Drug Value & Market Access Optimization

"Finding New & Better Avenues"

From Drug Cost to Payer Valuation

- How to get the best value? -

Excerpts

June 2016

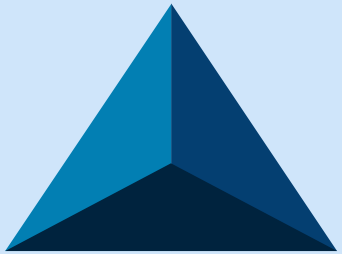

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Table of contents of the complete report

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The purpose of this report is to provide key information and robust analyses to better optimize drug valuation, from the pharmaceutical companies perspective

Context & Objective

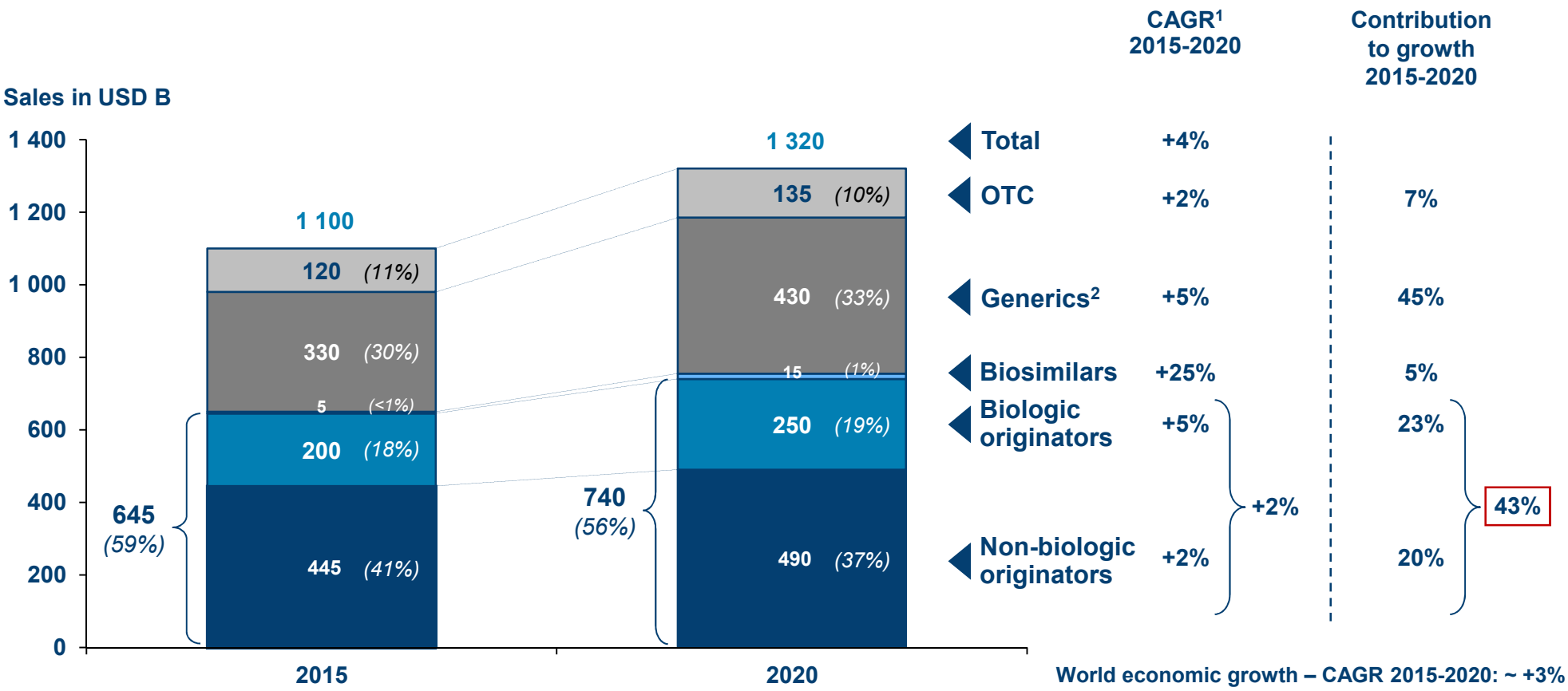
- To slowdown the increase of healthcare expenditure, governments and public or private payers implement a large array of cost-containment mechanisms
- Drugs are particularly affected by these measures, which include:
  - Drug prices control and regulations to favor the prescription of cheaper products like generics and biosimilars
  - Capping of the prescribed volumes
  - Selective reimbursement of drugs (e.g. limitation to a subset of patients or to the most severe cases)
- However, the way these measures are applied does not allow governments and payers to guarantee access to innovation to the largest number of patients
- Thus, governments and payers have no choice but to increase their pressure on drug prices and “force” pharma companies to accept affordable prices

- In this context, the following questions must be raised:
  - What is the value of innovative drugs for the community?
  - What is a fair price for pharmaceutical companies?
- This report reviews:
  - The economic and healthcare environment
  - The R&D cost of drugs
  - The drug pricing strategic approaches of pharma companies, governments and payers
  - The health economic evaluation methods
  - The market access processes in selected countries
  - The best practices in market access
  - The ways to leverage the corporate reputation of pharma companies
- Smart Pharma Consulting proposes new thoughts likely to help pharma companies to optimize the valuation of their drugs

Sources: Smart Pharma Consulting analyses

Sales of original drugs should keep on growing significantly by 2020, contributing to 43% of the global pharma market growth

Global pharmaceutical market growth by segment (2015 – 2020)

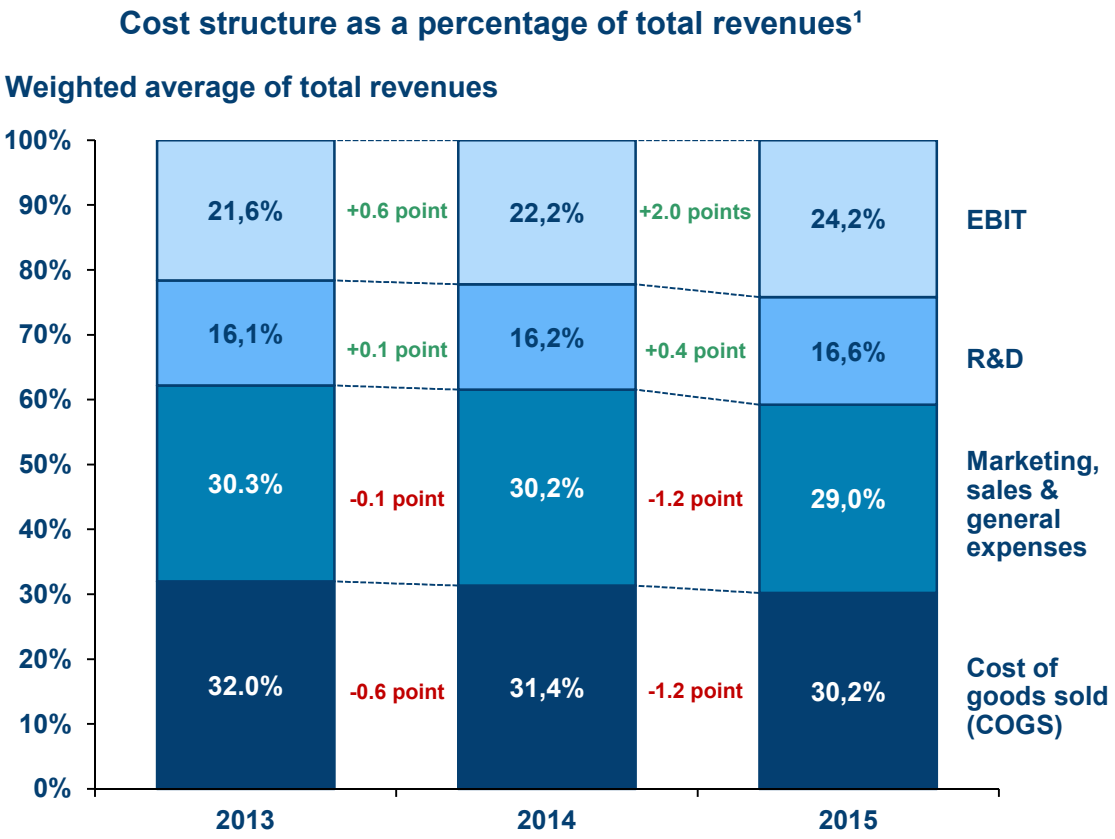


Sources: Nicholas Hall's OTC Yearbook 2015 – IMS World Review Executive 2015 – United Nations: World Economic Situation and Prospects 2016 – Smart Pharma consulting estimates

[1] Compound annual growth rate — [2] Including branded and unbranded generics, excluding OTC

Among the top 30 pharma companies, the trend goes toward an increase of the EBIT and of the R&D expenses while sales and manufacturing costs are slightly decreasing

