The French Pharma Market
2016 – 2022
Prospects
Strategic Implications for Pharma Companies
Business Report (Excerpts)
September 2017
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Glossary
This report analyzes the current situation and the key trends of the French Pharma market by the end of 2022 to provide pharma companies with key strategic insights

**2016 – 2022 French pharma market prospects & strategic implications**

- Despite an ever tougher environment, the French pharma market will remain a key priority for pharma companies
- Smart Pharma Consulting proposes pharma companies to address the following key issues related to the French healthcare system and pharma market evolution by the end of 2022, to better grasp its strategic impacts

- How is the healthcare system organized nationally and regionally?
- Who are the key stakeholders in the healthcare system and what are their respective role and influence?
- What are the major categories of healthcare expenditure?
- How does France stand in comparison with other countries?
- What are the recent evolutions of therapeutic classes, drugs and pharma companies sales?
- What are the estimated sales forecasts by strategic segment by 2022?
- What could be the strategic implications for pharma companies by 2022?
Healthcare expenditure will keep on growing faster than national economies due to demographic factors and willingness of citizens to have better access to healthcare

### Healthcare expenditure as a percentage of GDP

<table>
<thead>
<tr>
<th>Country</th>
<th>2005</th>
<th>2014 *</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>9%</td>
<td></td>
</tr>
</tbody>
</table>

Healthcare expenditure represented one of the largest public spending items in most developed economies: 1st (USA), 2nd (France, Germany, Japan, and UK) and 3rd (Italy and Spain).

At best, governments and payers will manage to slow down the rise of healthcare expenditure as a percentage of GDP but would not be able to stop it.

There is no optimal ratio of healthcare expenditure over GDP, it primarily results from:
- Public health conditions
- Governments investment prioritization
- Citizens willingness to seek for care
- Healthcare cost

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Sources: World Bank, as of September 2017 – OECD, as of September 2017 – Smart Pharma Consulting analyses

*Note: 2014 data excepted for France and the USA, 2015

1 After social protection
2 After social protection and general public services

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September 2017
By 2022, the sales growth of pharma companies should be essentially driven by generic and innovative biologic drugs, but they should lose two points of profitability.

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**Global pharmaceutical market attractiveness per strategic segment (2016 – 2022)**

- By 2022, the sales (incl. human drugs only for the non-OTC segments and medical devices and food supplements for the OTC segment) should reach USD 1,400 B and grow at a pace of +4% p.a.
- Pharma companies EBIT should decrease from ~24% to ~22% over the period due to increased price pressure.
- The OTC segment appears to be the least attractive.
- The biotech segment will remain very attractive but biosimilar competition will ramp up.

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Sources: Outlook for Global Medicines through 2021, Quintiles IMS (December 2016) – Global OTC Drugs Market, Mordor Intelligence (August 2016) – Global economic prospects, World Bank (June 2017) – Smart Pharma Consulting estimates

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1 Including branded and unbranded generics and biosimilars, excluding OTC
2 Excluding biosimilars, already included in the “Generics” segment
3 Earnings before interests and taxes
Stakeholders in the French healthcare system can be split according to their role as decision maker, payer, provider / supplier or consumer.

Mapping of key stakeholders

Sources: Smart Pharma Consulting analyses

1 The exact name of this ministry is: Ministry of Health and Solidarity, that will be named in this report Ministry of Health
Price and reimbursement settings depend on the status and on the clinical benefit of the drugs

**Overall reimbursement and pricing processes**

<table>
<thead>
<tr>
<th>ANSM / EMA</th>
<th>HAS</th>
<th>CT</th>
<th>CEESP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retail</td>
<td>Application for approval for hospital only use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>Approval by the Hospital Council</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Marketing authorization (MA)**

1. No request for reimbursement
2. Request for reimbursement
   - Medico-technical evaluation of clinical benefit (SMR) and of clinical benefit improvement (ASMR)
   - ASMR IV & V (which leads to savings in treatment costs)
   - ASMR I, II, III

**Non-reimbursable drug**
- Free price (no negotiation with CEPS)

**Reimbursable drug**
- Price Negotiation (or unilateral price setting) based on ASMR
- Reimbursement rate validated by UNCAM based on SMR
- Registration on the Social Security list

**Social Health Insurance**

- Retrocession drug list
- Setting of a reference price
- Inclusion in GHS

**CEPS**

- Expensive drug list

**Social Health Insurance**

- Free price

**UNCAM**

- DRG-related groups (DRGs)


1 After a favorable opinion of the MA commission (national level) or the EMA (European level) – 2 Similar to Diagnosis-related groups (DRGs) – 3 These drugs can be dispensed to outpatients by hospital pharmacies – 4 The cost of these drugs is not covered by the hospital but by the Social Health Insurance
Each type of evaluation compares alternative treatments from different perspectives

