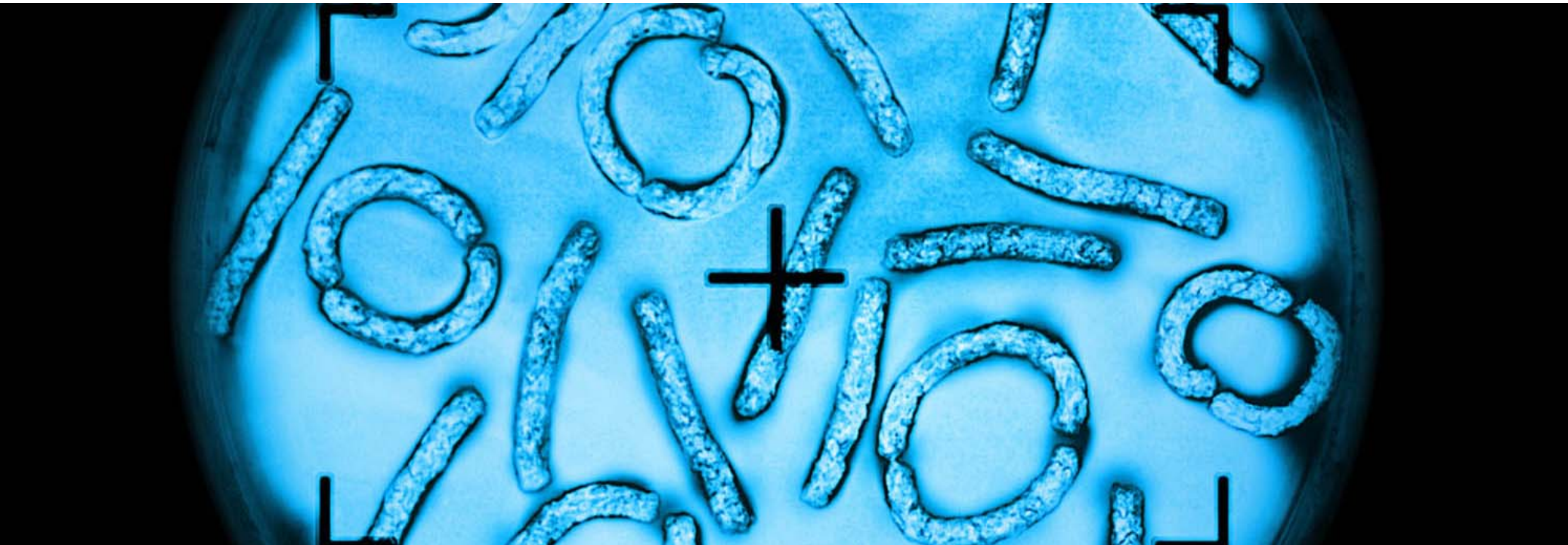
Can Healthcare Systems Afford Targeted Medicines



"Cook's private health insurer agreed to pay for eight months of treatment but has declined to fund it further. He has already sold his house to fund $12,000-a-year treatment"

(AUS, April 04)

"A woman with breast cancer has won the right to mount a High Court challenge against her local NHS to give her the drug Herceptin"

(UK, Jan 06)

General Motors says it all!

'Healthcare is putting our future at stake'
Rick Wagoner, CEO, General Motors announcing 25,000 job cuts in the USA'

(June 8 2005)

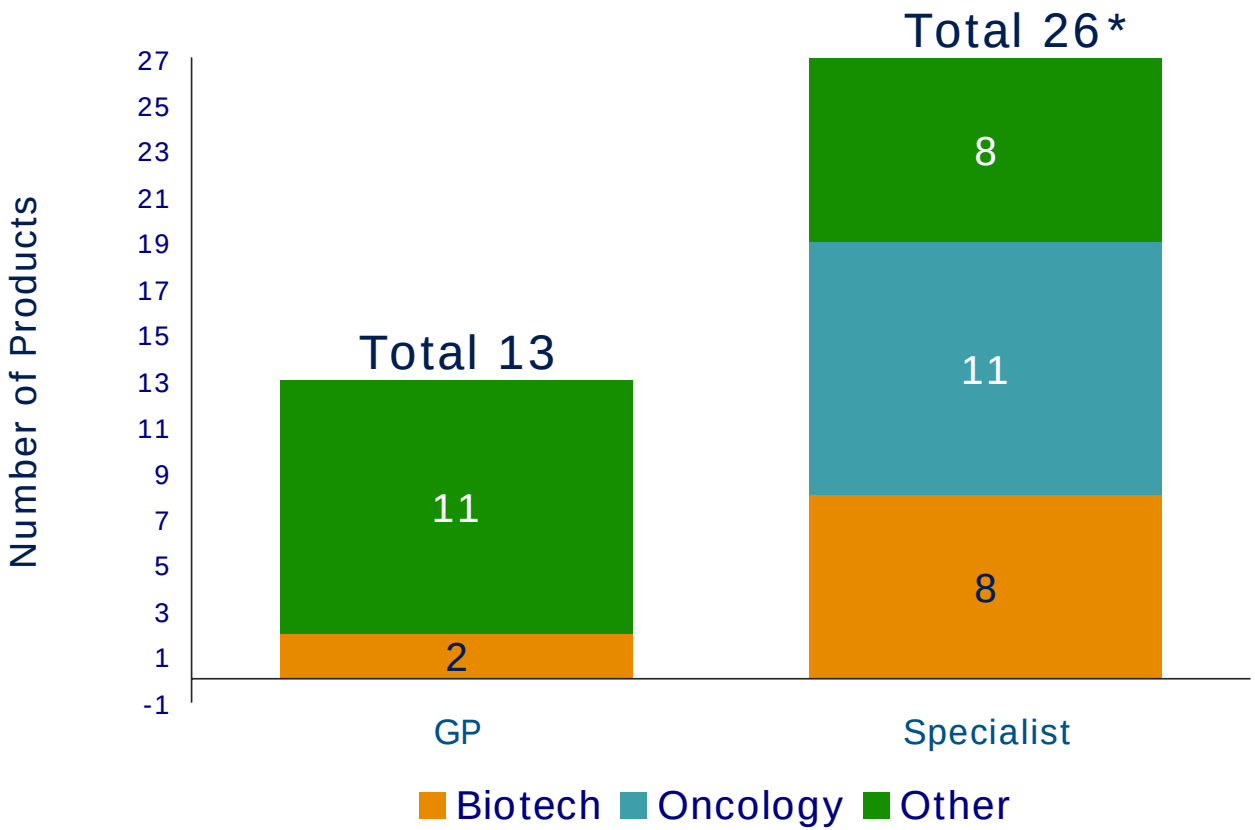
The oncology market is forecasted to be worth $55 billion in 2009