Evolution of the top 30 pharma cost structure (2013 – 2015)



- The analysis of the top 30 pharmaceutical companies in the world shows that their average profitability has increased by 2.6 points between 2013 and 2015
- This improvement can be explained by the restructuring of their product portfolio in which the weight of high priced secondary care products has been increasing
- Besides, the marketing and sales investment for these specialist-driven secondary care products is much lower than for GP-driven primary care products
- Restructuring and streamlining initiatives have also contributed to improve the economic performance of these companies
- These good performances are the Achilles heel of pharmaceutical companies when negotiating price and reimbursement of their drugs with governments and payers

Note: panel of the 30 biggest pharma companies in terms of prescription sales as of 2014

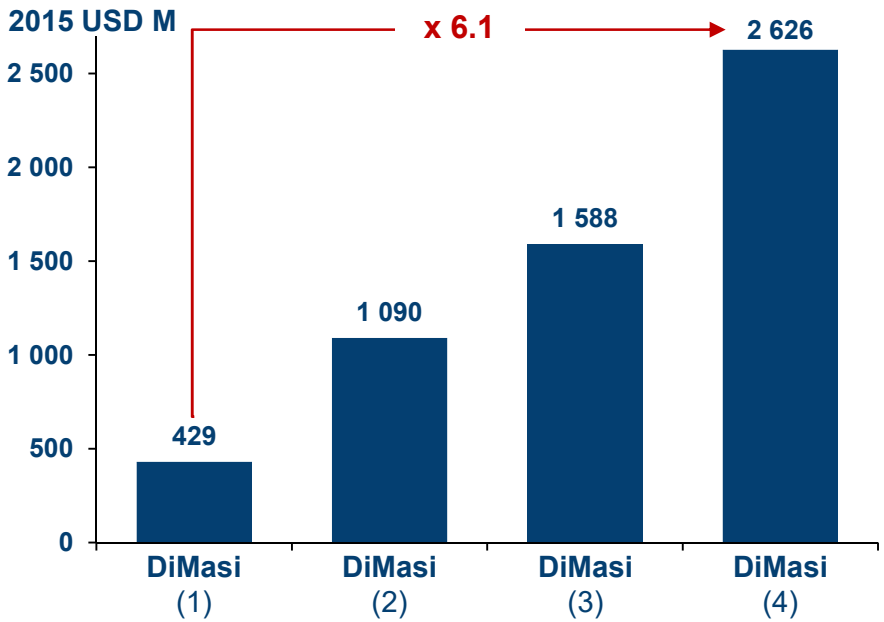
Sources: Companies annual reports – Federal Reserve annual exchange rates – Smart Pharma Consulting estimates

[1] Excluding Astellas, Daiichi Sankyo and Takeda for 2015, which have not published financial results at the moment of the study (due to their fiscal years ending in March) – Excluding for 2015 Actavis which merged with Allergan – Excluding Servier over the whole period for not publishing financial results and Boehringer Ingelheim for publishing non-standardized financial results

The analysis of four studies carried out with the same methodology, shows that the development cost of new drugs has more than sextupled over the last three decades

Evolution of R&D costs

Estimated capitalized cost per approved new drug (pre-tax)



	DiMasi (1)	DiMasi (2)	DiMasi (3)	DiMasi (4)
Mid-analysis year[1]	1976	1989	1997	2001
Publication date	1991	2003	2007	2014
Cost of capital used	9.0%	11.0%	11.5%	10.5%

- The evolution of the capitalized R&D costs per approved new drug, after neutralization of the inflation, can be mainly explained by:
  - The growth of the out-of-pocket costs, especially the growth of clinical trials spending: x10.8 between the 1991 and the 2014 estimates (vs. preclinical spending which grew less: x3.9)
  - The decrease of the success rates to reach approval from phase I, ranging from 23% in the first 1991 estimates to 12% in the 2014 estimates
  - The overall increase of the used cost of capital, even if, in the 2014 estimates a 10.5% cost of capital was used, in decrease of 1 point of percentage from the previous estimates. These assumptions of cost of capital seem overestimated compared to available data from NYU Stern School of Business for biotech products (9.2%, based on 411 firms) and for traditional pharma (7.7%, based on 157 firms)

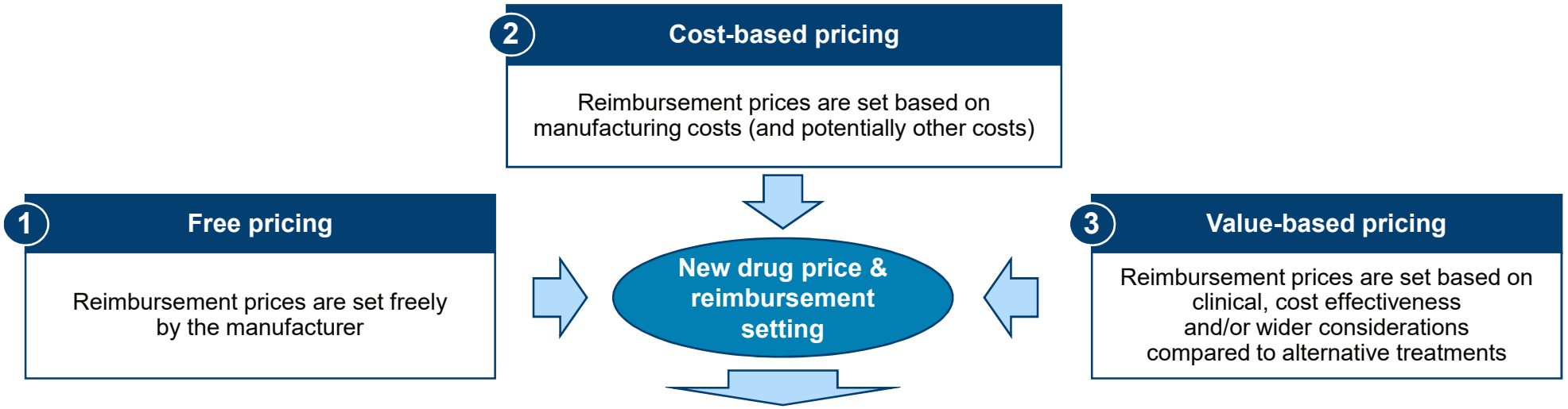
Note: For the sake of comparability, all values are adjusted to USD 2015 prices using data of the US GDP implicit price deflator from the US. Bureau of Economic Analysis. The GDP implicit deflator shows the rate of price change in the economy as a whole, being the ratio of GDP in current local currency to GDP in constant local currency

Sources: DiMasi (1991) – DiMasi et al. (2003) – DiMasi, Grabowski (2007) – DiMasi (2014) – Cost of Capital - NYU Stern School of Business, January 2016 – Smart Pharma Consulting analysis

[1] Products with first testing in humans over the analyzed period

The price and reimbursement of drugs are set according to three basic principles and implemented through different mechanisms during all their life-cycle

Drug price setting approaches and life-cycle evolutions[1]



Price & reimbursement setting mechanisms during the drugs life-cycle

Internal price referencing	International price referencing[2]	Managed entry agreements	Price cuts	Paybacks	Tenders	Compulsory licensing	Voluntary licensing	Tiered pricing
Reimbursement prices are set compared to prices of drugs of the same class	Reimbursement prices are set compared to prices in other countries	Price / volume agreements, risk-sharing agreements, etc.	Post-marketing reimbursement prices reevaluations	*A posteriori* rebates to healthcare system (PPRS, safeguard clause, etc.)	Competition between similar products	Licensing imposed by a government to a third party w/o the consent of the patent holder	Out-licensing by a patent holder to a third party to produce and/or market an invention	Differential pricing reflecting the willingness to pay across countries

Sources: "Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research", OECD – "Value-based pricing for pharmaceuticals: Implications of the shift from volume to value", Deloitte – Smart Pharma Consulting analysis