**CEESP – Possible types of health economic evaluations**

Six types of evaluations used by regulatory agencies

- **Cost Effectiveness Analysis (CEA)**
  - Compares costs and effects using final or surrogate outcomes

- **Cost Utility Analysis (CUA)**
  - Form of CEA that uses health-state-value scores (e.g.: QALY) as the outcome measure
  - Not widely used for ethical reasons and due to methodology biases
  - Most frequently recommended analysis in Europe

- **Cost Benefit Analysis (CBA)**
  - Comparative analysis of costs and money-valued benefits
  - Often used by purchasing groups (e.g. UNIHA)

- **Cost Minimization Analysis (CMA)**
  - Comparison of costs associated with products with the same effects (desired and undesired effects)
  - Only used in the UK

- **Cost Consequences Analysis (CCA)**
  - Variant of CEA (or of CBA) used when multiple consequences of a product have to be weighted
  - Only used in the UK

- **Budget Impact analysis (BIA)**
  - 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

Cost effectiveness and cost utility analyses are privileged by the CEESP to assess drugs

Source: EUnetHTA as of July 2017

1. The French healthcare system
1.1. Key stakeholders
When compared to the other EU5 countries, a wider array of indicators could be used by French health authorities to evaluate the economic value of drugs

**CEESP – Health economic evaluations: Submission requirements in Europe**

<table>
<thead>
<tr>
<th>Therapeutic benefit</th>
<th>Cost-effectiveness modeling</th>
<th>Budget impact modeling</th>
<th>HRQoL¹ data</th>
<th>Data vs. SoC²</th>
<th>Innovation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>Cost-effectiveness taken into account since 2013 with the creation of the CEESP (Economic committee for healthcare products)</td>
</tr>
<tr>
<td>Germany</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>Free pricing during the first six months on the market: i.e. before the assessment by IQWG (Institute for Quality and Efficiency in Health Care)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>One of the first countries to implement a form of value-based pricing including cost-effectiveness and QoL (Quality of Life) data</td>
</tr>
<tr>
<td>Italy</td>
<td>✔</td>
<td>(national or regional requirement)</td>
<td>(national and regional requirement)</td>
<td>✔</td>
<td>✔</td>
<td>Requirements may vary from a region to another</td>
</tr>
<tr>
<td>Spain</td>
<td>✔</td>
<td>(national or regional requirement)</td>
<td>(national and regional requirement)</td>
<td>✔</td>
<td>✔</td>
<td>Requirements may vary from a region to another</td>
</tr>
</tbody>
</table>

Sources: “An Introduction to European Market Access”, PRMA Consulting – Smart Pharma Consulting updates

¹ Health-Related Quality of Life  
² Standard of Care
French health authorities will keep on limiting the number of ASMR I, II & III to quantum leap innovations in order to contain the cost of reimbursed drugs

CT – SMR and ASMR granting over time (2012 – 2016)

Distribution of granted SMR levels¹

Distribution of granted ASMR levels¹

Sources: HAS Annual Activity Reports (2011-2016) – Smart Pharma Consulting analyses

¹ Applications for first registration only, all procedures combined. An application may result in several different SMR / ASMR, depending on the considered indications

*2016 data not available in September 2017
The price level accepted by the CEPS (Economic Committee on Healthcare Products) depends on the level of ASMR granted by the Transparency Committee

CEPS – Price setting for reimbursable ambulatory drugs

Rating of ASMR

- ASMR I to III (significant improvement)
- ASMR IV (Minor improvement)
- ASMR V (No improvement)

Pricing principles

- Consistent pricing with prices in the four other major European markets
- No increase in the cost of medical treatment
- Savings in the cost of medical treatment
  - Referent: Comparator used by the CT during its evaluation or, in the case of a product line extension, the cheapest competitors
  - Level of price reduction:
    - Low: If it is considered that the new product will only take part of the market of other products already in the market
    - High: If it is estimated that the new product may increase consumption

Specific clauses may be added to the price agreement between the CEPS and the pharma companies:

- Risk sharing clause: The company is bound to pay financial compensation by refunding any excess costs to the Health Insurance if sales exceed those forecasted for the first four years after launch
- Price revision clauses:
  - Volume clauses: are used where the ASMR for a drug has only changed for one of its indications; here sales volumes are monitored to make sure the product is used in-label. If these volume clauses are not respected, prices will be lowered or a rebate due from the companies
  - Cost clauses for daily dosages: these clauses are used when there is a range of dosages; the aim is to ensure the use of the most appropriate dose by controlling the average daily cost of the range of products. If the distribution of the consumption of different dosages is different from that forecasted, the price is revised in order to re-establish the daily treatment cost which was forecasted initially
  - Dosage or posology clauses: the treatment cost is initially calculated on the basis of the average dose; these clauses result in a price reduction if the average stated dose is exceeded