2004 – 2009 Leading Therapy Classes

2004 Therapy Class	Sales ($,bn)	2009 Therapy Class	Sales ($,bn)
Statins	27	Oncology	55
Oncology	24	Statins	38
Proton pump inhibitors	22	Antidepressants	26
Antidepressants	21	Proton pump inhibitors	26
Antipsychotics	14	Angiotension II inhibitors	
Angiotension II inhibitors	12	Antipsychotics	20
Erythropoetin products	12	Platelet aggr. inhibitors	18
Anti-epiletptics	11	Erythropoetin products	16
Oral antidiabetics	10	Osteoporosis	16
Osteoporosis	9	Anti-epileptics	15

Source: IMS Health: MIDAS, MAT Dec 2004; Therapy Forecaster 2005

2006 potential launches reflect emphasis for specialist sector with many targeted medicines

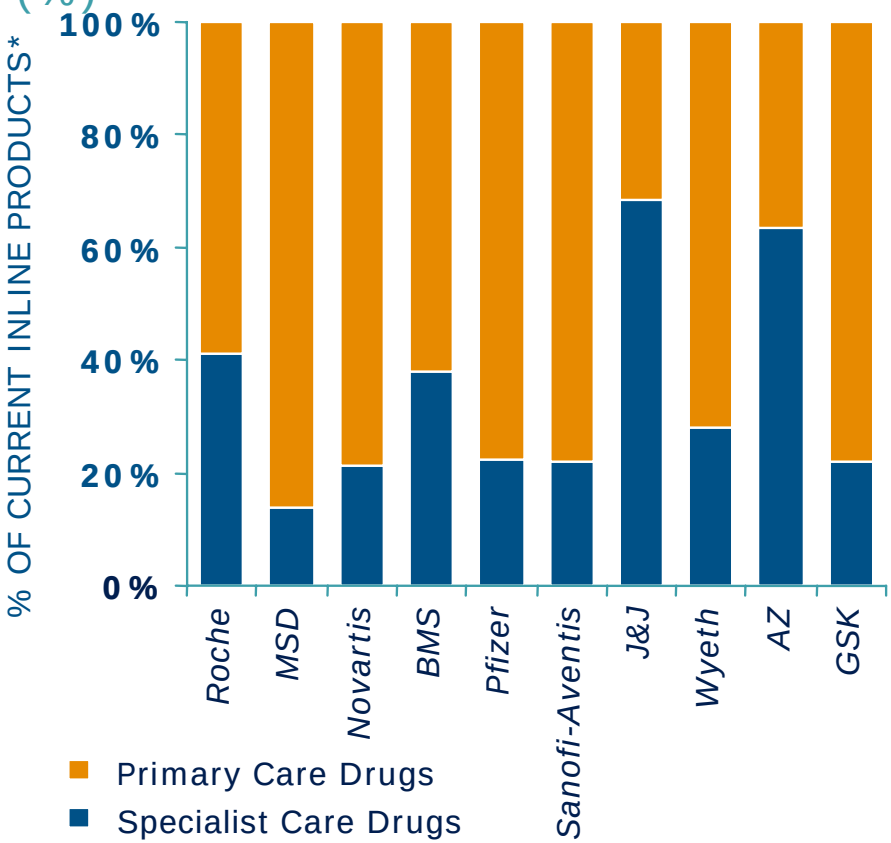


* Individual segments add to 27 because one product (oblimersen) is both biotech and oncology

