes
- Patient-oriented information/ educational activities
- Prescribing targets to monitor the efficiency of prescribing
- Financial incentives and budget devolution to enhance cost consciousness amongst physicians
- Monitoring prescribing of restricted drugs including registries. Registries also used to monitor effectiveness and safety of new drugs in reality, e.g. rimonabant for obesity

Prescribing targets have also be instigated in Sweden mirroring initiatives elsewhere

- Prescribing targets have also been introduced in Sweden as well as across the counties to enhance the quality and efficiency of prescribing
- This mirror initiatives in other countries, e.g. prescribing targets have been introduced in Spain (Catalonia) and the UK
- Targets include % of PPI prescriptions as generic omeprazole, % of statins as generic simvastatin and % of renin-angiotensin drugs as ACE inhibitors. County targets typically developed after extensive consultation and reviews with physicians and medical opinion leaders
- UK goals similar for instance to Stockholm County Council

National Prescribing targets include some of the following for benchmarking among counties:

Medical (Quality of care)

- % of people >80 years purchasing ten or more prescribed drugs concomitantly
- Proportion of the population treated with antibiotics
- % of patients with prescribed and dispensed diabetes drugs who are also prescribed lipid lowering drugs
- % of stroke patients with atrial fibrillation dispensed anticoagulation therapy 12 months after discharge
- % of post acute myocardial infarction (AMI) patients dispensed lipid lowering therapy 12 to 18 months after discharge

Efficiency

- % of patients prescribed generic omeprazole as a % of all PPIs
- % of patients prescribed either generic simvastatin or generic pravastatin as a % of all statins
- Proportion of patients treated on ARB therapy not prescribed an ACE inhibitor prior to ARB initiation

Prescribing targets in counties such as Stockholm County Council include:

Category	Target	2007
% of PPI prescriptions as generic omeprazole	>80% of DDDs	72%
Reducing the prescribing of PPIs for non-specific dyspepsia	<20DDD/ thousand inhabitants per day	26 DDD/TID
% of antithrombotic drugs as low dose acetylsalicylic acid	>95% of DDDs	96%
% of statin prescriptions as generic simvastatin	>80% of DDDs	74%
% of renin-angiotensin products as ACE inhibitors	>75% of DDDs	57%
% generic mirtazapine as a % of all mirtazapine	>90% of DDDs	51%
% of quinolones prescribed to treat urinary tract infections (UTIs) as opposed to other antibiotics such as trimethoprim, nitrofurantoin, and pivmecillinam	< 30% of prescriptions	30%
% of patients prescribed generic nasal budenoside versus other nasal steroids for the treatment of hay fever and other pertinent conditions	> 15% of DDDs	25%

Prescribing targets in Östergötland include (for benchmarking to help PHCs with savings)

Indicators of cost-effective prescribing	Characteristics
Indicators of quality of prescribing	<ul style="list-style-type: none">• Number of patients with diabetes reported to the national quality register for diabetes mellitus• % of patients with diabetes reaching agreed targets for HbA1c levels• % of patients with diabetes >40 years prescribed statins• % of patients with diabetes >40 years prescribed angiotensin-converting enzyme inhibitors or angiotensin-II receptor antagonists
Indicators of equity	<ul style="list-style-type: none">• Number of defined daily doses (DDD) adjusted for the age and sex of different ATC-groups dispensed to patients listed to PHCs regardless of the prescriber• Costs in SEK adjusted for the age and sex for the different ATC-groups dispensed to patients listed to PHCs

Prescribing targets in England linked with incentives to improve rates. This will grow

	Average in England (July 2006)	Level PCTs to deliver estimated savings	Level most efficient PCT (July 2006) to act as future guidance
% Statins as generic simvastatin	52%	66%	84%
% Renin-angiotensin drugs as ACE inhibitors	79%	84%	89%
% PPIs as generics such as generic omeprazole	82%	87%	95%
Volume clopidogrel prescribed (DDD/1000 age-sex weighted patients)	149	111	61

- Similar utilisation of generic simvastatin, omeprazole and ACE inhibitors between England and Stockholm County Council
- Estimated that annual savings of £227mn can be achieved if all PCTs reach prescribing targets as part of the 'Better care/better value' initiatives. Financial and improved care incentives for PCT GPs to attain targets