Sources: CEPS 2015 annual report (Appendix 4), published in 2016 – Smart Pharma Consulting analyses

1 Apply to the initial registration of drugs – 2 Germany, Spain, Italy and the UK; This situation is monitored over time and the proposed price is modified if it differs from that in other European countries – 3 The cost may be calculated based on the price per pack or on the daily treatment cost for chronic diseases
**CEPS – Criteria for inscription on / radiation of the list of Off-T2A¹ expensive hospital drugs**

<table>
<thead>
<tr>
<th>Criterion n°1</th>
<th>The drug must be mainly used in the hospital setting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- If it is not the case, the CEPS considers that its cost can be funded under the hospital service tariffs (T2A system)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Criterion n°2</th>
<th>The drug must provide an important Clinical Benefit (important SMR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Suggesting that the drug has a positive risk/benefit ratio and that it covers an actual medical need</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Criterion n°3</th>
<th>The drug must provide a Clinical Added Value (ASMR I to III)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Suggesting that the drug is innovative vs. available alternatives</td>
</tr>
<tr>
<td></td>
<td>- An exception can be made for products with ASMR IV with no therapeutic alternatives</td>
</tr>
<tr>
<td></td>
<td>- For equity reasons, when a product receives an ASMR IV or V and its comparators are already listed, the product will also be listed, despite its poor ASMR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Criterion n°4</th>
<th>The cost of the drug is incompatible with the T2A system</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- The threshold is fixed at a cost of the drug representing &gt; 30% of the GHS (as set under the hospital service tariffs for a given disease)</td>
</tr>
</tbody>
</table>

**Criteria for radiation of the list**

When a product does not meet inclusion criteria anymore, it may be excluded:

- When there is a reevaluation by the HAS of the SMR / ASMR
- When prices have decreased enough to make the product compatible with the T2A system

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Sources: Decree of March 25th, 2016 regarding modalities of inscription to the “liste en sus” – Smart Pharma Consulting analyses

¹ Activity-based costing system similar to a Diagnosis related group-based funding
Managed entry agreements may be considered by the CEPS when the level of medical evidence is too low and/or the financial impact is too high

**CEPS – Options for a newly approved product**

- **Decision of reimbursement**
  - **Reimbursement with no additional evidence**
    - Payers estimate that the adequate level of evidence is provided to cover the drug
  - **Reimbursement with managed entry agreements**
    - Payers have uncertainties regarding evidence provided by the company
  - **No reimbursement**
    - The manufacturers have the option to reapply with more evidence

- **Managed entry agreement**
  - **Outcomes-based contract**
    - Payers have uncertainties regarding the medical outcomes / cost-effectiveness of the drug
  - **Financially-based contract**
    - Payers have uncertainties regarding the budgetary impact of the drug
  - **No contract**
The implementation of managed entry agreements are most often time-consuming and costly for payers and/or pharma companies, outweighing their benefits

### CEPS – Pros & Cons of managed entry agreements

#### Pros

<table>
<thead>
<tr>
<th>CEPS</th>
<th>Pharma companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Potential to re-evaluate the effectiveness of drugs at a later stage and re-negotiate the price based on real-world evidence</td>
<td></td>
</tr>
<tr>
<td>- Help address post-licensing uncertainty by offering flexibility in dealing with new and often expensive treatments</td>
<td></td>
</tr>
<tr>
<td>- Improve the cost-effectiveness through a discount or a payback agreement for non-responders</td>
<td></td>
</tr>
<tr>
<td>- Enable different types of schemes addressing different needs, both financial and non-financial</td>
<td></td>
</tr>
<tr>
<td>- Speed up pricing negotiations and reimbursement</td>
<td></td>
</tr>
<tr>
<td>- 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</td>
<td></td>
</tr>
<tr>
<td>- Potential to reinforce the long-term collaboration between payers, health authorities and pharmaceutical companies</td>
<td></td>
</tr>
<tr>
<td>- Enable discounts without impacting list prices</td>
<td></td>
</tr>
</tbody>
</table>