[1] Non-exhaustive list – [2] Also called External price referencing

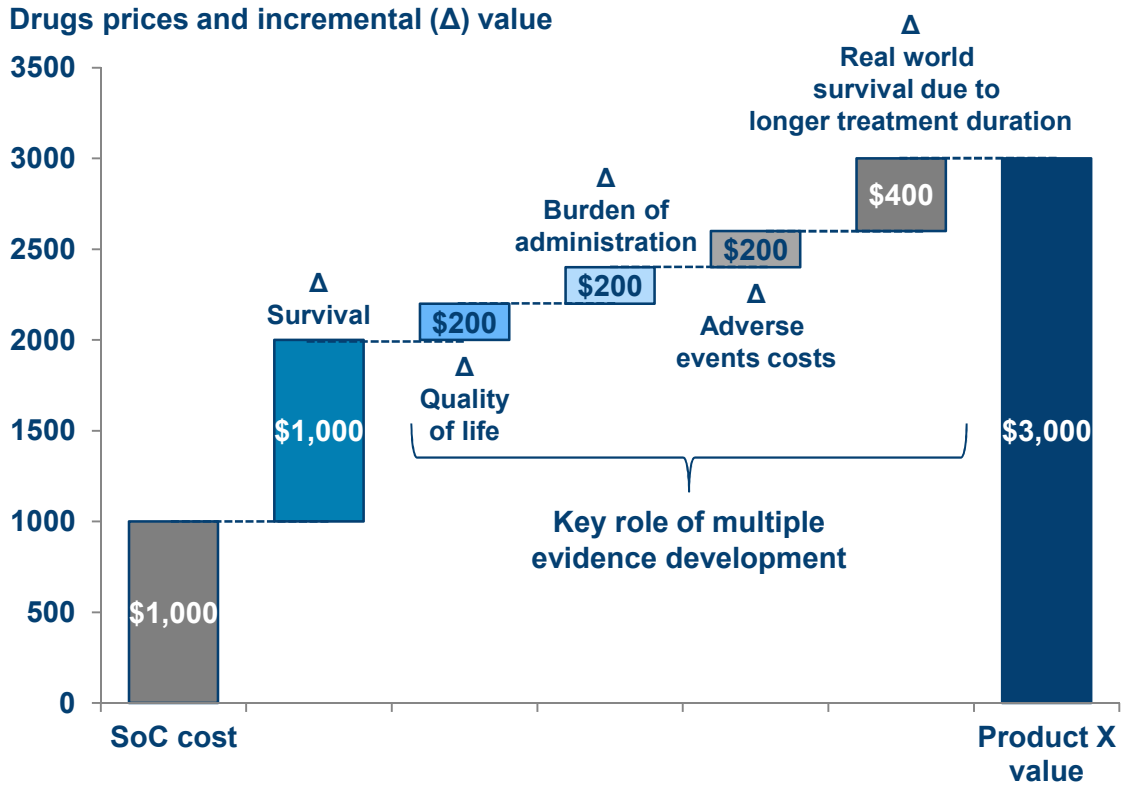
Value-based pricing aims to set drug prices based on multiple criteria to assess their general impact on the healthcare system or on the society, as a whole

3 Value-based pricing – Approach

Definition & analysis

- Value-based pricing (VBP) sets prices based on a value assessment that takes into account several criteria such as clinical efficacy, cost-effectiveness, or a wider range of criteria including the burden and severity of the disease and the long-term benefits of the treatment
- VBP consists in negotiating prices for new pharmaceuticals based on their value for the society as assessed through Health Technology Assessments (HTA)
- By ensuring access to cost-effective drugs today and incentivizing manufacturers to invest in cost-effective products for the future, VBP seeks to provide a sustainable solution to pharmaceutical price regulation. But while it aims to reward innovation, establishing a clear relationship between the level of innovation and the price is not straightforward

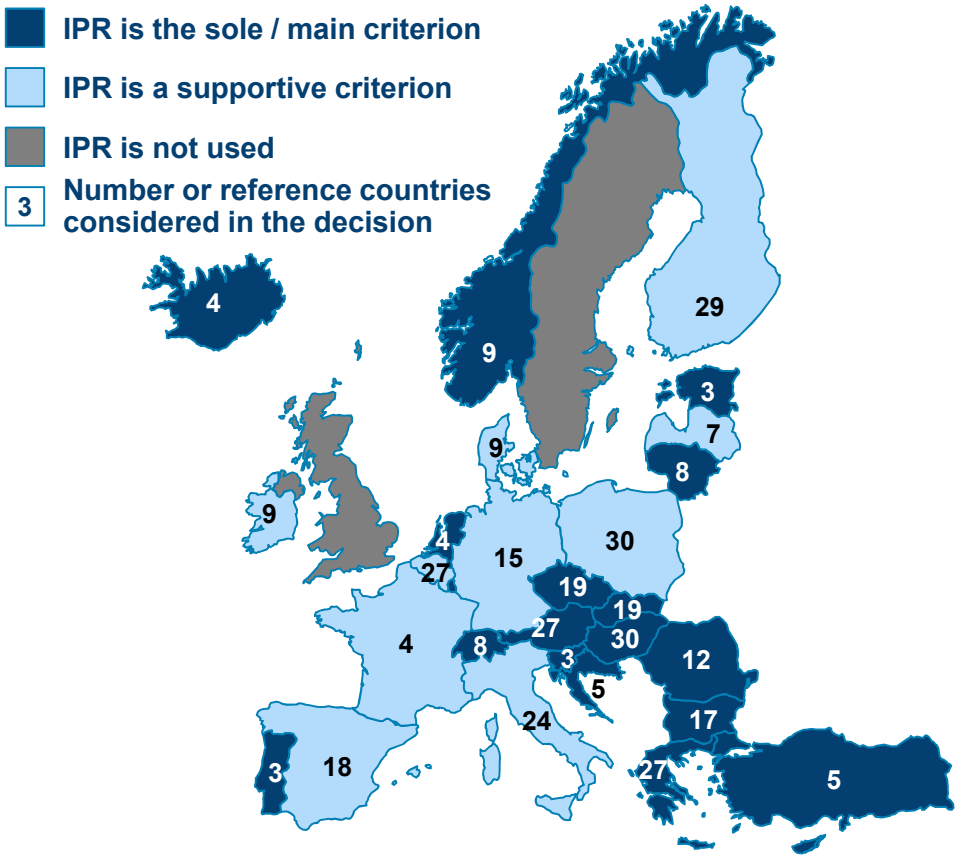
Product X value vs. standard of care (SoC)



Sources: "Future strategies for pricing and market access in oncology", Analysis Group, Oct. 2014 – "Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research", OECD – Smart Pharma Consulting analysis

International Price Referencing (IPR) is used in most European countries to set drug prices but its scope may vary from one country to another

International price referencing



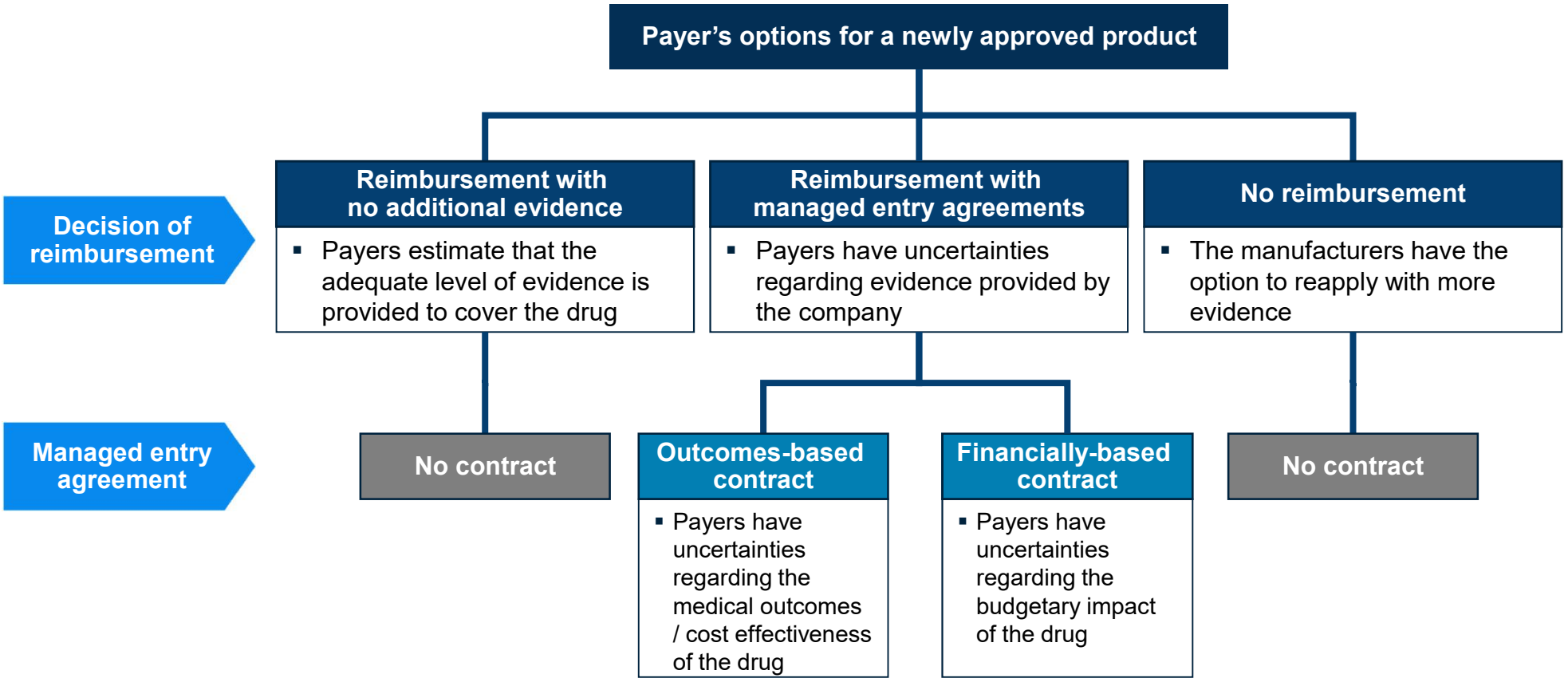
- If most European countries use the International Price Referencing to set the price of drugs, there are some disparities in its usage and calculation:
  - The scope of the use of IPR may depend on the country. For example, in Italy, all reimbursed medicines are concerned while in Spain only new reimbursed medicines with no comparator available are concerned
  - The calculation may also vary. In France, prices should be similar to those in the reference countries and should not be lower than the lowest price in one of the four reference countries while in Belgium prices are based on the average price in reference countries
  - The revision frequency might also depend on the country with bi-annual revisions in the Netherlands or annual revisions in Spain
  - Ex-factory prices are considered in most European countries but Norway, Denmark or the Netherlands consider pharmacy purchasing prices

