Analysis of the Global TB Drug Market and Country-Specific Case Studies of TB Drug Distribution Channels

France Case Study

Prepared with IMS Consulting  November 2006
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- Procurement and Distribution of TB Drugs
- Value and Volume of the French TB Market
- Appendix
In France, the TB notification rates fell steadily for 20 years

**Notification**
- Between 1972 and 1988 the number of notified cases of TB in France fell by 71%, more recently cases have begun to level off
- In total 6,242 cases were reported in mainland France in 2004

**Detection**
- Physicians are required to notify the Department of Health and Social Affairs (DDASS) of all suspected cases of TB
- Despite this obligatory declaration it is estimated that only 50% of cases are reported due to physicians failing to notify the DDASS

Source: Superior Council for Public Hygiene Guidelines; Bulletin Epidemiologique Hebdomadaire
Prevalence of TB is highest in Paris and, in particular, amongst immigrant populations

**Epidemiology**

- A majority of cases of TB in France are seen in immigrants
- Prevalence in highest in Paris as a result of the large concentration of high risk groups (i.e. PLWHA and immigrants from endemic countries) and high levels of poverty
There are three major bodies involved in TB care at a national level

1. Directions Départementales des Affaires Sanitaires et Sociales (DDASS)
   - Sub-department of the Department of Health and Social Affairs
   - Responsible for surveillance and monitoring

2. Statutory health insurers
   - Receive funding from the treasury
   - Responsible for distributing funding to healthcare providers

3. Superior Council for Public Hygiene
   - Independent body consulted by the Minister of Health
   - Responsible for development of treatment guidelines

Source: Superior Council for Public Hygiene Guidelines, PQ Systems, Interviews, DH Website
Directions Départementales des Affaires Sanitaires et Sociales (DDASS) is a national body responsible for TB surveillance and monitoring and acts as the de facto national TB program.

**Physicians** are required by law to report all cases of TB to the DDASS.

- The DDASS then traces and screens all contacts of TB patient and records epidemiological data about the patients.
- This data is passed to the Institut de Veille Sanitaire (InVS) for collation.
- Data on treatment outcomes are not routinely reported, but default rates are estimated at 22%.
- Data on HIV infection among TB cases is not routinely reported.

*Source: Department of Health and Social Affairs, interviews*
Statutory health insurers set budgets for all public and semi-private sector GPs and hospitals for all diseases

**Flow of funding**

- **Treasury**
  - Money is collected from taxpayers by the treasury
  - The Agence Centrale des Organismes de Securite Sociale (ACOSS) is responsible for distributing funding to the health insurers

- **Statutory health insurers**
  - Distribute funding to the hospitals and GPs in both the public and semi-private sector

- **Healthcare providers**
  - Responsible for providing care to patients
  - Receive block funding from the health insurers which they are able to spend without restriction by the insurers
  - Size of patient contributions depend on whether the facility is public or semi-private

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Source: PQ Systems
The Superior Council for Public Hygiene makes clinical recommendations, one of which is the use of BCG vaccination in all children under the age of six.

**Age Group**
- **Children under 6 years old**
  - **Recommendation:** Vaccination is obligatory. Administered at birth to children at medium to high risk and before starting school for all others.

- **Children over 6 years old**
  - **Recommendation:** Vaccination is obligatory. Administered when first entering an educational establishment.

- **Adults**
  - **Recommendation:** Vaccination on a case-by-case basis. Strongly recommended to people in certain occupations, certain ethnic communities and people exposed to infected persons.