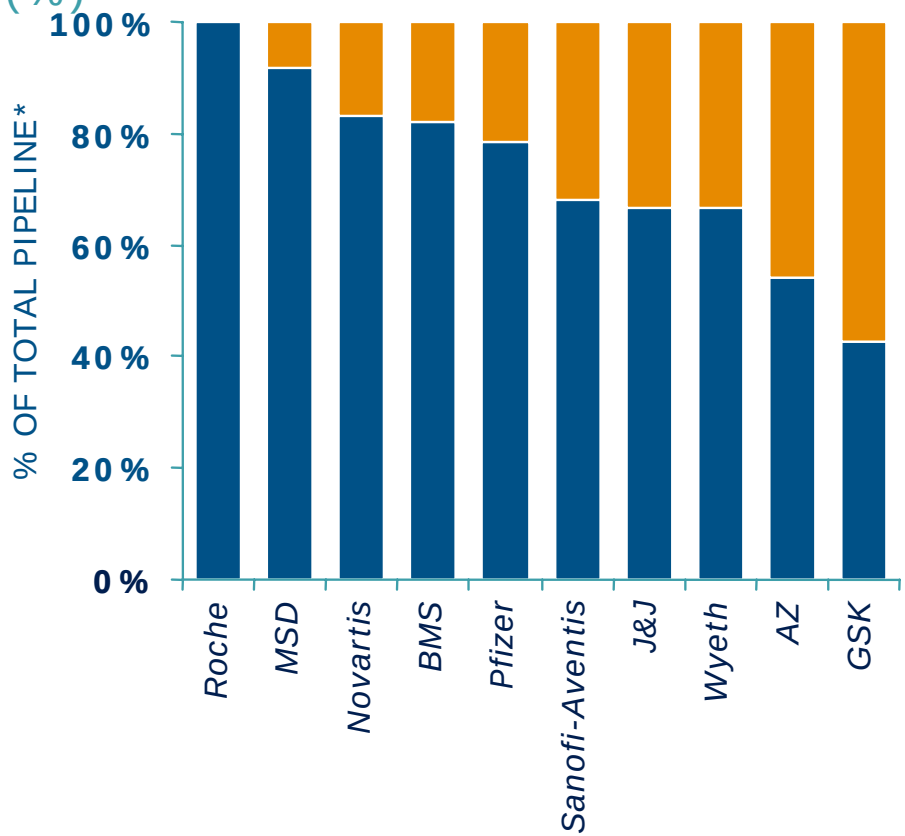
Source: R&D Focus, IMS Management Consulting

Indeed, pharmaceutical companies are turning to specialist care to drive growth

In-line Products

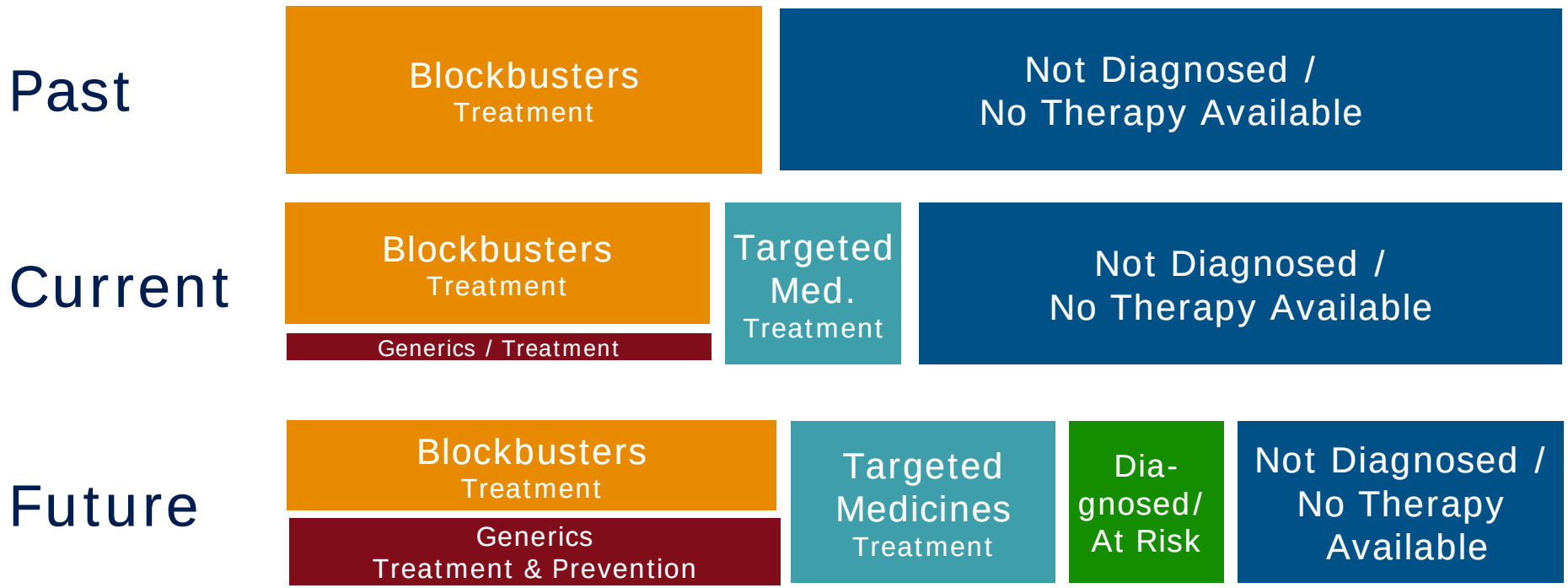


Pipeline Products



Source: R&D Focus, IMS Management Consulting; * Based on the number of drugs

New approaches of healthcare provision for therapy and prevention are developing



Source: IMS Management Consulting

Health care costs as are growing faster than economic growth in all OECD countries