Sources: "Study on enhanced cross-country coordination in the area of pharmaceutical product pricing", European Commission, Dec. 2015 – "External reference pricing of medicinal products: simulation based considerations for cross-country coordination" , European Commission, 2014 – Smart Pharma Consulting analysis

Note: Germany should use the International Price Referencing to set drugs prices but it is not used in practice

Managed entry agreements may be considered by payers when the level of medical evidence is too low and/or the financial impact is too high

Payer's options for a newly approved product



Sources: "Can't Get No Satisfaction? Will Pay for Performance Help? Toward an Economic Framework for Understanding Performance-Based Risk-Sharing Agreements for Innovative Medical Products", Adrian Towse and Louis P. Garrison Jr, 2010 – Smart Pharma Consulting analysis

Managed entry agreements are expanding to reduce the risk for the payer (efficacy, safety, etc.) and/or to enable pharma companies to negotiate better prices

Classification of the managed entry agreements

	Outcomes-based contracts	Financially-based contracts
	▪ Reimbursement consistent with the public interest, based on the results provided by the pharma company	▪ Limit the economical consequences of the negotiated price

Patient level

1 Biomarker-linked payment

- Reimbursement based on the results of biomarker tests
- e.g.: Herceptin (Roche)
  Erbitux (Merck)
  Enbrel, Australia (Pfizer)

2 Pay-for-performance

- Reimbursement based on clinical endpoints:
  - Morbidity-mortality
  - Clinical efficacy
  - Better adherence
- e.g.: Velcade, UK (Janssen)
  Imnovid, FR (Celgene)
  Aclasta, GE (Novartis)
  Janumet/Januvia, USA (MSD)

4 Per patient cost capitation deals

- Maximum cost set per patient (number of doses, daily cost of treatment, total cost of treatment, etc.)
- e.g.: Lucentis, UK (Novartis)

Population level

3 Coverage with evidence development (CED)

- Funding granted if efficacy proven through real life studies
- Evidence needed to decide whether or not to maintain funding
- e.g.: Risperdal Consta, FR (Janssen), many high cost drugs in Italy

5 Overall sales capitation

- Annual sales volume agreement as part of the initial price negotiation
- Annual value capping with rebates for exceeding sales
- e.g.: most high cost drugs in France, Enbrel (etanercept) in Australia

Sources: "Innovation et prix du médicament contrats d'accès au marché des médicaments remboursables : choix des schémas d'étude et des critères de jugement", Réseau d'Evaluation en Economie de la Santé, Jan. 2014 – "Unpacking Risk Sharing and Alternative Pricing Schemes"; Pharmaceutical Commerce, Feb. 2010 – "Mechanism Of Coordinated Access (MOCA) and transparent value framework, managed entry agreements", AIFA – Smart Pharma Consulting analysis

Celgene agreed to implement a pay-for-performance scheme based on an ad-hoc registry for Imnovid in France

2 Case study: Imnovid pay-for-performance scheme in France (2015)

Background

Concerned indication

- Imnovid is indicated as a **3rd line** therapy (second relapse after Revlimid and Velcade treatment) in the treatment of **multiple myeloma**

Initial evaluation of Imnovid

- The "Commission de la Transparence" (CT) gave Imnovid an **ASMR III** (moderate improvement of the medical benefit)
- Imnovid was granted an **initial price** of € 8,900 per cycle of treatment of 21 days, with 5 to 6 cycles per patient
- The target population was estimated at ~ 2,000 patients

Existing registry

- Celgene initially implemented a **patients registry** for Imnovid with the aim of:
  - Measuring the efficacy of **the risk minimization** and **pregnancy prevention** plans
  - Controlling the **good use** of Imnovid

Pay-for-performance scheme

- Celgene agreed with the CEPS[1] to implement a **pay-for-performance scheme**
- The rationale of this agreement is to support with real world data (RWD) the clinical results observed with Imnovid during the clinical phase studies
- The **exact terms** of the scheme are **not disclosed** so that physicians should not be influenced in their prescriptions (but terms were determined jointly with the HAS[2] and the CEPS, based on the International Myeloma Working Group (IMWG) recommendations)
- The scheme uses Imnovid **registry** to collect **efficacy data**, which is **shared with the CEPS** on an annual basis to calculate rebates due by Celgene to the national sickness fund (through its financial arm, the Acoss[3])

Sources: "Médicaments : quand les laboratoires sont rémunérés à la performance", Les Echos – "Celgene a conclu un accord "efficace ou remboursé" avec le CEPS pour Imnovid"; APMnews

[1] Comité Economique des Produits de Santé → Economic Committee on Healthcare Products – [2] Haute Autorité de Santé → National Authority for Health – [3] Agence Centrale des Organismes de Sécurité Sociale → Central Office for Social Security Organizations

Managed entry agreements enable an early access of patients to innovation while also facilitating reimbursement negotiations and limiting the budgetary risk for payers

Opportunity analysis

	Opportunities	Relative importance[1]
Payers	▪ Potential to **re-evaluate** the effectiveness of the drugs at a later stage and **re-negotiate** the price based on **real-world evidence** and thus to move towards a **value-based pricing system**	5
	▪ Help **address post-licensing uncertainty** by offering flexibility in dealing with new and often expensive treatments	5
	▪ Improve the **cost-effectiveness** through a **discount** or a **payback** agreement for non-responders	4
	▪ Potential to create **synergies** with existing **initiatives** on **registries** in **Europe**: pulling evidence from different countries could allow to generate a **large pool** of data and **increase the statistical significance** of the results	3
	▪ Enable **different types of schemes** addressing **different needs**, both **financial** and **non financial**	3
Manufacturers	▪ Speed up **reimbursement** negotiations for drugs which were likely to be rejected by drug reimbursement agencies	5
	▪ Potential to benefit from a better **corporate reputation** as a result of the willingness to take responsibility for the use of the drug in real-life	4
	▪ Potential to **reinforce** the **long-term collaboration** between **payers**, **health authorities** and **pharmaceutical companies**	4
	▪ Enables **discounts** without impacting list prices	4
Patients	▪ Ability to gain **faster access** to **innovative medicines**	5

Sources: "Managed entry agreements for pharmaceuticals: the European experience", Alessandra Ferrario and Panos Kanavos, April 2013 – Smart Pharma Consulting analysis

[1] Rating from 5 = very important to 1 = limited importance

Due to their impact on public budgets, French authorities voted a budget capping for all innovative hepatitis C drugs sales

Case study: HCV budget capping in France

Background

Initial issue

- In 2014, a **new generation** of treatments of **hepatitis C** such as Solvaldi (sofosbuvir) was launched
- These treatments reached high volumes from their **first year** on the market and **impacted public budgets**

French government solution

- French government, through the vote of the annual law of financing of the Assurance Maladie for 2015 (LFSS 2015), implemented an ad-hoc **mechanism of budget control** for hepatitis C drugs
- This mechanism is running till a reevaluation, expected by October 2016

Hepatitis C budget capping scheme

- The **HAS** (health authority) **sets the list** of products concerned by the capping
- **Clawback payments** are due by pharma companies **to the Assurance Maladie** if sales of these products (jointly):
  - **Exceed a fixed amount** called "Montant W" (€ 450 M for 2014, € 700 M since 2015)…
  - … and **increased by more than 10%** over the previous year
- **Clawback payments** calculation:
  - For sales between **W and W+10%: 50%** clawback = € 35 M since 2015
  - For sales between **W+10% and W+20%: 60%** clawback = € 42 M since 2015
  - For sales **> W+20%: 70%** clawback
- A company that signs an ad-hoc **agreement** with the CEPS may be **exempted** from the clawback payments for hepatitis C if the **amount** due to the Assurance Maladie according to this ad-hoc agreement is **over or equal to 90% of what would be due under the hepatitis C scheme**