#### Cons

| Additional efforts required to make a new drug available to patients, such as negotiation time, monitoring of patient response, data gathering, development of registries, etc. |
| Threat that manufacturers could start proposing higher entry prices in the expectancy of having to engage managed entry agreements |
| Limited capacity to implement and assess evidence, notably if implementation takes place at regional/hospital level |
| Costs related to the implementation of the managed entry agreement can, in some cases, totally outweigh benefits |
| Concessions required such as refunds for non-respondent patients, discounts, gathering of additional data |
| Voluntary versus no voluntary nature of such contracts leading to a variability in stakeholders’ perception |

Sources: “Managed entry agreements for pharmaceuticals: the European experience”, Alessandra Ferrario and Panos Kanavos, April 2013 – Smart Pharma Consulting analyses
In eight European countries, including France, pharma companies and patients must wait, one year or more, after marketing authorization, to get a new drug reimbursed\(^1\)

### Average time to market vs. European countries

- **In Europe**, the delay between marketing authorization of a drug and its availability on the market may vary widely, due to the time required to obtain its inclusion on reimbursement list and a price agreement.
- **In countries such as France, Italy or Spain**, this delay exceeds the 180 days recommended by the European Commission.
- An important delay may be harmful both for patients who do not have full access to innovative therapies and for companies which face a loss of revenues\(^1\).
- **The UK and Germany** have no delay since the price and reimbursement negotiations occur once the product has reached the market.

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Sources: Patients W.A.I.T. Indicator – EFPIA (2015)

\(^1\) Excluding early access programs for breakthrough innovations (e.g. ATU / post-ATU in France) – \(^2\) For drugs receiving their first marketing authorization between 2011 and 2014
If mutual funds are in a greater number, they are often smaller than private insurance companies and provident funds in terms of activity

**Complementary health cover organizations**

<table>
<thead>
<tr>
<th></th>
<th>Private organizations</th>
<th>Public schemes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mutual fund</td>
<td>CMU Fund¹</td>
</tr>
<tr>
<td>Legal status</td>
<td>Private non-profit organization</td>
<td>Public institution of administrative nature</td>
</tr>
<tr>
<td>Applicable law</td>
<td>Mutual societies code</td>
<td>Social Security code</td>
</tr>
<tr>
<td>Description</td>
<td></td>
<td>Insurance code</td>
</tr>
<tr>
<td></td>
<td>▪ Self-management</td>
<td>▪ Financing of the CMU-C² and ACS³:</td>
</tr>
<tr>
<td></td>
<td>▪ No discrimination</td>
<td>▪ ‒ Support the out of pocket of a basket of goods and health services for CMU beneficiaries with a lower level of resources ceiling</td>
</tr>
<tr>
<td></td>
<td>▪ Level of contributions independent of the health status of the person</td>
<td>▪ ‒ CMU-C and ACS are agreed for one year</td>
</tr>
<tr>
<td></td>
<td>▪ The complementary health cover accounts for 2/3 of the activity of the mutual funds</td>
<td></td>
</tr>
<tr>
<td>% of organizations</td>
<td>74%</td>
<td>20%</td>
</tr>
<tr>
<td>% of insured people</td>
<td>58%</td>
<td>25%</td>
</tr>
</tbody>
</table>
In 2016, generics accounted for 19% of the retail pharmacies’ sales on average and for 29% of their margin, due to the high rebates offered by generics companies.

Economic structure of retail pharmacies in France (2016)

Average annual turnover of a retail pharmacy in 2016: €1,558 K

Average profitability by segment:
- Reimbursable drugs (ethicals & semi-ethicals): 43% (€216 K)
- Reimbursable generics: 29% (€145 K)
- Non-reimbursable drugs (OTC & "lifestyle" Rx products): 25% (€216 K)
- Other healthcare products (non-drugs): 17% (€82 K)
- Other healthcare products: 11% (€56 K)
- Other healthcare products: 49% (€296 K)
- Reimbursable drugs (ethicals & semi-ethicals): 55% (€857 K)

Relative weight of each segment in pharmacies commercial margin:
- Reimbursable drugs (ethicals & semi-ethicals): 33% (€499 K)
- Reimbursable generics: 35% (€82 K)
- Non-reimbursable drugs (OTC & "lifestyle" Rx products): 15% (€145 K)
- Other healthcare products (non-drugs): 11% (€56 K)
- Other healthcare products: 19% (€296 K)

Sources: KPMG (2016) – Smart Pharma Consulting analyses

1 Inclusive of legal margin, rebates, commercial agreements and remuneration for pharmaceutical services, notably those corresponding to the public health objectives (e.g. generics substitution objectives, pharmaceutical interviews with patients, etc.)
Former Health Minister, Marisol Touraine, made the Health System Modernization Act be enacted from January 26th, 2016