Healthcare Spend

- Healthcare spend as % of GDP: US 15%, 8.8% average OECD, 5.6-6.5% (Slovakia, Poland
- Spending on drugs has risen more than a third in real terms since 1997

Positive Drivers

- Smoking in decline
- Alcohol in decline

Negative Drivers

- Ageing population – could add another 3% points of GDP to expenditure
  - Over 80y to increase 3-4 times by 2050
- Obesity rising
  - US 31% alone are obese: healthcare costs 36% higher, cost for medication alone for 77% higher
  - In Top 10 OECD countries, if overweight included more than half of population

Source: IMS Management Consulting, Financial Express

Across Europe a number of interventions are in place to limit price and demand growth

MEASURE	PRICE	DEMAND
Price Cuts	X	
Claw-backs/Discounts	X	
Reference Prices	X	
Reduced Margins	X	
Generic Substitution	X	
Parallel Import Incentives	X	
Drug Evaluation	X	X
Prescribing Guidelines		X
Drug Budgets		X
Strict Criteria For Reimbursement		X
De-listing		X
Condition On Use		X
Co-payments On Drugs		X
Co-payments On Visits		X
Gate Keeper Systems		X

Source: IMS Management Consulting

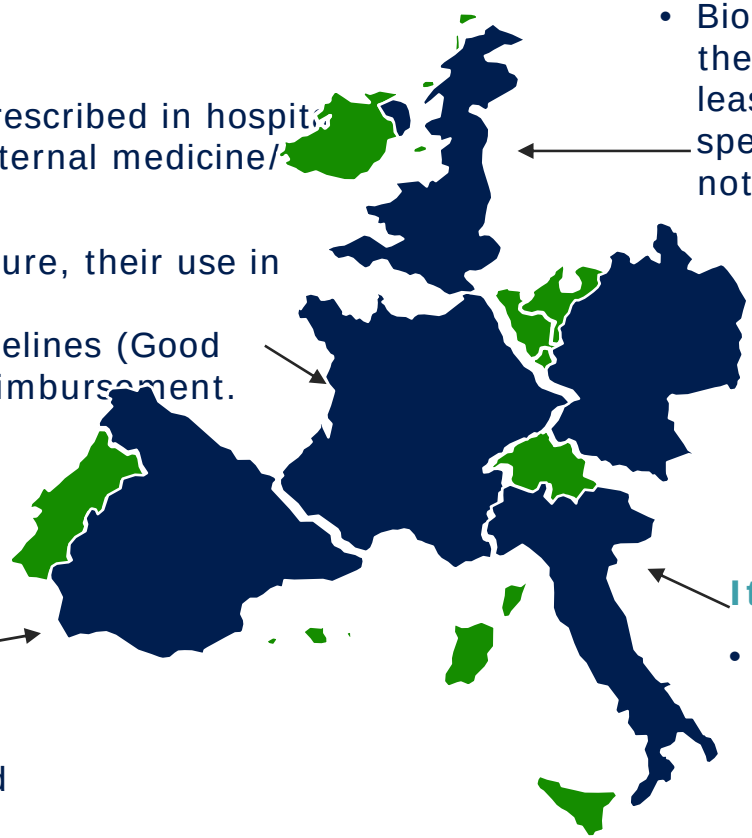
In EU, severe restrictions exist for biologics in RA despite meeting unmet needs

UK: Restrictions

- Biologics should be used according to the NICE guidance - have failed on at least two DMARDs and must be specialist-initiated (consultant level, not junior doctor)

France: Restrictions

- Remicade can only be prescribed in hospit by certain specialists (internal medicine/ haematologists)
- Changes: in the near future, their use in hospitals will be governed by guidelines (Good Drug Practice) tied to reimbursement.



Germany: Restrictions

- Strict guidelines on when biologics can be used (3rd line to DMARDs) – if patients fulfil these criteria then the sick funds have to reimburse them

Italy: Restrictions

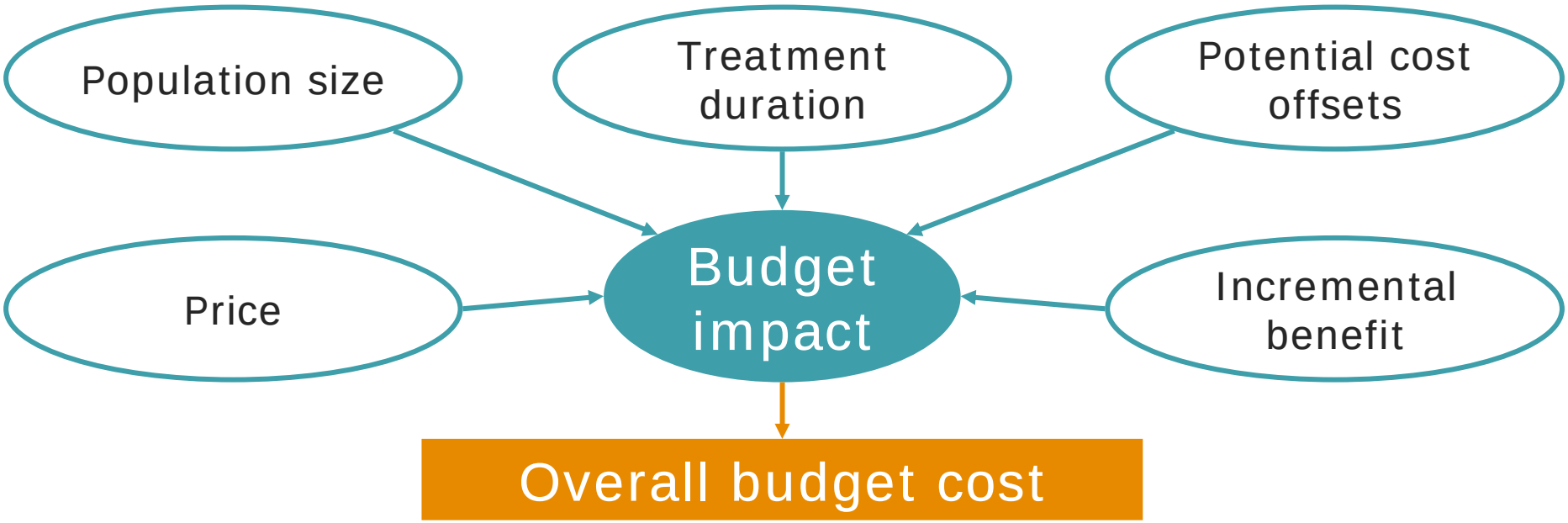
- Biologics are covered under File F, under this funding they can only be prescribed by certain hospitals and patients have to fulfil treatment criteria