Impact of the scheme

- This scheme **allows a broad access** to hepatitis C treatments by **not rationalizing prescriptions**
- **Clawback payments** by companies for the fiscal year **2014 amounted € 76.5 M**
- **France** is considered to be **well positioned** (from the public payer perspective) in terms of **net price of HCV drugs vs. other European countries**

Sources: "Contribution au titre de médicaments destinés au traitement de l'hépatite C", URSSAF – LFSS 2015 et 2016 – "Produits de santé à l'heure des comptes", APICCS – CEPS 2014/2015 annual report – Smart Pharma Consulting analysis

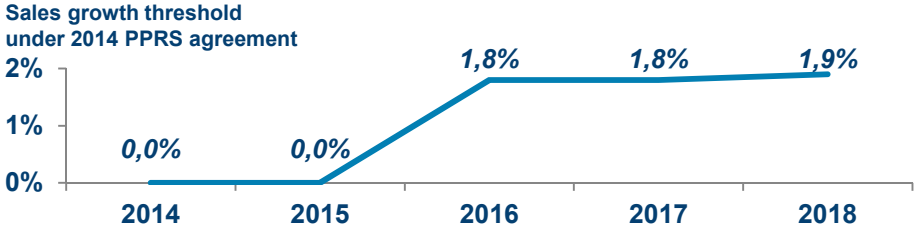
UK 2014 PPRS (Pharmaceutical Price Regulation Scheme) includes one total pharmaceutical sales capping and one profitability capping for the 2014-2018 period

Case study: UK 2014 PPRS

The 2014 PPRS is a voluntary agreement between the British Department of Health (DH) and the Association of British Pharmaceutical Industry (ABPI) which regulates the supply of branded medicines to the NHS[1] by 2018

Sales growth paybacks

- Due to the current state of the global economy and the **financial challenges** facing the NHS, the DH and the ABPI have agreed to introduce a **limit on** the **growth** of the **overall cost** of the branded medicines purchased by the NHS
- Payments are made by pharma companies on a quarterly basis of net sales to the NHS of **branded medicines**, i.e. after any other discounts already given
- **Smaller companies** with sales to the NHS of less than £5m are exempt from payments and to stimulate innovation, **products with first sales after January 2014** are **not concerned** by this scheme either



Profitability paybacks

- The scheme provides a framework for determining **reasonable limits to the profits** to be made from the supply of branded medicines to the NHS
- There are two **profitability thresholds** that pharma companies choose to refer to (they are designed to be similar):
  - One level of **return on sales** (ROS) target: **6%**
  - One level of **return on capital** (ROC) targets: **21%**
- **Within either limits**, companies are **allowed to set and change prices** in line with commercial considerations and NICE[2] appraisals
- If companies **reach the profit threshold**, they have to **pay 50% of the additional profit** to the NHS and are **not allowed to increase their prices**
- Companies must submit an **Annual Financial Return** to the DH for **control** purpose

Sources: "Understanding the 2014 PPRS", ABPI – Smart Pharma Consulting analysis

[1] National Health Service – [2] National Institute for Health and Care Excellence

An EU collaboration for Health Technologies Assessment exists since 2005 with the aim to set a better communication between HTA bodies and to standardize methodologies

Initiatives of assessment collaborations in Europe

About EUnetHTA

- EUnetHTA was established in 2005 to create an effective and sustainable network for HTAs (Health Technologies Assessments) across Europe
- EUnetHTA helps develop reliable, timely, transparent and transferable information to contribute to HTAs in European countries
- EUnetHTA supports collaboration between European HTA organizations at the European, national and regional level through:
  - Facilitating efficient use of resources available for HTA
  - Creating a sustainable system of HTA knowledge sharing
  - Promoting good practices in HTA methods and processes

EUnetHTA Joint Action 1 strategic objectives (2010-2012)

- To develop principles, methodological guidance and functional online tools and policies to:
  - Produce, publish, store and retrieve structured HTA information
  - Improve Relative Effectiveness Assessment (REA) by identifying areas where methodological guidance is needed and by providing it, suggesting ways to integrate REA of pharmaceuticals as a special version of the HTA Core Model (methodological framework for production and sharing of HTA information)
  - Structure exchanges and storage of information on evidence generation on new technologies (e.g. registries and trials)
- To test and implement:
  - A web-based toolkit for structured exchanges and storage of information on evidence generation on new technologies
  - The application of the HTA Core model in common production of at least 2 Core HTAs
  - A REA of (a group) of pharmaceuticals in line with the core HTA development
  - Real life support of information flow on new technologies prompting those where parallel assessments of same technologies are detected and alerting on opportunities for information sharing and closer collaboration
  - Provision of a contemporary information management system which supports collaborative HTA work and ensures rapid dissemination of HTA results

EUnetHTA Joint Action 2 strategic objectives (2012-2015)

- To strengthen the practical application of tools and approaches to cross-border HTA collaboration
- To aim at bringing collaboration to a higher level resulting in better understanding for the Commission and Member States (MS) of the ways to establish a sustainable structure for HTA in the EU
- To develop a general strategy, principles and an implementation proposal for a sustainable European HTA collaboration

Sources: EUnetHTA website – Smart Pharma Consulting analysis

Note: Were implemented in Europe some other collaborative initiatives such as SEED (Shaping European Early Dialogues For Health Technologies), with the aim to implement early discussions between pharma companies and HTA bodies, to align product development with the future HTA requirements

Each type of evaluation compares alternative treatments from different perspectives

Types of health economic evaluations

Six types of evaluations used by regulatory agencies

Cost Effectiveness Analysis (CEA)	Cost Utility Analysis (CUA)	Cost Benefit Analysis (CBA)	Cost Minimization Analysis (CMA)	Cost Consequences Analysis (CCA)	Budget Impact analysis (BIA)
▪ Compare costs and effects using final or surrogate outcomes	▪ Form of CEA that uses health-state-value scores (e.g.: QALY) as the outcome measure ▪ Most frequently recommended analysis in Europe	▪ Comparative analysis of costs and money-valued benefits ▪ Not widely used due to frequent methodologic biases	▪ Comparison of costs associated with products with the same effects (desired and undesired effects)	▪ Variant of CEA (or of CBA) used when multiple consequences of a product has to be weighted ▪ Only used in the UK	▪ Considers the affordability of a technology ▪ Measures how a change in the treatment strategy will impact spending

Informs on the most economically efficient way to use healthcare resources, taking into account health consequences

Informs on financial and organizational consequences, without taking into account health consequences

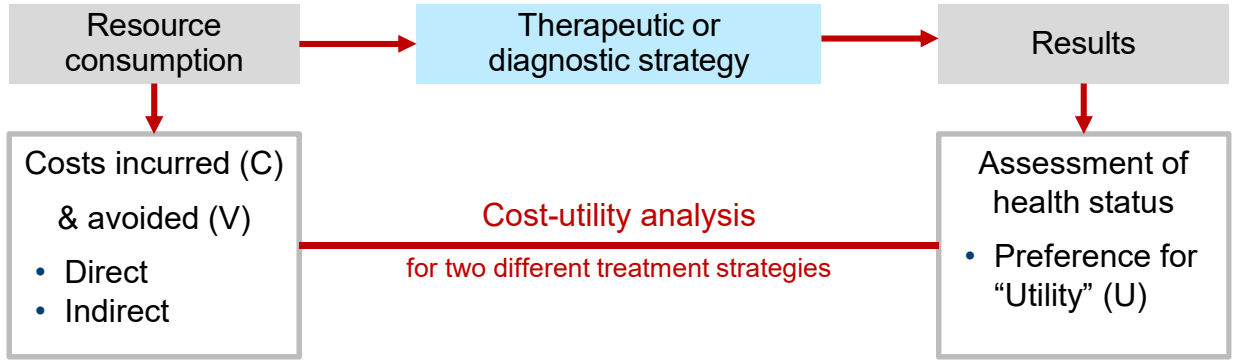
Sources: EUnetHTA 2015 – Smart Pharma Consulting analysis

The cost-utility analysis compares two treatment strategies based on their cost and their impact on a quality criterion aggregated with an efficacy criterion called QALY

Cost-utility analysis (CUA)

Definition

- The cost-utility analysis compares the costs associated with a medical strategy and its utility, which is a criterion combining the efficacy and the quality
- Thus, saving a life is important but not enough, the quality of life should also be considered
- The cost-utility analysis is a particular form of cost-effectiveness analysis for which results are measured by the number of years of life gained, adjusted with the quality of life, so called “quality-adjusted life year” (QALY)