**Health System Modernization Act**

“One objective: equality. Only one method: innovation”, Marisol Touraine

<table>
<thead>
<tr>
<th>Priority 1: “Innovate to better prevent”</th>
<th>Priority 2: “Innovate to better care in close proximity”</th>
<th>Priority 3: “Innovate to strengthen patients rights and safety”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention should be at the heart of the healthcare system</td>
<td>Redirecting the health system on community-based care</td>
<td>New concrete rights to patients, progression of health democracy and reinforced patients’ safety</td>
</tr>
<tr>
<td>▪ Measure 1: Deploy a health education pathway from kindergarten to high school</td>
<td>▪ Measure 8: Develop a community-based care around GPs</td>
<td>▪ Measure 14: Creating a right to oblivion for former patients with serious diseases</td>
</tr>
<tr>
<td>▪ Measure 2: Refer to GPs for children (up to 16 years)</td>
<td>▪ Measure 9: Set up a third-party payment system for physicians</td>
<td>▪ Measure 15: Allowing “class action” in healthcare</td>
</tr>
<tr>
<td>▪ Measure 3: Strengthen nutrition information on food packaging</td>
<td>▪ Measure 10: Create a national helpline to call on-call physicians</td>
<td>▪ Measure 16: Improve access to abortion throughout the country</td>
</tr>
<tr>
<td>▪ Measure 4: Reduce the phenomenon of massive alcoholism among young people</td>
<td>▪ Measure 11: Expand the competencies of selected health professions</td>
<td>▪ Measure 17: Open access to health data</td>
</tr>
<tr>
<td>▪ Measure 5: Actively fight against smoking</td>
<td>▪ Measure 12: Relaunch the “shared medical record”</td>
<td>▪ Measure 18: Ensuring more transparency on links of interest in health</td>
</tr>
<tr>
<td>▪ Measure 6: Improve screening for sexually transmitted infections</td>
<td>▪ Measure 13: Strengthen the “public hospital service”</td>
<td>▪ Measure 19: Increasing the safety of medicines and medical devices</td>
</tr>
<tr>
<td>▪ Measure 7: Encourage risk reduction among drug users</td>
<td>▪ 4 other secondary measures, including the creation of GHT(^1)</td>
<td>▪ 6 other secondary measures</td>
</tr>
<tr>
<td>▪ 7 other secondary measures, including the access to emergency contraception for secondary level schools</td>
<td>▪ 4 other secondary measures, including the creation of GHT(^1)</td>
<td></td>
</tr>
</tbody>
</table>

Sources: Press kit “Loi de Modernisation de notre système de Santé”, French Health ministry January 28th, 2016 – Smartt Pharma Consulting Analyses

\(^1\) GHT: “Groupement Hospitalier de Territoire”: grouping which governs cooperation between several public health establishments in the same territory. 135 GHTs were created on July 5th, 2017
1. The French healthcare system

1.2. Recent reforms

The shared medical project is the heart of the GHT because it guarantees a proximity and a reference offer.

**GHT – Community hospitable territory**

**Members**

- Public health facilities including CHU and CH authorized in psychiatry
- CH associates authorized in psychiatry
- Public medico-social institutions
- Private facilities’ partners
- Armed Forces hospitals
- Public home hospital facilities

**Organization & Governance**

- Each GHT is attached to a teaching hospital (CHU)
- A support institution is designated to provide shared functions on behalf of all participating institutions:
  - Hospital information system
  - Department of Medical Information
  - Purchasing function
  - School, formation, ongoing professional development
- A constitutive convention adopted for 10 years and approved by the general director of the ARS describes:
  - The shared medical project
  - The operating method of the GHT
- The governance is ensured by different instances:
  - The strategic committee
  - The medical board or medical committee of the grouping
  - The CSIRMT
  - The territorial committee of local representatives
  - The users committee or commission
  - The conference on territorial cohesion

Sources: “Rapport intermédiaire de Jacqueline Hubert et de Frédéric Martineau sur les GHT”, May 2015 – Smart Pharma Consulting Analyses

1 A CHU may be part of a GHT and be associated with several other GHTs
2 CSIRMT: “Commission des Soins Infirmiers, de Réd éducation et Médico-Techniques”: Commission on nursing, rehabilitation and medico-technical care


September 2017
In 2015, total expenditure for healthcare goods and services amounted to € 195 billion (of which ~47% from hospitals) and was mostly funded by the Social Security