Spain: Restrictions

- Hospital only (prescribed and dispensed)

Source: IMS Management Consulting

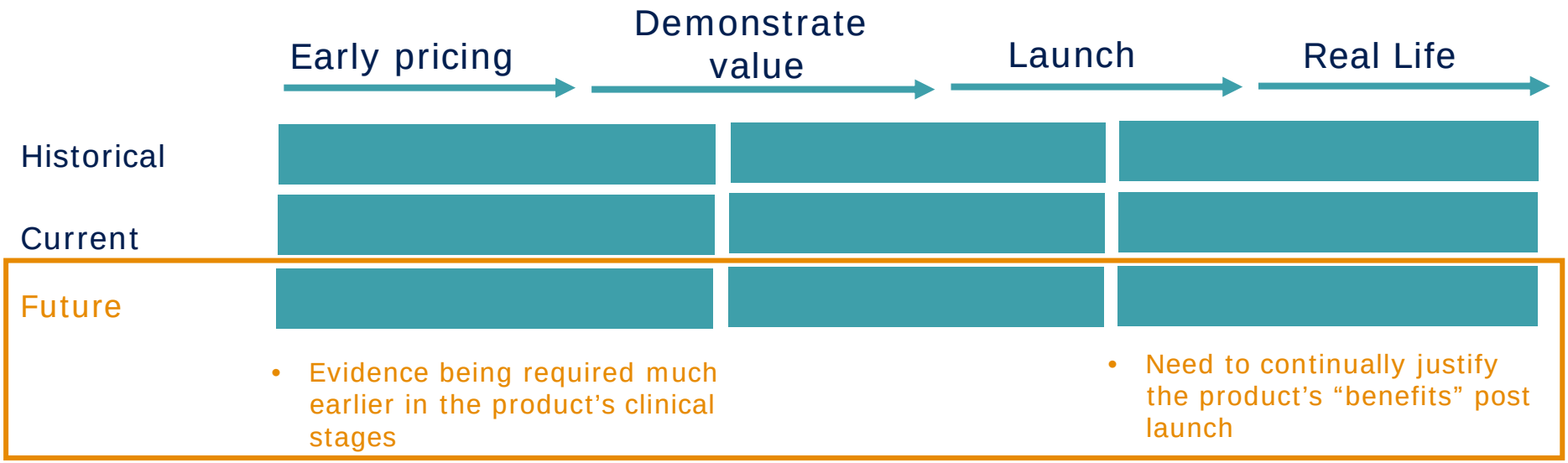
From a payers perspective, the main concern is the overall budget impact



Payers strategy has been to control market access and are increasingly aware of pharma industry approaches

Source: IMS Management Consulting

Providing an expanded need for health economics and outcomes research across the product's lifecycle



- Early insight into outcome and benefits
- Clinical trial design
  - Establish end points
  - Establish sample sizes
- R&D investment decisions
  - Go vs. No-go decisions
- Licensing & valuations