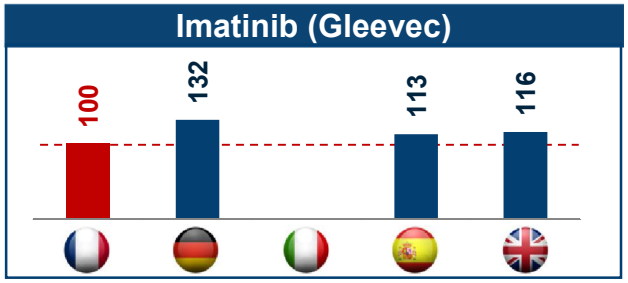


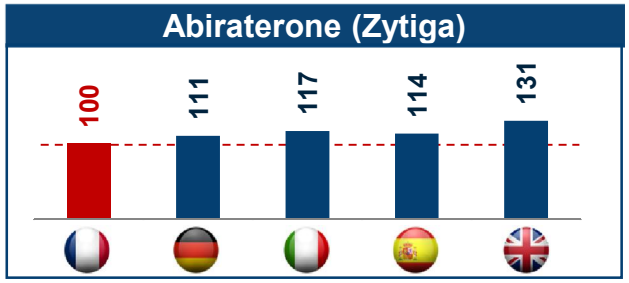
- “Utilities” of health states are generally expressed on a numerical scale ranging from 0 to 1 (0 represents the “utility” of the state “Dead” and 1 the utility of a state lived in "perfect health“)
- Thus, a year of healthy life accounts for 1 year of life and a year of lower health state accounts for a fraction of a year (<1). Some health states may be considered worse than death and have negative scores
- QALYs are used to compare protocols where the impact on quality of life is engaged
- This is the case for anticancer drugs comparisons which can improve response and/or survival time, and particularly living comfort; the results are then expressed using QALYs

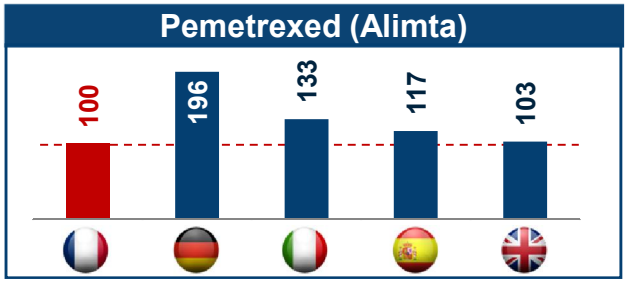
Sources: Marie-Christine Woronoff-Lemsi, Georges Weil 2011 – HAS 2014 – EUnetHTA 2015 – Smart Pharma Consulting analysis

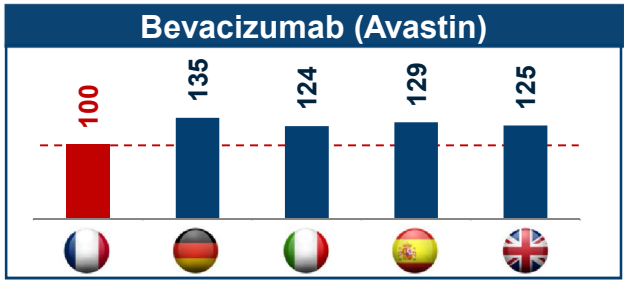
The analysis of a selection of onco-hematology treatments shows that prices are in general lower in France than in the other EU 5 countries

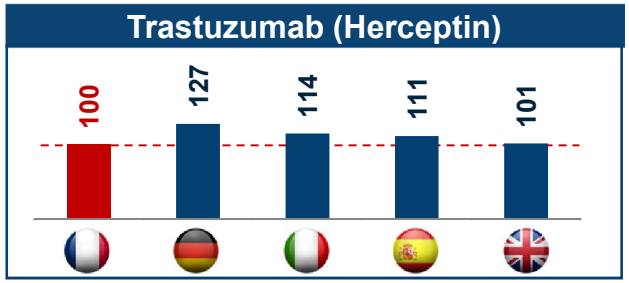
Oncology drugs price comparison in Europe

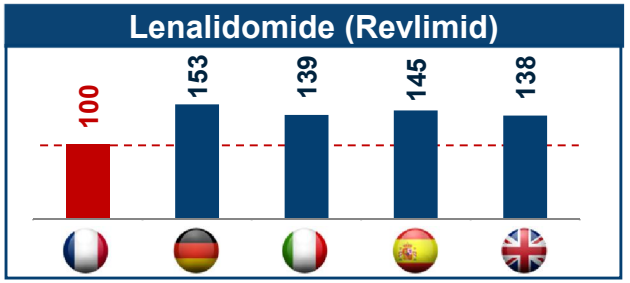


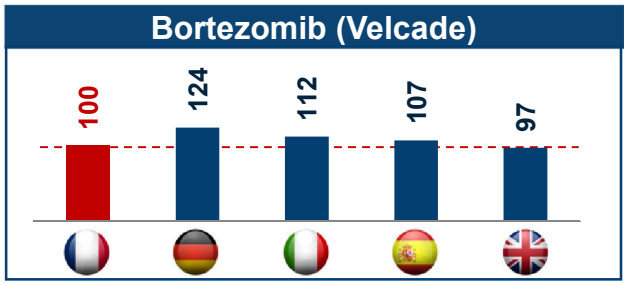


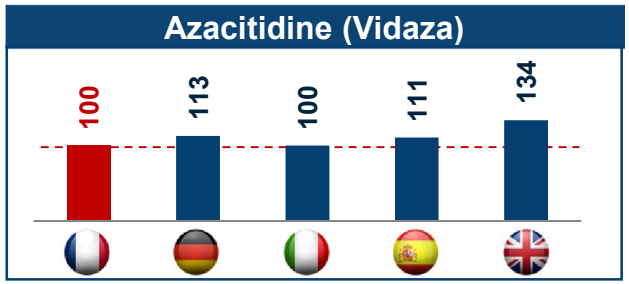


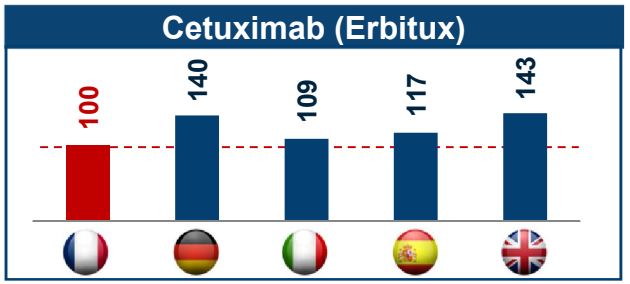












Sources: CEPS annual report 2014/2015 – Smart Pharma Consulting analysis

Note: Ex-factory prices, without rebates/discounts, based on HIS database as of July 2015

Drug reimbursement is automatic following marketing authorization* and price free up to 12 months, period during which an early benefit assessment (EBA)** is carried out

National market access considerations in Germany (1/3)

Timelines (months)

3

Marketing Authorization (at national level)

Dossier submission following marketing authorization granted by the Federal Institute for Drugs and Medical Devices (BfArM)

1

3

Early Benefit Assessment

- The Federal Joint Committee (G-BA) evaluates if the product has an additional benefit over the appropriate comparator (six categories: from lower benefit to major benefit vs comparator or IRP[1] in 15 EU countries)
- The G-BA also issues drug prescribing guidelines for physicians that will specify reimbursement conditions

2

3

Health Technology Assessment

- The Institute for Quality and Efficiency in Health (IQWIG) is responsible for producing independent evidence-based reports based on international standards on G-BA request
- The IQWIG may be asked by the G-BA to assess the benefits of new drugs under AMNOG (reform including mandatory pricing assessment for newly introduced drugs introduced in 2011)
- The IQWIG has also started undertaking cost-benefit assessments

4a

4b

6 (+3 if arbitration)

Pricing (if additional benefit)

- If the G-BA agrees that the product has an added benefit and if it is qualified for reimbursement by the Federal Association of Health Insurance Funds (GKV-SV), the price is then negotiated[2,3]
- If no agreement is reached, an arbitration board determines the price using European pricing levels as its standard

Pricing (if no additional benefit)

- If the drug is considered **as having no added benefit** over comparators, it will be included in the reference price system within six months after launch
- The annual treatment costs must not exceed those of the appropriate comparator or the cheapest alternative
- Reference prices are annually reviewed by the GKV-SV. Revisions are based on changes in market conditions, prescription patterns, and market prices