Source: Superior Council for Public Hygiene Guidelines
The Superior Council for Public Hygiene recommends a four drug regimen for active TB patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
<th>Initial Phase</th>
<th>Continuation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>New patient</td>
<td>Smear positive patient not having previously received care</td>
<td>2HRZE</td>
<td>4HR</td>
</tr>
<tr>
<td>Isoniazid resistance</td>
<td>Infected with TB resistant to isoniazid</td>
<td>2RZ</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3RE</td>
<td>-</td>
</tr>
<tr>
<td>MDR TB</td>
<td>Infected with TB resistant to two or more 1st line drugs</td>
<td>5 drugs the organism is susceptible to (at least 2 of which, preferably 3, should not have been used before) – until sputum negative</td>
<td>At least 3 drugs the organism is susceptible to for a further 9 months (up to 24 months)</td>
</tr>
<tr>
<td>Latent</td>
<td>Positive Mantoux test or interferon-gamma immunological test. No symptoms</td>
<td>6-12H</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3RH*</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4R</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2RZ</td>
<td>-</td>
</tr>
</tbody>
</table>

*The most common approach to treating latent TB in France

As there are not explicit guidelines for the treatment of MDR TB specialists treating a patient with it are able to contact a specified member of the National Reference Laboratory for treatment advice at the beginning of treatment. Those requiring extra assistance are able to contact refer their patient for treatment by this person.
TB patients can be treated in government or non-government funded sectors, although most are treated in the government funded sector.

Most patients will receive all treatment in the government funded sector.
Patients can visit their GP, but most go directly to a hospital Accident and Emergency Department.

**Patient flow through initial diagnosis**

1. **Patient presents with TB symptoms**
   - General practitioner
   - Hospital/Accidents and emergencies
   - Hospital outpatient/Hospital specialist

A majority of patients (75%) will go directly to Accident and Emergency. It is cheaper than paying to see a GP. Those identified by Accident and Emergency as potentially having TB are sent straight to the hospital specialist for diagnosis and treatment.

After visiting their GP, patients are referred to hospital specialists for diagnosis and treatment – GPs play no further role in treatment.

2. **Initial diagnosis for TB through chest x-ray**
   - If confirmed patient referred to specialist for further diagnosis and treatment

Patient suspected of having TB after initial chest x-ray are referred to a hospital specialist for further diagnosis and treatment. Patients may be referred to a public or private hospital specialist.

Source: PQ Systems, Interviews
Specialists confirm the initial diagnosis, categorize and treat TB patients

*Patient flow through confirmation of diagnosis and treatment*

Specialists use sputum samples to confirm diagnosis and check for drug resistance. Samples are sent to a 'Centre National de Référence' Laboratory.

All patients are treated as inpatients until no longer contagious at which point they are discharged. Receive the rest of their treatment as outpatients.

Patients collect almost all of their drugs from retail pharmacies. Due to French cost saving initiatives only more specialized drugs are dispensed by outpatient pharmacies (e.g. streptomycin).

Source: Superior Council for Public Hygiene Guidelines, Interviews
TB treatment and drugs have a special listing under the French healthcare system and so are completely free of charge to patients.

*Charges for TB drugs in each healthcare setting*

- **Public hospital**
  - Inpatient: Drugs dispensed by hospital inpatient pharmacy
  - Outpatient: Drugs dispensed by hospital outpatient or retail pharmacy

- **Semi private hospital**
  - Inpatient: Drugs dispensed by hospital inpatient pharmacy
  - Outpatient: Drugs dispensed by retail pharmacy

TB is classified as an Affection de Longue Duree (ALD) and so exempt from all consultation fees, hospital charges and drug co-pays irrespective of sector. All treatment and drugs are always 100% covered by social security and free of charge.

*Source: PQ Systems, interviews*
Social security also funds the treatment of TB for immigrants living in France