Financial incentive schemes appear to be working alongside budget devolution

- A variety of financial incentive models have been introduced across Sweden providing examples to other countries to improve quality and efficiency, e.g. for Stockholm includes:
 - ❑ Improved guideline adherence to recommended drugs
 - ❑ Physicians identifying areas of improvement including limiting prescribing where weak evidence and safety issues
 - ❑ Savings greater than 30,000SEK/ GP for every % increase in adherence to recommended drugs. These estimated at least five times greater than programme costs
 - ❑ Consequently, far more efficient than UK (QoF targets)
- The future must include measures to optimise utilisation of new expensive drugs. This likely to include:
 - ❑ greater co-ordination of identification, forecasting and critical drug evaluation activities to optimise utilisation
 - ❑ post launch activities including registries to ensure prescribing in accordance with guidance

Horizon Scanning activities growing to optimise resources. Sweden provides direction

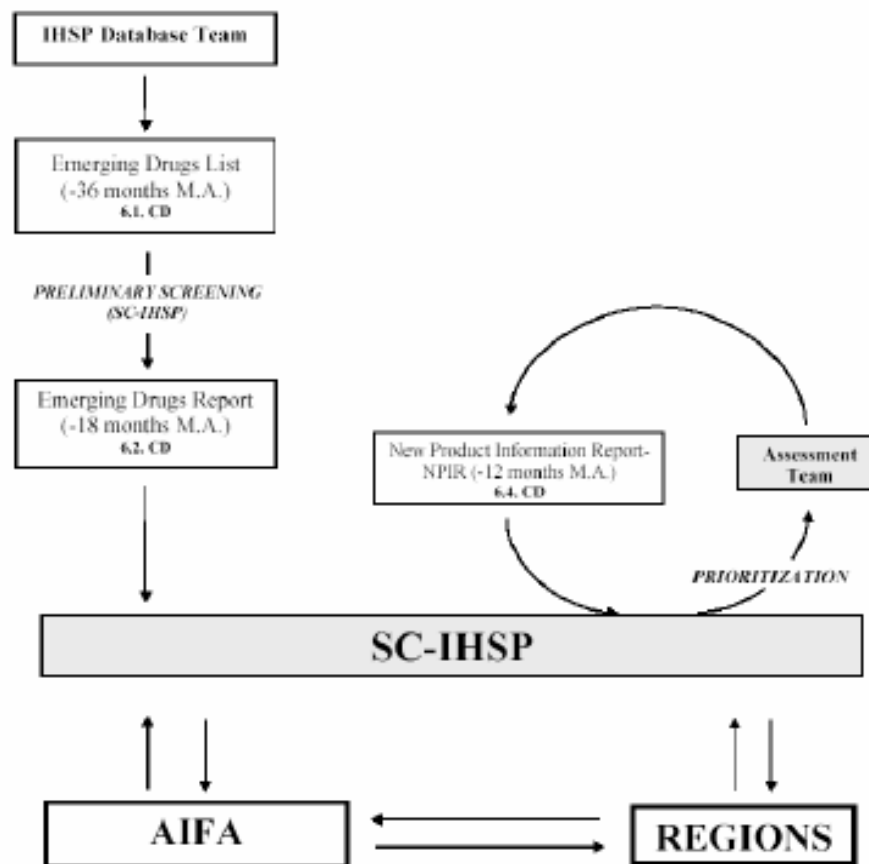
- Horizon Scanning, forecasting and critical drug evaluation activities are growing pre-launch across Europe to help optimise the use of scarce resources with the cost of new expensive drugs seen as the greatest challenge to European healthcare activities
- Activities in Austria, Italy, Sweden, and UK (Liverpool and SMC) provide direction to other countries in Europe
- The use of registries to monitor prescribing and outcomes in practice is also growing across Europe building on experiences in Italy and Sweden (nationally and among the counties)

Horizon Scanning activities growing to optimise resources providing direction to others

- SKL as well as the counties are introducing models to optimise the diffusion of new expensive drugs across all sectors, e.g. the model in Stockholm consists of early detection, forecasting, critical drug evaluation and structured protocols to assess value in practice
- Estimated growth in expenditure for new and existing products/ classes in for instance the Stockholm County forecasting model is based on:
 - Their position in the product life cycle
 - Envisaged reforms or other expected changes over the time scale for the model
 - Envisaged new drugs, their prices and likely prescribing
- Model robustness enhanced through using local experts
- DTC personnel play a key role in these activities, with the models increasingly providing direction to other countries

Italian Horizon Scanning activities start 36 months before likely EMEA approval. Input enhanced nearer launch