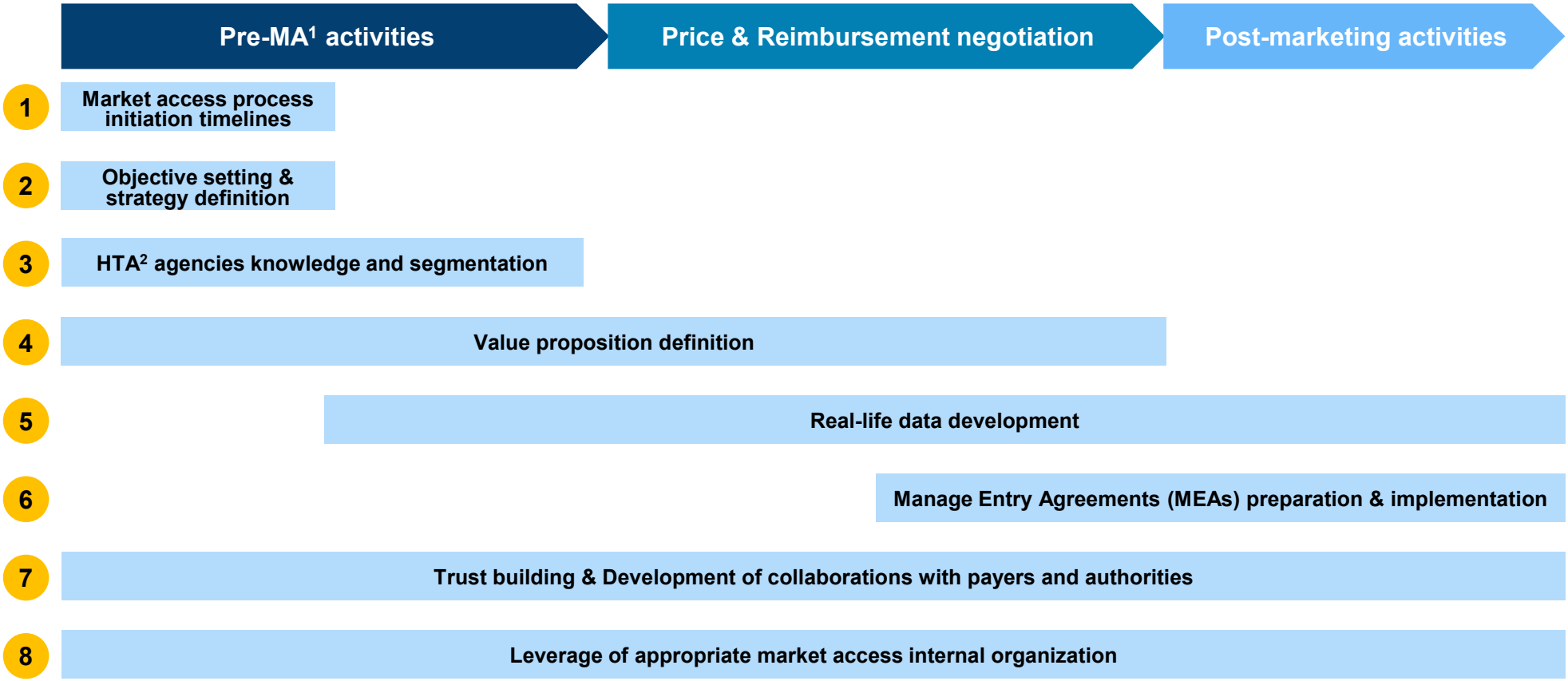
** Exceptions: non-prescription drugs, lifestyle drug*
*** Exemptions for non reimbursed drugs, hospital-only drugs and generics*

Sources: FirstWord 2013 – IMS – GVK – "Reimbursement Systems for Pharmaceuticals in Europe Concept Mechanism and Perspective", EMAUD – Smart Pharma Consulting analysis

[1] International Reference Price – [2] Since June 2013, where there have been several appropriate comparators, price negotiation should be based on the cheapest comparator – [3] Since 2007, German health insurers are able to negotiate drug price contracts directly with pharma companies through a tendering process

The best practices related to the market access process are well identified from the pre- to the post-marketing authorization phases of products

Market access best practices



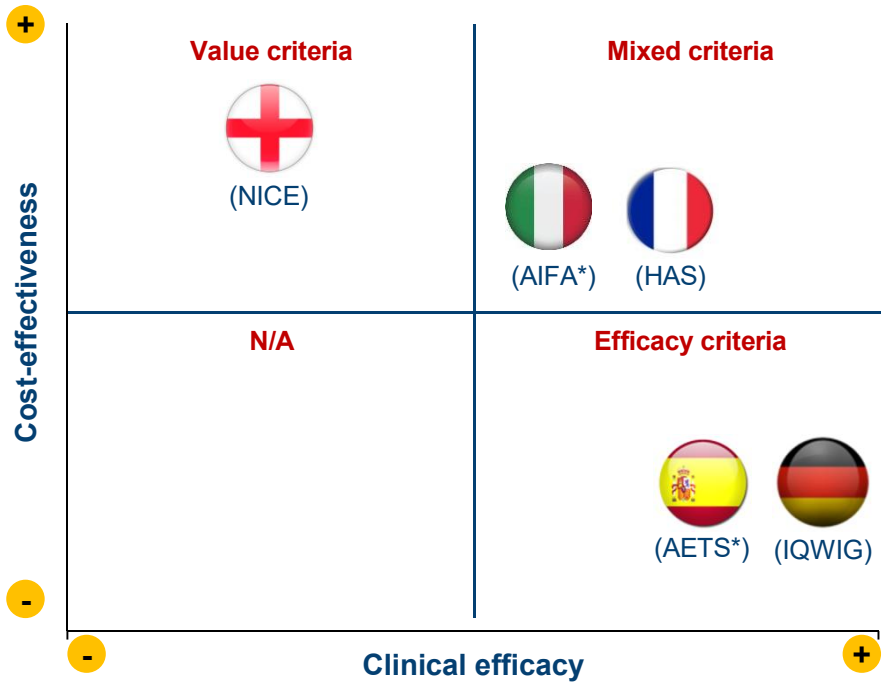
Sources: Smart Pharma Consulting analysis

[1] Marketing Authorization – [2] Health Technology Assessment

Pharma companies may cluster HTA agencies according to the assessment criteria they value the most and then develop a specific value proposition for each of them

3 Payers knowledge and segmentation

Segmentation of EU countries based on HTA criteria
(clinical efficacy vs. cost-effectiveness)



- The first step for market access activities planning is to understand **what will drive national HTA** (Health Technology Assessment) agencies **decisions** when it comes to drug evaluation
- A good understanding of their requirements will allow to define an **appropriate value proposition** for each of them
- The **"one fits all" strategy is no longer valid** since each country has different requirements
- **HTA agencies** can be **segmented** according to the importance they grant to the following **criteria**:
  - **Clinical efficacy** vs. **cost-effectiveness**
  - **Absolute**[1] vs **relative therapeutic value**[2]
  - **Narrow** view vs. **holistic** view of the impact of the drug (Health Related Quality-of-Life, societal impact, etc.)
  - Importance of **subpopulations**

Sources: "Reimbursement Systems for Pharmaceuticals in Europe Concept Mechanism and Perspective", EMAUD – Smart Pharma Consulting analysis

** Note: In Spain and Italy, policies may differ from a region to another*
[1] Disease severity and burden, unmet needs, efficacy/safety of the product –
[2] Incremental efficacy/safety versus available comparators

Value dossiers may help to develop targeted key messages for the different stakeholders

4 Value proposition definition – The value dossier: Example

Disease description

- Colorectal cancer is still a life-threatening disease with an average survival of 1.3 year despites available therapies
- In France, 10,000 patients are concerned by this disease each year

Value story / value proposition

Patients oriented value messages	Prescribers oriented value messages	Regulators oriented value messages	Payers oriented value messages
▪ Increases lifespan compared with normal care ▪ Mild side effects are mostly observed ▪ Improves the ability to perform normal activities	▪ Provides 15% longer progression-free survival compared with standard of care ▪ Acceptable benefit-risk profile ▪ Improves quality of life	▪ Provides statistically significant and clinically relevant longer progression-free survival compared with standard of care with an acceptable benefit-risk profile	▪ Provides cost-effective benefits based on cost per life-year gained (LYG) and quality-adjusted life-year (QALY)