**Immigrant entitlement to healthcare within the government funded sector**

<table>
<thead>
<tr>
<th>Status</th>
<th>GPs</th>
<th>Hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immigrants who have lived in France for &lt;3 months</td>
<td>100% healthcare coverage “for urgent treatments whose absence could lead to death or a serious deterioration in health of that person or their unborn child”</td>
<td></td>
</tr>
<tr>
<td>Asylum seekers</td>
<td></td>
<td>Covered by AME (Aide médicale de l’Etat) and so patients are entitled to receive treatments covered by the CMU (Couverture Maladie Universelle) free of charge</td>
</tr>
<tr>
<td>Immigrants who have lived in France for &gt;3 months earning less than €597.16 per month</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- CMU is a statutory health insurance provided to people who do not qualify for any other statutory insurance
- As they are covered by CMU, immigrants are entitled to free access to the French healthcare system as they do not have complementary insurance they must usually pay co-pays
- However, as TB is an *Affection de Longue Durée* there are no co-pays associated with it and so immigrants receive treatment for TB free of charge

Source: www.cyes.info
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In the France, TB drug procurement mechanisms vary according to the setting in which drugs are dispensed.

**Procurement mechanisms**

- **Hospital buying groups**
  - Public hospitals located within cities with buying groups
  - Semi-private hospitals
  - Retail pharmacy

- **Direct negotiations**
  - Public hospitals not located within cities with buying groups

*NB: GPs do not treat TB patients and so are not included here*

Source: PQ Systems, Interviews
A number of public hospitals within the large cities have formed buying groups which procure drugs on their behalf.

**Procurement mechanisms**

- **Hospital buying group**
- **Direct negotiations**

**Public Hospitals**

- Public hospitals within the cities of Paris, Lyon and Marseilles operate buying groups, which negotiate directly with manufacturers on behalf of all group members.

- These groups must use a bid and tender system for all purchases of £100,000 or more (mandatory under EU law for public hospitals).

*Source: PQ Systems, interviews*
Procurement and Distribution of TB Drugs

These drugs are distributed by manufacturers to a centralized group warehouse from which each hospital pharmacy sources its drugs.

**Drug Flow: Public Hospitals (buying group)**

1st point of sale: Manufacturers holding the contract with the buying group supply drugs direct to a centralized warehouse at the agreed price.

2nd point of sale: Drugs are purchased by the buying group and held in the warehouse until required by a hospital within the group. The hospital receiving the drugs issues a payment to the buying group.

Hospital sale: Hospitals distribute drugs to the patient. The patient, or their complementary insurer, will pay a certain level of co-pay and the remainder is paid by social security.

Source: PQ Systems, interviews
All other public and semi-private hospitals must negotiate directly with suppliers to procure drugs.

**Procurement mechanisms**

- Hospital buying group
- Direct negotiations

**Public and Semi-Private Sector Hospitals**

- Public hospitals that do not belong to buying groups and semi-private hospitals negotiate individually with manufacturers.

- Must also operate a bid and tender system for all purchases of £100,000 or more (mandatory under EU law).

Source: PQ Systems, interviews
Suppliers then distribute drugs **directly** to the hospital pharmacies

**Drug Flow: Public (non-purchasing group)/Semi-private Hospitals**

1st point of sale: Manufacturers holding the contract supply drugs at the agreed price direct to hospitals or, if they lack a distribution network, via a wholesaler.

Hospital sale: Hospitals then distribute drugs to the patient. The patient, or their complementary insurer, will pay a certain level of co-pay and the remainder is paid by social security.

*Source: PQ Systems, interviews*
Retail pharmacies are not entitled to form chains and so negotiate individually

**Procurement mechanisms**

- **Hospital buying group**
- **Direct negotiations**

**Retail Pharmacies**

- Retail pharmacies are not permitted to form pharmacy chains in France
- Instead, each pharmacy individually negotiates prices with wholesalers or manufacturers (in rare cases)
  - Suppliers may only offer authorised margins and discounts to pharmacists, in turn, pharmacists are only permitted to use specified mark-ups, thus profitability is limited

Source: PQ Systems, interviews
Wholesalers and manufacturers then distribute drugs directly to the purchasing retail pharmacy

**1st point of sale:** Manufacturers supply drugs to wholesalers or direct to the purchasing pharmacies

**2nd point of sale:** Wholesalers sell drugs to pharmacies. Margins are limited for most generic (covers most TB drugs) and all branded products to roughly 10% of ex-manufacturers price