Supply, consumption and funding of healthcare and medical goods in 2015

<table>
<thead>
<tr>
<th>Suppliers</th>
<th>Consumers</th>
<th>Payers</th>
<th>Financial Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public Hospitals</td>
<td>Patients</td>
<td>National Health Insurance Fund</td>
<td>Employers</td>
</tr>
<tr>
<td>Primary care</td>
<td></td>
<td>CMU / AME²</td>
<td>Salaried and Households</td>
</tr>
<tr>
<td>Retail pharmacies</td>
<td></td>
<td>Households³</td>
<td>Public administration</td>
</tr>
<tr>
<td>Private hospital</td>
<td>Healthcare goods and</td>
<td>Mutual Insurance Funds</td>
<td></td>
</tr>
<tr>
<td></td>
<td>services expenses in 2015</td>
<td>Private Insurance companies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>€ 195 billion</td>
<td>Provident Institutions</td>
<td></td>
</tr>
<tr>
<td>Others¹</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


¹ Optics, prostheses, small devices, hygiene and first aid, etc. – ² CMU / AME: “Couverture Médicale Universelle Complémentaire / Aide Médicale d’Etat”; Complementary universal medical coverage / State medical assistance – ³ Non reimbursed, deductible, etc.
The increase of on top of “T2A” drug sales was mainly driven by the growth of Imnovid, Imbruvica, Viekirax, Keytruda and Entyvio

Sales of drugs on top of “T2A” (2012 – 2016)

- **Imnovid** (Pomalidomid), monoclonal antibody used for multiple myeloma in relapse and refractory in adult patients, marketed by Celgene
- **Imbruvica** (Ibrutinib), monoclonal antibody for adults with leukemia marketed by Janssen
- **Viekirax** (Ombitasvir + Paritaprevir + Ritonavir), antiviral complex indicated for chronic hepatitis in adults, marketed by AbbVie
- **Keytruda** (Pembrolizumab), humanized monoclonal antibody for adult patients suffering from advanced melanoma and non-small-cell lung cancer, marketed by MSD
- **Entyvio** (Vedolizumab), humanized monoclonal antibody indicated for the treatment ulcerative colitis and Crohn’s disease, marketed by Takeda

Sources: “Tableau de bord” GERS SAS – Smart Pharma Consulting analyses

1 Drugs retroceded and which can also be purchased at retail pharmacies (double channel) such as for: hepatic antiviral drugs, anti-HIV drugs and certain oncology products – 2 Excluding new hepatic antiviral drugs accounting for € 1,096 M in 2014
In 2016, the national objective of substitution was set at 86%, while individual objectives have also been set for 27 molecules with important saving potential.

**Top 10 generics with the highest potential savings (2016)**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>% of Substitution</th>
<th>Substitution rate Dec. 2016</th>
<th>Objective rate 2016</th>
<th>Potential savings</th>
<th>Potential savings for 2016 in € M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatine (TAHOR)</td>
<td>90%</td>
<td>91%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esomeprazole (INEXIUM)</td>
<td>85%</td>
<td>83%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel (PLAVIX)</td>
<td>80%</td>
<td>80%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole (MOPRAL)</td>
<td>95%</td>
<td>99%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine (ZYPREXA)</td>
<td>90%</td>
<td>89%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escitalopram (SEROPLEX)</td>
<td>90%</td>
<td>87%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatine (ELISOR)</td>
<td>95%</td>
<td>96%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montelukast (SINGULAIR)</td>
<td>85%</td>
<td>85%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatine (ZOCOR)</td>
<td>96%</td>
<td>97%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol+ Paracetamol (IXPRIM)</td>
<td>90%</td>
<td>83%</td>
<td>83%</td>
<td>83%</td>
<td>7.8</td>
</tr>
</tbody>
</table>

Sources: Amendments 8, 9 and 10 of National Convention, Official Gazette, June 2016 – GERS – Smart Pharma Consulting analyses
Sales of biosimilars, which were launched in 2007 and belonged to six therapeutic classes until May 2016, reached a total ~ € 212 million on the total market in 2016.

**Evolution of the biosimilars market (2007 – 2016)**

![Graph showing the evolution of the biosimilars market](image)

**Sources:**
- GERS – ¹ Ex-factory prices excluding rebates – ² CAGR: Compound annual growth rate – ³ GH: Growth hormones – ⁴ ESA: Erythropoiesis stimulating agents – ⁵ G-CSF: Granulocyte colony stimulating factors – ⁶ mAb: Monoclonal antibodies – ⁷ FSH: Follicle Stimulating Hormone – ⁸ Ratiogastrim was removed from market in 2016 – ⁹ Eporatio is not a biosimilar per se but is rather a "me-too" product. It was first launched by Ratiopharm, before to be acquired by Teva in March 2010 – ¹⁰ No sales in the GERS 2016
In 2016, the self-medication market accounted for 5.6% of the retail pharmaceutical market and included both reimbursable and non-reimbursable non prescribed drugs.