Supporting evidence

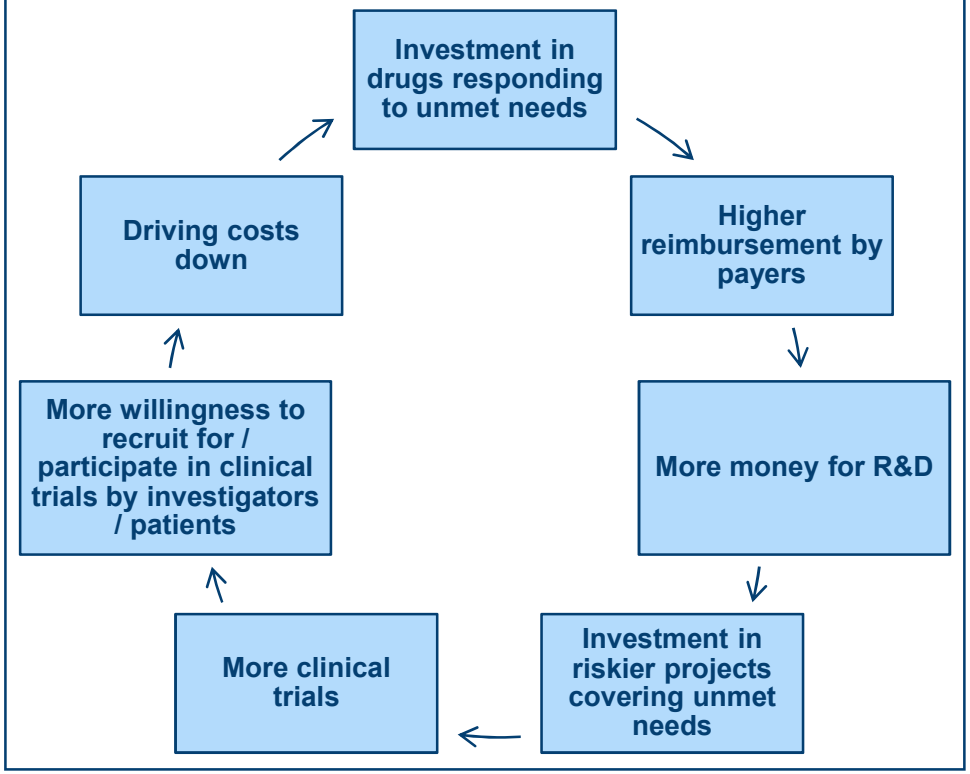
Value message	Target	Source of evidence	Type of evidence	Strength of evidence	Probability of success	Comments
▪ Improves the ability to perform normal activities / quality of life	▪ Patients ▪ Physicians ▪ Payers	▪ Phase III trials (#1 & #2)	▪ Patient-reported outcome endpoint data gathered with validated questionnaires	▪ Medium	▪ Medium	▪ N/A

Sources: ISPOR 14th annual meeting presentation, RTI Health – Smart Pharma Consulting analysis

Pharma companies corporate reputation is directly related to their research announcements responding to previously unmet needs

Corporate reputation building – Involvement in R&D

R&D investment in innovation virtuous cycle



Patient-centric mindset for an improved corporate reputation

- A reputation benchmark performed by Alva showed that pharma companies **reputation peaked** when were announced **patient-driven breakthrough research initiatives**:
  - **AstraZeneca** reputation improved when was announced in 2014 a partnership with Eli Lilly for the development of **Alzheimer** treatments based on **genome-editing technology**. It also peaked when was announced its partnership with **PatientsLikeMe** in 2015
  - **Merck** reputation peaked in 2015 with the announcement of its partnership with Genea Biomedx and with Illumina for the development of **pioneering assisted reproductive treatments**
  - **GSK** reputation also peaked with the announcement of R&D innovations such as **Ebola vaccine** reaching phase II during late 2014 or **malaria vaccine** being approved by the EMA and soon to be used in Africa

Sources: "Pharma industry improves its tarnished reputation", CenterWatch News Online – "R&D innovation – a reputation differentiator for pharma", Alva – Smart Pharma Consulting analysis – Merck press release

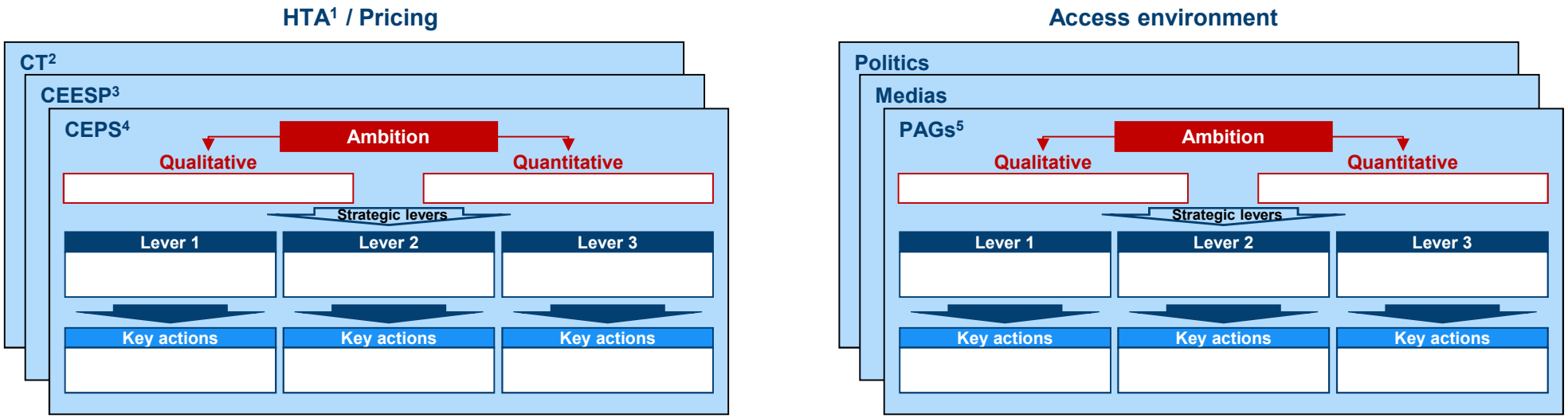
The Pharma Corporate Reputation Audit developed by Smart Pharma Consulting facilitates the identification of key challenges to improve corporate reputation

Corporate reputation strategy & tactics

Assessment | Strategy & tactics | Management

Illustrative – France

Pharma Reputation Strategy Card



- Strategy and related actions aim at achieving the set ambition in terms of corporate reputation improvement
- The Pharma Reputation Strategy Card can be applied for one stakeholder group (i.e. HTA / Pricing, Access environment…) or sub-group (i.e. CT, CEESP, CEPS, Etc.), or even for one individual stakeholder (i.e. President of the CEPS)
- Strategic levers correspond to strengths on which the company should capitalize to create a competitive advantage or weaknesses to be corrected

Sources: Smart Pharma Consulting analysis

[1] Health Technology Assessment – [2] Transparency Commission – [3] Health economic evaluation committee – [4] Drug pricing committee – [5] Patient Advocacy Groups

Market access strategy and corporate reputation play a key role to optimize drug price valuation and to take the advantage over competition…

Selected key takeaways

- Pressure of governments and payers on drug prices will keep on increasing but the impact within the same category of drugs will significantly differ, depending on market access strategy design and execution by pharma companies

DON'Ts	DOs
▪ Justify the price of innovation by the level of investment in R&D which is almost half the one invested in marketing, sales and general expenses ▪ Invoke the high level of risk, knowing that there is no case of bankruptcy amongst pharma companies ▪ Invest in sophisticated and expansive health economic studies which will be most likely criticized and not taken into consideration to grant you a better price ▪ Propose managed entry agreements for which the uncertainty associated with outcomes is high ▪ Underestimate the importance of corporate reputation	▪ Pharma companies should act in good faith and put themselves in governments and payers shoes ▪ Put forward evidence that are well-documented and articulated in a convincing argument to support the asking price ▪ Managed entry agreements should remain as simple as possible and generate a minimum of controlled associated costs ▪ Each pharma company should strengthen its corporate reputation to differentiate itself positively from others and thus get preferred (vs. competitors)

… knowing that pharma companies are not considered as all equal by governments and payers in the context of drug pricing & reimbursement

Sources: Smart Pharma Consulting analyses

Smart Pharma Consulting

Consulting company dedicated to the pharmaceutical sector operating in the complementary domains of strategy, management and organization

Core capabilities

1 Strategy

- **Assessing the attractiveness of markets** (Hospital / retail innovative products - Vaccines - OTC - Generics)
- **Growth strategy**
  - Optimization of marketing / sales investments
  - Development of a company in the hospital market Business
  - Valuation for acquisition
  - Portfolio / franchise assessment
- **Extension of product life cycle performance**
  - Improvement mature products performance
  - Adaptation of price strategy
- **Defense strategies vs. new entrants**
- **Competitive strategies in the hospital market**
- **Strategic partnerships companies / pharmacies**

2 Management

- **Facilitation and structuring of strategic thinking for multidisciplinary product teams**
  - Key challenges identification
  - Strategic options formalization
  - Resource allocation optimization program
- **Training of marketing and market research teams to sales forecast techniques (modeling and scenarios development)**
- **Development and implementation of a "coaching program" for area managers**
  - Sales reps coaching
  - Regional action plans roll-out
- **Development and implementation of a "sales techniques program" for sales forces (STAR[1])**

[1] *Sales Techniques Application for Results (training courser*

3 Organization

- **Rethink of operational units organization**
- **Improvement of sales force effectiveness**
- **Improvement of the distribution channels covering the hospital and retail markets**
- **Development of a strategic planning process**

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