**Pharmacy sale:** Drugs are always reimbursed at the list price so the larger the discount the pharmacist can obtain the greater the profit

Source: PQ Systems, interviews
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The 1st line TB drug market has been relatively stable over the past five years and is currently valued at 3.6M USD

Note: Includes 1st line drugs that may be used in the 2nd line treatment

*Fluctuations were interpreted around limitations of IMS data base around percent sales of use for TB
The volume of the 1\textsuperscript{st} line market has also been stable—9.2M units were dispensed in 2005.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Value and Volume of the French TB Market}
\end{figure}

Note: Includes 1\textsuperscript{st} line drugs that may be used in the 2\textsuperscript{nd} line treatment. Volume refers to the number of units (e.g. tablets) dispensed.

Source: IMS MIDAS data
FDCs currently account for 50% (1.8M USD) of the French market value and 39% (3.6M units) of the volume.

**Total 1st Line TB Market Value by Formulation in 2005 (3.6M USD)**

- Fixed Dose Combinations: 50%
- Loose Drugs: 50%

**Total 1st Line TB Market Volume by Formulation in 2005 (9.2M USD)**

- Fixed Dose Combinations: 39%
- Loose Drug: 61%

*Note: Includes 1st line drugs that may be used in the 2nd line treatment.*

*Volume refers to the number of units (e.g. tablets) dispensed.*

*Source: IMS MIDAS data*
Bottoms up estimates confirm the top line value data and give a 1st line market estimate of between 3.2-3.6M USD

<table>
<thead>
<tr>
<th></th>
<th>Active</th>
<th>Resistant</th>
<th>Latent</th>
<th>Retreated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total patients</td>
<td>5,252</td>
<td>236</td>
<td>452</td>
<td>276</td>
</tr>
<tr>
<td>Patients per category*</td>
<td>270.92</td>
<td>349.05</td>
<td>69.27</td>
<td>270.92</td>
</tr>
<tr>
<td><strong>Total cost per category</strong></td>
<td>1,422,862</td>
<td>82,375</td>
<td>31,310</td>
<td>74,774</td>
</tr>
<tr>
<td><strong>1st line estimate</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st line estimate</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>1st line adjusted estimate</strong></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**A number of studies have suggested that only 50% of cases are reported in France – hence we can increase the estimate by a factor of 2

Note: Does not 1st line drugs that may also be used in the 2nd line treatment

Source: EuroTB, IMS MIDAS data, IMS analysis, BNF. See appendix for details of calculation
Value and Volume of the French TB Market

The market value of all 2\textsuperscript{nd} line TB drugs is growing overall and is currently valued at 4M USD.

Source: IMS MIDAS data

\textit{Note: Includes 1\textsuperscript{st} line drugs that may be used in the 2\textsuperscript{nd} line treatment}

*Data was not available for all 2\textsuperscript{nd} line drugs used in this country. Drugs listed do not comprise full 2\textsuperscript{nd} line treatment regimen in this country.
Other than a steep increase in 2004, the volume of 2nd line TB drugs dispensed has remained stable and currently stands at 1.9M units.

Source: IMS MIDAS data

Note: Includes 1st line drugs that may be used in the 2nd line treatment

Volume refers to the number of units (e.g. tablets) dispensed

*Data was not available for all 2nd line drugs used in this country. Drugs listed do not comprise full 2nd line treatment regimen in this country.
Ciprofloxacin dominates the 2nd line market value with sales of 1.8M USD, whereas clavulanic acid has the greatest volume of sales with 1.2M units in 2005.