OTC market size and structure (2016)

- The strictly defined OTC market accounts for 82% of the self medication market.
- OTX or semi-ethical drugs (non-prescription-bound, reimbursed only if prescribed) are massively prescribed by physicians (sometimes on patient request), which limits the growth of the reconstituted self-medication sales.

Total pharmaceutical retail market (Manufacturer prices excl. tax)
€ 20.0 B

OTC market (prescribed or not)
8.6% (€ 1.7 B)

Reimbursable/non-reimbursable prescription-bound drugs (either prescribed or not)
83.7% (€ 16.8 B)

Non-prescribed OTC
(i.e. non prescription-bound non reimbursable drugs)
4.7% (€ 0.9 B)

Prescribed OTC
(i.e. non-prescription-bound non-reimbursable drugs)
3.9% (€ 0.8 B)

Non-prescribed OTX
(i.e. non prescription-bound reimbursable drugs)
0.9% (€ 0.2 B)

Prescribed OTX
(i.e. non-prescription-bound reimbursable drugs)
6.8% (€ 1.4 B)

Non-prescribed OTX
(i.e. non prescription-bound reimbursable drugs)
0.9% (€ 0.2 B)

Sources: Smart Pharma Consulting estimates based on data from GERS and pharmastat-IMS heath
In 2016, on the French pharmaceutical market, the top 10 pharma companies accounted for almost 48% of the market, with Novartis and Sanofi standing on the top.

Top 10 pharma companies retail and hospital market – In value (2016)

<table>
<thead>
<tr>
<th>Company</th>
<th>Market Share</th>
<th>2015-2016 Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novartis</td>
<td>7.8%</td>
<td>+6.9%</td>
</tr>
<tr>
<td>Sanofi²</td>
<td>6.5%</td>
<td>-4.4%</td>
</tr>
<tr>
<td>Roche</td>
<td>5.1%</td>
<td>+1.2%</td>
</tr>
<tr>
<td>MSD</td>
<td>4.5%</td>
<td>-1.9%</td>
</tr>
<tr>
<td>Servier²</td>
<td>4.4%</td>
<td>+1.7%</td>
</tr>
<tr>
<td>Gilead</td>
<td>4.2%</td>
<td>-10.7%</td>
</tr>
<tr>
<td>Mylan</td>
<td>4.0%</td>
<td>+1.3%</td>
</tr>
<tr>
<td>Pfizer</td>
<td>3.9%</td>
<td>-11.8%</td>
</tr>
<tr>
<td>J&amp;J³</td>
<td>3.8%</td>
<td>+5.4%</td>
</tr>
<tr>
<td>BMS²</td>
<td>3.5%</td>
<td>+22.3%</td>
</tr>
</tbody>
</table>

Sources: GERS and Top Pharma – Smart Pharma Consulting analyses

1 Constant ex-factory prices, excluding taxes and rebates, with the exception of hospital sales for which rebated sales have been estimated including hospital sales of biosimilars, products invoiced in addition of the hospitalization charges (on top of T2A) and reassigned medicine sales – 
2 Including respectively, from left to right: Sandoz, Zentiva, Biogaran and UPSA (in a logic of group of companies) – 
3 Drugs sector only
2. The French pharmaceutical market

2.3. Future market trends

By 2022, the pharmaceutical market should be mainly driven by innovative hospital products, biosimilars and generics


<table>
<thead>
<tr>
<th>Year</th>
<th>Total Market</th>
<th>Hospital sales</th>
<th>Not reimbursed</th>
<th>Reimbursed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>€26.3 B¹</td>
<td>€5.4</td>
<td>€12.1</td>
<td>€8.8</td>
</tr>
<tr>
<td>2016</td>
<td>€27.4</td>
<td>€7.4</td>
<td>€11.9</td>
<td>€8.1</td>
</tr>
<tr>
<td>2022</td>
<td>€28.3</td>
<td>€7.8</td>
<td>€11.6</td>
<td>€8.9</td>
</tr>
</tbody>
</table>

**Retail sales**
- 2012: €20.9
- 2016: €20.0
- 2022: €20.5

**CAGR**
- 2012-2016: +1.0%
- 2016-2022: +0.5%

Sources: GERS and Top GERS data – Smart Pharma Consulting analyses

¹ Constant ex-factory prices – ² Estimated rebated sales including hospital sales of biosimilars, products invoiced in addition of the hospitalization charges (on top of T2A) and reassigned medicine sales – ³ Reimbursable generics and quasi-generics – ⁴ Sales of medicines whose patents have not expired and of other specific products (calcium, sodium, potassium, paracetamol, etc.) – ⁵ Compound Annual Growth Rate