IHSP Flow Chart



Legend

SC-IHSP: Italian Horizon Scanning Project - Scientific Committee

M.A.: EU Marketing Authorization

AIFA: Italian Medicines Agency

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- 4. Future for DTC activities and members**

Further reforms essential including strict criteria for granting premium prices for new drugs

- Further reforms will be implemented across Europe to ensure comprehensive and equitable healthcare without prohibitively raising taxes or insurance premiums
- Alongside this will see improved planning for new drugs including forecasting, critical drug evaluation, monitoring of prescribing against guidance and monitoring outcomes in practice. This may include 'risk sharing' arrangements and setting minimum effectiveness criteria for funding especially where concerns with surrogate markers
- This will require increased DTC activity especially for specialist drugs with clinical pharmacists playing a key role. As a result, DTCs will become an increasing target for pharmaceutical company activity

DTCs can provide direction across Europe to enhance the rational use of medicines

DTCs can provide direction in Sweden and Europe with:

- Establishing minimum effectiveness criteria for premium pricing of new expensive drugs such as new cancer drugs
- Ensuring Pharmaceutical companies routinely provide outcome rather than surrogate data to support formulary listing of new products; otherwise no listing/ funding
- Playing a key role to optimise the utilisation of new expensive drugs through planned introduction and follow-up
- Driving forward refinement of incentive schemes/ budget devolution schemes to enhance rational use of drugs
- Driving forward initiatives to enhance compliance especially for non-symptomatic diseases such as hypertension
- Helping develop new quality targets for prescribing linked to outcomes, e.g. QoF targets in the UK
- Help further refine financial incentive schemes
- Enhancing synergy between national and regional groups

Critical drug evaluation will include greater scrutiny with surrogate markers where concerns

- Examples where concerns with surrogate markers include:
 - Flecainide - helps decrease arrhythmias but increases overall mortality
 - Oestrogens for HRT - help improve the lipid profile (HDL) but do not decrease CV events
 - Fibrates - have a variable impact on CV events and overall mortality despite all universally improving lipid profiles
 - Ezetimibe lowers LDL levels but no impact on carotid intima–media thickness (surrogate for CVD). In addition, concerns with increasing the risk of certain cancers
 - Raloxifene - helps improve BMD in patients with osteoporosis but has no impact on hip fracture rates
 - The glitazones - help improve Hba1c levels in patients with T2DM but increase heart failure rates, etc.
 - Certain cancer drugs significantly improve response rates but have limited impact on overall survival
 - Etc.

Composite measures are also a concern as they can give a false impression of health benefit

The use of composite measures in STEMI patients (patients with ST-elevation myocardial infarction - STEMI) gave a misleading picture of the overall effectiveness of clopidogrel

End Point	Clopidogrel	Placebo	p
Death	45 (2.6%)	38 (2.2%)	0.49
Recurrent ischemia	44 (2.5%)	63 (3.8%)	0.08
Coronary artery occlusion	192 (11.7%)	301 (18.4%)	<0.001
Composite	262 (15.0%)	377 (21.7%)	<0.001

Increased survival was the key criteria for funding premium priced cancer drugs in the UK

Minimum effectiveness and data quality for new cancer drugs

Effectiveness	Criteria
A	Median survival improved > 9months + improved QoL
B	Median survival improved 3 - 6 mnths. + improved QoL
C	Improved QoL, no impact on survival
D	Minimal impact QoL, no impact survival
Data Quality	Criteria
alpha +	Meta analysis or two high quality RCTs
alpha -	One high quality RCTs and supporting Phase II data
beta	One poor quality RCT and/or several Phase II studies

- Ferguson and colleagues believed only new products with A and B effectiveness criteria and alpha data quality should be funded at premium prices
- Cost/ QALYs should be a subsequent consideration to approve funding once minimum standards attained

Compliance is a key consideration in ambulatory care. There are ways to enhance this

- Potential ways that DTCs can help improve patient compliance especially for chronic diseases include:
 - Helping physicians provide information to patients to enhance their understanding of the medicines prescribed including dosing recognising differences between patients. This includes dealing with side-effects where this is an issue as well as potential drug: drug interactions
 - Ensuring robust systems and information when patients are transferred between services
 - Helping professionals monitor prescribing and refill rates and subsequently communicating with patients
 - Initiating research with patients on potential ways to enhance adherence/ reduce barriers for poor adherence for new and existing drugs in the disease area, and including the results in future physician/ patient/ DTC activities

DTCs can co-ordinate activities to further enhance quality and efficiency of prescribing