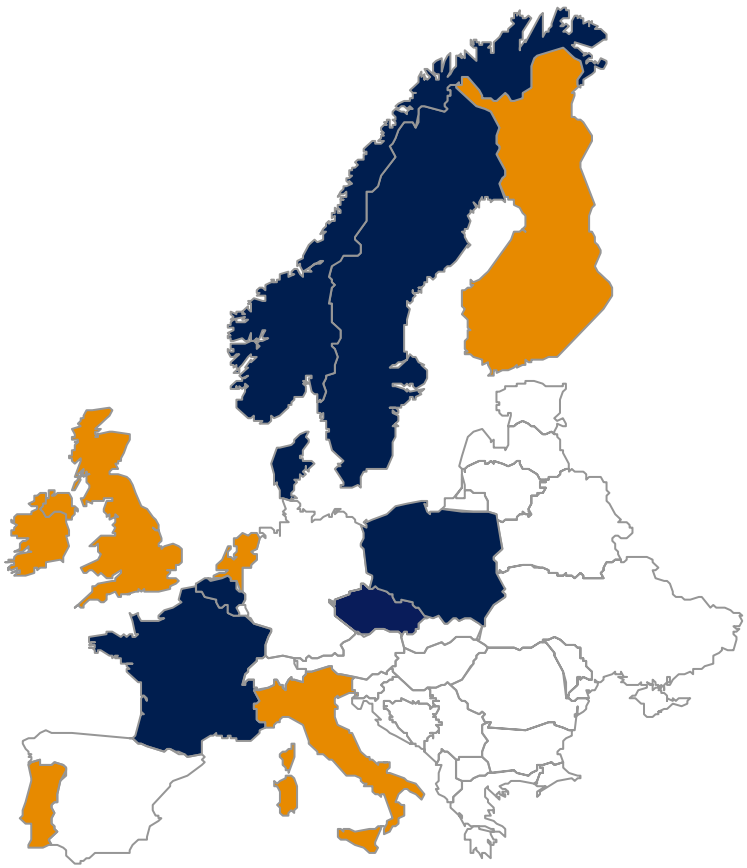
- Compliance with the guidelines
- Burden of disease and outcomes
- Therapy persistence
- Real life switches and use of resources
- Co-prescriptions
- Target populations (indications)

Limited Frequent Extensive

Source: IMS Management Consulting

Hence the number of governments and payers requiring economic argumentation is increasing

Healtheconomic Data Requirements for Approval in Europe



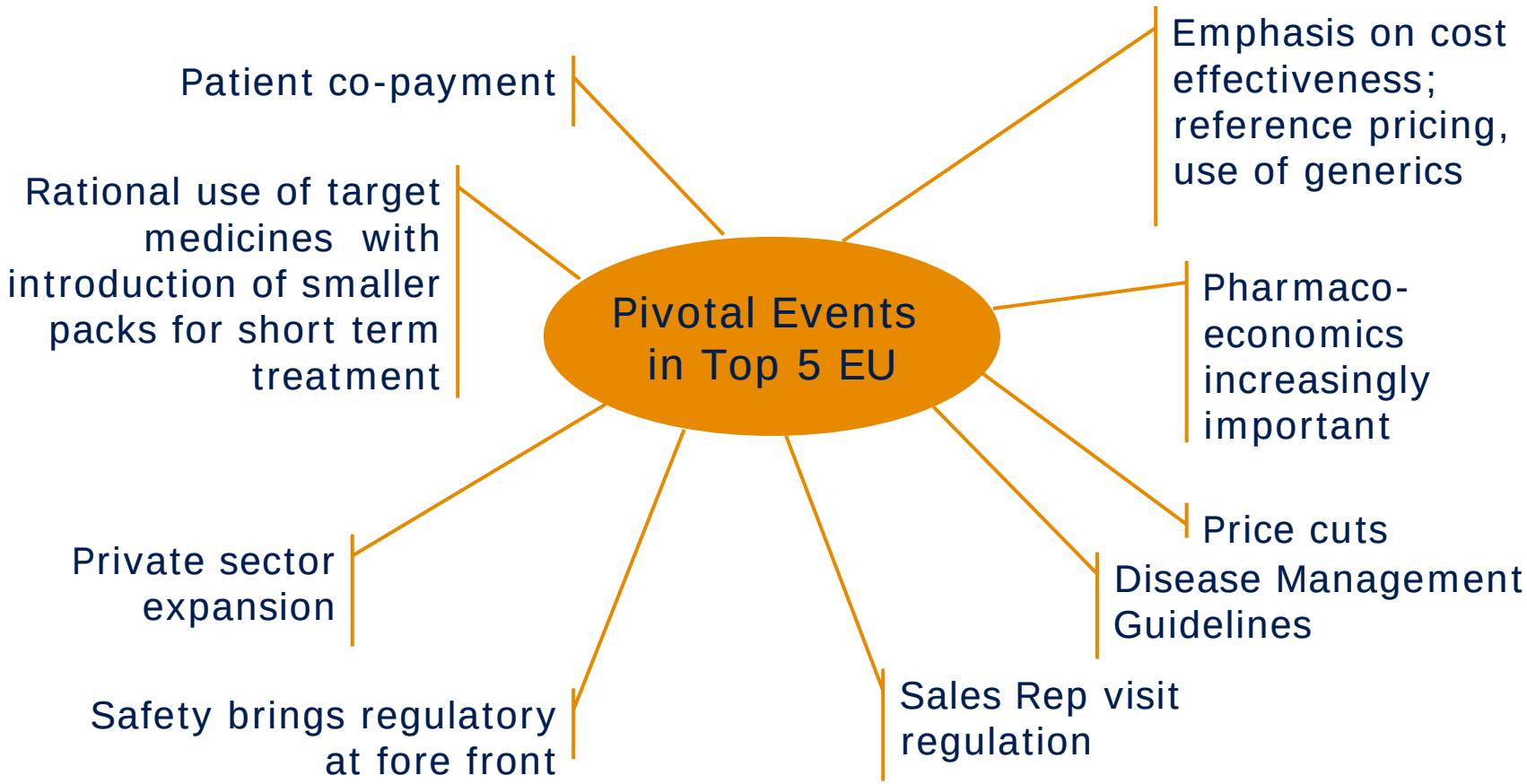
Requirements in the approval process

- Mandatory
- Optional

Mandatory in
- Canada
- Australia

Source: IMS Management Consulting

The use of targeted medicines will be impacted by further pressures on healthcare systems