* Hospital rebates are estimated to -30% of total hospital sales
Pharmaceutical companies’ strategic priorities by 2022 will be linked with the behavior of the “7 Ps” stakeholders

The 7 Ps

- Policy makers
- Pharma competitors
- Physicians
- Pharmacists
- Patients & PAGs
- Payers
- Payers

Sources: Smart Pharma Consulting analyses

* Patients Advocacy Groups
Policy makers & Payers will work jointly to secure the sustainability of the healthcare system, implying its redesign and the introduction of new measures and new taxes

### Stakeholder behavioral trends: Policy makers & Payers (1/4)

<table>
<thead>
<tr>
<th>2016 – 2022 Trends</th>
<th>Driving factors</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global cost optimization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Research of new funding mechanisms to ensure a better sustainability of the healthcare system</td>
<td>- Ageing of population associated to low economic growth leading to larger deficits over the 2017-2022 period, and beyond</td>
<td>- Increase of the CSG and the possibility to introduce new taxes to reduce dependency on social contributions and thus, on the employment</td>
</tr>
</tbody>
</table>
| - Reorganization of the healthcare system to improve its efficacy and efficiency | - ~2/3 of the National Health Insurance Fund revenues generated by social contributions (linked to national economy and employment) | - Redesign of the healthcare system:
  - Shift from hospital to home care
  - Improve hospital / open care markets coordination
  - Develop effective patient journeys |
| - Reduction / prevention of National Health Insurance Fund deficit | - French GDP is expected to grow by 1.6% p.a. until 2022 | - Introduction of measures and tools:
  - Tighter control of hospital costs
  - Increase price pressure on reimbursed drugs
  - Reinforcement of the ROSP\(^1\) contracts plan for physicians |
| - Capping of the mid to long term healthcare expenditure objective by the government at \(\leq +2.3\%\) p.a. on average by the end of 2022 | - National Health Insurance Fund cumulated deficit reaching a total of €70 B, over the 2007-2016 period | - Limit access to ALD\(^2\)
  - Budgeting control generalization |

**Sources:** Smart Pharma Consulting analyses

\(^1\) Bonus program to encourage physicians to comply with “best prescribing practices” for a better efficacy/cost ratio – \(^2\) 100% cost coverage for chronic and long lasting diseases
Pharma companies must position their products, services and themselves to be perceived by policy makers and payers as offering superior value than competition.

**Strategic priorities induced by Policy makers & Payers behavioral trends**

**Behavioral trends**

1. **Stricter control of reimbursed drug expenditure**
2. **Measures to boost generics & biosimilars**
3. **Shift from hospital to ambulatory care**
4. **Promotion of R&D investments in France**

**Strategic priorities for pharma companies**

- Enhance their global value proposition (incl. corporate identity, product and service offering) through:
  - Dedicated corporate reputation programs targeted at policy makers and government
  - Generation of RWD (Real Word Data) and ... high quality medico-economic studies (if relevant)
  - Initiation / support of specific projects to improve patient care

- Participate to working groups with health authorities and other stakeholders to:
  - Facilitate the change management
  - Ensure this change will have a positive, or at least a neutral effect, on pharma company performance

- Increase or maintain R&D activities in France to be in a more favorable position vis-à-vis health authorities to get reimbursement and to negotiate price of drugs

*Sources: Smart Pharma Consulting analyses*
Smart Pharma Consulting Editions

- Besides our consulting activities which take 85% of our time, we are engaged in sharing our knowledge and thoughts through our:
  - Teaching and training activities
  - Publication of articles, booklets, books and business reports

- Since 2012, we have published **15 business reports** covering the following topics:
  - Market access and drug valuation (2016)
  - Global biosimilars drugs market (2015, 2012)
  - Best pharma performers (2015)
  - French pharma distribution (2015, 2012)
  - Digital marketing (2012)
  - French OTC market (2012)

- We expect that this new publication will be helpful

  Best regards,

  Jean-Michel Peny

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- Our business reports have in common to:
  - Be well-documented with recent facts and figures
  - Highlight the key points to better understand situations
  - Propose in-depth analyses
  - Determine the business implications for stakeholders

The French Pharma Market 2016 – 2022 Prospects

- This report has been conceived as a working tool to:
  - Strengthen and align the level of knowledge and understanding of the French pharma market and its key trends by the executives of French affiliates
  - Facilitate the communication, with correspondents of affiliates at the European and/or Global headquarters, regarding the specificities and major trends in France
  - Support the strategic decisions over the 5 coming years

- The purchase of this report includes:
  - A two-hour working session to address one or more specific points covered in this report
  - A free access to all collaborators of the pharma group