- DTCs can potentially co-ordinate activities to further enhance quality and efficiency of prescribing through:
 - Helping TLV with further reviews of new classes as well as routinely instigating activities to support implementation of current guidance, e.g. ACEis/ ARBs
 - Putting pressure on TLV to review all new products and not just ambulatory care products as loop hole exploited
 - Combining activities for horizon scanning, critical drug evaluation and needs based forecasting linked to SKL
 - Join forces to develop and implement registries – funding through national sources independent of the industry
 - Push for price: volume or other risk sharing agreements such as price caps and outcome schemes where pertinent administered by TLV to minimise county budgetary pressures

Examples of price cap schemes in Europe and the US include:

Country	Current schemes and arrangements
Italy	<ul style="list-style-type: none">▪ Costs of bevacizumab in approved cancers can not exceed €25,941 per patient per year▪ This is in addition to other schemes to reduce costs for bevacizumab and other anti-cancer drugs in Italy
England and Wales	<ul style="list-style-type: none">▪ Under the RANIBIZUMAB Reimbursement Scheme, the first 14 injections in the eye for wet AMD are paid for by the NHS▪ The costs of any subsequent injections reimbursed by the company either as free drug or a credit note
US	<ul style="list-style-type: none">▪ Programmes were introduced by Genetech in 2006 to cap total costs of bevacizumab at \$55,000 per year for certain patients; initiated to address public concern. This is in addition to existing programmes to help patients pay for cancer drugs▪ Alongside this, MCOs have also instigated maximum dose policies to reduce their exposure, e.g. United Healthcare

DTCs can co-ordinate activities to further enhance quality and efficiency of prescribing

- DTCs can potentially co-ordinate activities to further enhance quality and efficiency of prescribing through (continued):
 - Helping co-ordinate the development of decision support tools such as drug: drug interactions. DTCs can play an active role ensuring systems meet physician and patient needs
 - Undertaking studies showing local DTC networks effective in enhancing guideline implementation as **local** and only a 'soft regulation'. This builds on the existing literature
 - Pushing for government funded independent studies to answer questions unlikely to be funded by the industry building on models in Italy and UK. DTCs active part of any subsequent research activities
 - Helping counties proactively prepare for ever changing environment through developing and refining action plans

Significant number of independent projects have been funded in the past three years in Italy

- Examples of the independent research currently funded in Italy through a tax on industry promotion (5%) includes:
 - ❑ drugs for mood disorders
 - ❑ antipsychotics in patients with AD
 - ❑ low-dose aspirin in diabetes patients on statins (ACCEPT-D)
 - ❑ LMWH in women with previous pregnancy complications
 - ❑ Sildenafil/ Bosentan in patients with severe pulmonary hypertension
 - ❑ pharmacists' outreach visits
 - ❑ cancer pain analgesia
 - ❑ bevacizumab and cetuximab in colorectal cancer
 - ❑ depression in primary care (ISDB)

HTA and research programme extensive in the UK funded by government and charities

- There are a number of ongoing independent research programmes in the UK. These include HTA programmes:
- Research studies, e.g.
 - Trials comparing three diagnostic techniques for the assessment of patients with lung cancer
 - TACIT Trial – TNF inhibitors vs. combination DMARDs at intensive doses in patients with established RA
 - PERSEPHONE – Duration of trastuzumab (6 vs. 12 months) with chemotherapy in early breast cancer
- Technology Assessment Reports for new technologies
- Decision support - Horizon Scanning, UK Cochrane, and the Centre for Reviews and Dissemination of the Evidence

The politically agreed 5 point long term strategy for Stockholm County Council includes

Decision support, e.g.

- Electronic system providing an overview of patients' medicine profiles
- Drug interactions and warnings of adverse events
- E-Prescribing and Janus website
- Wise Drug List, Wise Drug Advice

Continuous professional education and communication e.g.

- Education strategy, dialogue with prescribers
- Relations with the pharmaceutical industry

Economic incentives, e.g.