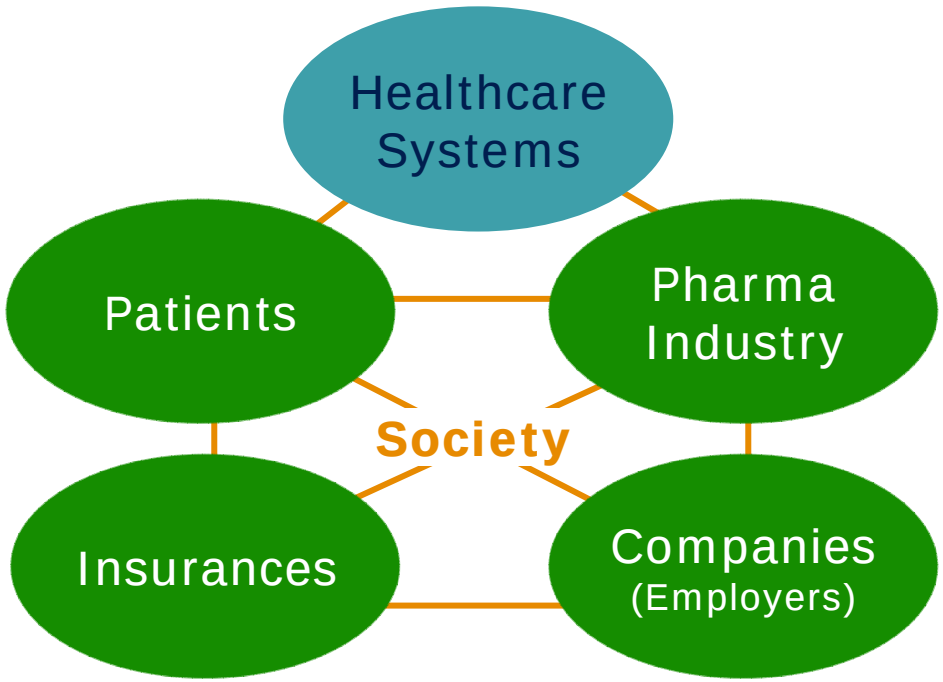


Source: IMS Management Consulting

Multiple actors are becoming responsible for financing the provision of healthcare

Today → Future

- Classical model in most European countries



Source: IMS Management Consulting

Personalised medicines is a multiple step process

- In discussion; long term implementation
- Who should get the test? How should the information used?
- Based on large population risk

- Second priority focus
- Symptoms driven (selection of right therapy – targeted or not)

- First priority focus
- More effective and reduced side effects
- Cost effective in only subgroups

- In discussion; short term implementation

Source: IMS Management Consulting

Cost impact evaluations for pharmacogenomics and targeted therapies are particularly complex

Cost-Benefit	Cost-Effectiveness	Cost-Utility
• Evaluates all costs and all benefits in monetary terms	• Evaluates all costs in monetary terms and comparison of treatment approaches in clinical terms	• Evaluates all costs in monetary terms and all effects are measured in quality adjusted life years (QALYs)
• Evaluation can be challenging (measuring benefits) • Not well accepted by payers	• Impossible to compare approaches across disease areas	• Comparable across disease areas • Difficult to assess meaning • Widely accepted

Points to consider

- Define clear research questions
- Identification of all intervention and setting of time horizon
- Delimit patient population
- Information sources
- Testing: potential additional costs (follow-up, family members) to be included
- Prevalence of genetic mutation
- Availability of effective intervention
- Isolated assessment vs ultimate beneficiary

Source: IMS Management Consulting

There are no clear guidelines of which efficacy measures to adopt

- What are the right survival data?
  - What incremental value needs to be achieved?
    - Consensus that a couple of months will not be sufficient
  - Not all cancer types can be measured on the same scale
    - Dependent on level on unmet need and therapeutic alternatives
- How to measure quality of life improvement?
  - Which value to needs to be achieved in terms of impact on disease progression?

Source: IMS Management Consulting

The current diagnostic environment is not ready for pharmacogenetics

	General	Pharmacogenetics
Provision	• Private and public with different scope and quality of provision • Public labs often underfunded • Fragmented but with increased consolidation • Trend to bring test closer to patient (POC) • Established kits available	• Current test still labour intensive • Capacity for large scale testing by far not sufficient • Difficult to coordinate & rationalise large scale testing • POC testing unlikely in near future • Test still largely experimental "home-brew" tests; mainly in private labs, often in conjunction with pharma (regulatory authorities to be more stringent on tests) • Regulation on patents for proprietary kits required • Samples going cross-border in Europe

Source: IMS Management Consulting

Funding of appropriate diagnostic environments is a great challenge

	General	Pharmacogenetics
Funding	• Various forms: ex.: payment of true cost vs flat fee; set reimbursement fee, covered by hospital or GP budget • Cost containment; pressure on physicians to reduce tests • Labs often forced to provide tests at reduced rates	• Health services to delegate some services to large centralised private labs • Co-payment model as option

Source: IMS Management Consulting

Applying diagnostics – involves a changing paradigm in physician behaviour

	General	Pharmacogenetics
Physician	• Genetic tests ordered by specialists • GPs refer for budget reasons	• Generally low awareness/ knowledge amongst physicians • Need for counselling services • Gaterkeeper model considered (referral to geneticist) but risk to wider adoption of testing • General physicians will have a very real impact on the rate these technologies are adopted

Source: IMS Management Consulting

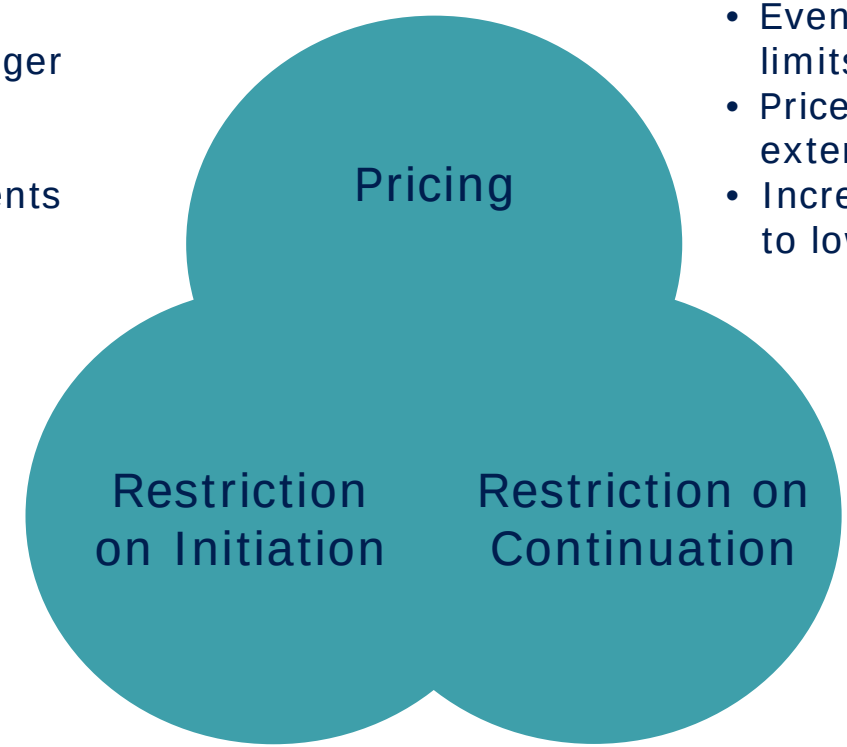
There are a number of challenges for the adoption of pharmacogenomics

- Proof of clinical utility will be necessary
  - Improvement of patient care (reduced side effects, increased survival, quality of life)
  - And/or reduction in health care costs
- Role of pharma companies is important
  - Collaboration with labs to fund test development
  - Pharma may not be interested as will limit blockbuster potential
- Role of payers
  - Payers will push for rationalisation of tests and affordability
  - Need to gain better understanding, need to
- Patients
  - May not be able to get reimbursed if test shows that drug is not working
  - Concern how results are used (treatment, insurance cover, etc)

Source: IMS Management Consulting

Restriction on usage of targeted medicines will be further strengthened

- Impact of survival data
- More emphasis on stronger clinical endpoints
- Competition with more efficacious/targeted agents



- Even free pricing markets, limits are to be set
- Price regulation on label extension
- Increased use of comparators to lower prices

- Availability of other treatment approaches
- Evidence of response failure to existing treatment
- Specific tests to check for likelihood of response; reimbursement dependent on it
- Limitation of off-label

- Clinical evidence: reduction of tumour size, etc.
- Appropriate biological tests

Source: IMS Management Consulting

The Herceptin case

No rush to prescribe for early breast cancer

- If Herceptin turns out to be as powerful in early breast cancer; it may be cost effective in certain sub-groups
- Using it as adjuvant therapy in early disease represents a significant financial burden
  - High drug price
  - Long duration of treatment
  - Large number of women who could be eligible
  - Belgium: 6,600 cases a year, 45% stage II/III, with ¼ to respond to Herceptin

➔750 patients representing €25,5m/y= € 34,000 per patient

➔extending to stage I would double the cost (ie >€50m/y)

(depending on country even more difference as prices vary by country)

Source: Neyt (University of Ghent) European Society for Medical Oncology (2005)

The ultimate question is how much society is willing to pay

Political Pressures

- Budgetary pressures will further increase
- Governments will put pressure on pharma industry rather than openly limit access
- Demand for health economics data to ensure that cost effective therapies are used first line

Patient's Associations

- Different cancers have different lobbying activity with increased support from pharma
- More patient advocacy groups will get organised with increased influence

Special Status

- Media interest and emotional sensitivity means that cancer will not loose its protected status in next years
- How much is society willing to pay for a quality adjusted life year: US €85,000 vs UK €48,000

Source: IMS Management Consulting

Targeted therapies offer time in a bottle; what price tag should we place on prolonged life?

- Personalised medicines are perhaps over hyped; widespread use still 15-20 years away
- Introducing financial incentives for pharma companies to develop pharmacogenic drugs with smaller market potential (mini-blockbusters) and support testing initiatives
- Healthcare system need to better manage over-prescribing of multiple drugs for common conditions such as cholesterol, blood pressure, etc
- If healthcare authorities want to pay for targeted medicines, than discussion over price is inevitable, and authorities must be willing to delist older non-cost effective treatments
- Healthcare systems need to be revisited overall including all stakeholders to provide funding for targeted medicines

Source: IMS Management Consulting

Thank you!

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