- Local quality incentive
- Incentives for meeting agreed targets

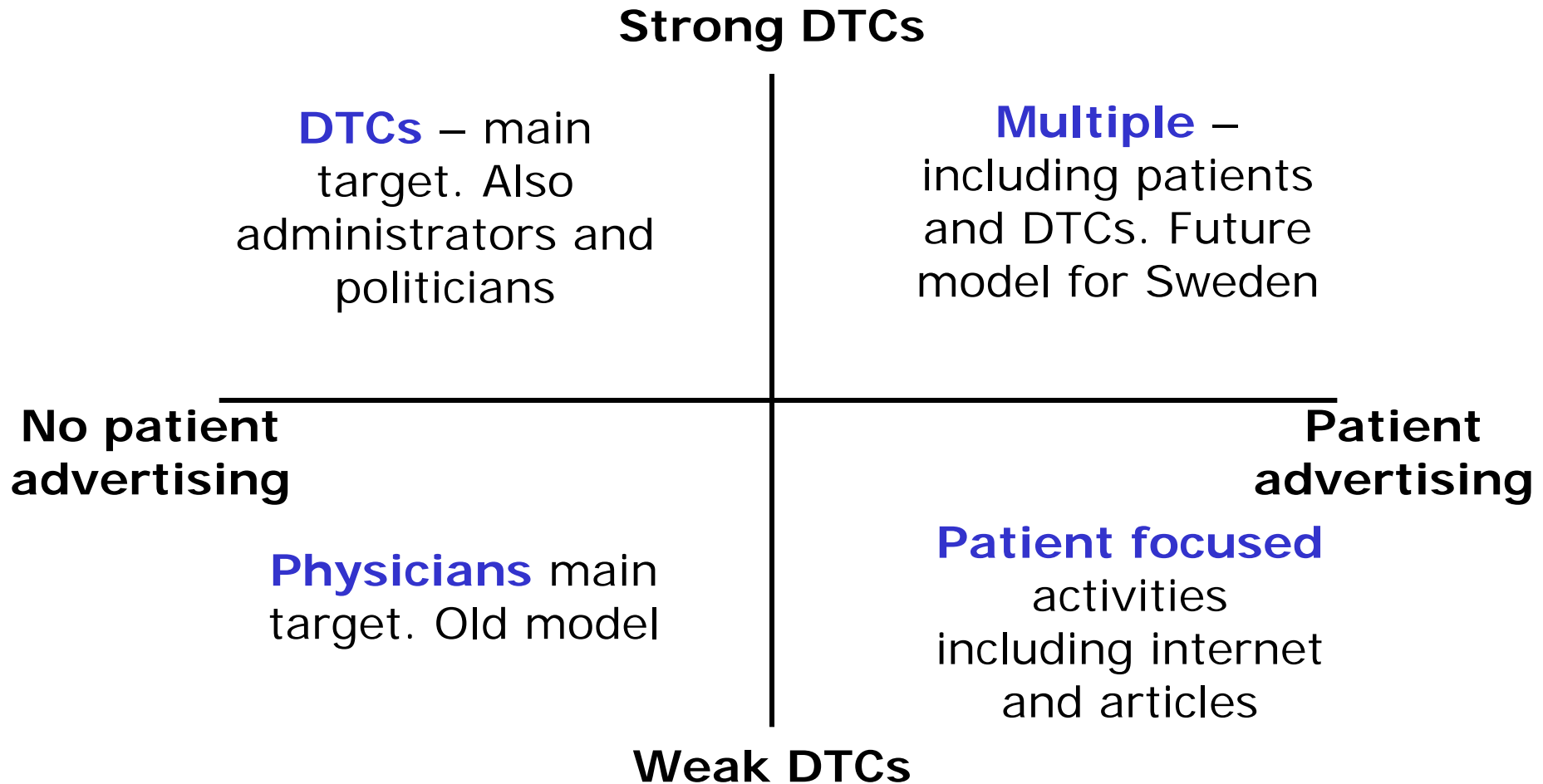
Drugs and the elderly

Improvement areas with future implications, e.g.

- Strategies for introducing new expensive drugs in hospitals
- Environmental issues, research and development

DTCs will become an increasing target for pharmaceutical company activity

Direction pharmaceutical company marketing/
communication efforts



The Piperska 3-day course in Scotland in July 2009 will tackle a number of subjects

- The Piperska educational course grew out of the need to exchange knowledge to help optimise utilisation of new drugs
- Planned subjects involving Swedish personnel include:
 - HTA and managed entry practices in Europe
 - Horizon scanning activities including identification, forecasting, critical drug evaluation and guidance
 - Local formulary and guideline development
 - Workshops around SMC submission
 - Potential ways to change and influence behaviour
 - Independent studies
 - Monitoring of effectiveness of new drugs in practice
 - Development of risk sharing arrangements
- All are welcome – fee is GB£340 for the three days

Thank You

Any Questions!

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