**Total 2nd Line TB Market Value by Drug in 2005 (4M USD)**

- Ciprofloxacin: 43%
- Moxifloxacin: 7%
- Ofloxacin: 21%
- Clarithromycin: 5%
- Clavulanic acid: 24%

**Total 2nd Line TB Market Volume by Drug in 2005 (1.8M units)**

- Clavulanic acid: 66%
- Ofloxacin: 10%
- Clarithromycin: 6%
- Ciprofloxacin: 14%
- Levofoxacin: 0%

*Source: IMS MIDAS data*

*Data was not available for all 2nd line drugs used in this country. Drugs listed do not comprise full 2nd line treatment regimen in this country.*
Top line value figures and bottom up calculations suggest the 2nd line market value is 0.8M to 4M USD

<table>
<thead>
<tr>
<th></th>
<th>Diagnosed in 2003</th>
<th>Diagnosed in 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patients receiving treatment in 2004</strong></td>
<td></td>
<td>51</td>
</tr>
<tr>
<td><strong>Patients per category</strong>*</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td><strong>Average cost of treatment</strong></td>
<td>5635</td>
<td>9049</td>
</tr>
<tr>
<td><strong>2nd line estimate</strong></td>
<td></td>
<td>376,131</td>
</tr>
<tr>
<td><strong>Adjusted 2nd line estimate</strong>**</td>
<td></td>
<td>752,263</td>
</tr>
</tbody>
</table>

Note: Does not include 1st line drugs that may also be used in the 2nd line treatment. **A number of studies have suggested that only 50% of cases are reported in France – hence we increase the estimate by a factor of 2

Source: EuroTB, IMS MIDAS data, IMS analysis, WHO, interviews. See appendix for details of calculation
However, it is impossible to perform an accurate bottom up calculation for 2\textsuperscript{nd} line drugs due to large numbers of uncertainties, hence, value is estimated to be 4M USD

- A bottom up calculation involves assumptions about which drugs are administered to 2\textsuperscript{nd} line patients, the dose at which they are given and the duration of treatment, all of which vary widely between patients

- Additionally, in 1\textsuperscript{st} line patients suffering from side effects the 1\textsuperscript{st} line drug responsible for those side effects is often substituted for a 2\textsuperscript{nd} line drug

- Physicians estimated the incidence of side effects to be between 5-30\%, however it is impossible to be certain how many 1\textsuperscript{st} line drugs are substituted in these cases and which 2\textsuperscript{nd} line drugs they are substituted for

- Hence, there are too many uncertainties for an accurate bottoms-up calculation and value is estimated to be $4M USD (based on IMS MIDAS figures)
If we combine the value and volume of 1\textsuperscript{st} and 2\textsuperscript{nd} line drugs we have a market value of 7.6M USD and volume of 11M units.
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### Total market value and volume figures for all 1st line drugs in 2005*

<table>
<thead>
<tr>
<th>1st line drug</th>
<th>Volume (units)</th>
<th>Value (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>599,613</td>
<td>395,006</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>4,250,000</td>
<td>1,313,542</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>794,490</td>
<td>99,189</td>
</tr>
<tr>
<td>Rifampicin/isoniazid combinations</td>
<td>1,555,396</td>
<td>1,032,207</td>
</tr>
<tr>
<td>Rifampicin/isoniazid/pyrazinamide</td>
<td>2,046,442</td>
<td>789,165</td>
</tr>
</tbody>
</table>

*Figures for ethambutol and isoniazid/ethambutol combinations were not available for 2005, thus data from earlier years were used.

Source: IMS MIDAS
## Total market value and volume figures for all 2\textsuperscript{nd} line drugs in 2005*

<table>
<thead>
<tr>
<th>2\textsuperscript{nd} line drug</th>
<th>Volume (units)</th>
<th>Value (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clavulanic acid</td>
<td>1,239,410</td>
<td>962,702</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>111,343</td>
<td>181,662</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>184,270</td>
<td>856,686</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>268,896</td>
<td>1,735,659</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>70,056</td>
<td>294,753</td>
</tr>
</tbody>
</table>

*Figures for levofloxacin were not available for 2005, thus data from earlier years were used.

Source: IMS MIDAS
## Manufacturers of 1st line drugs in France

<table>
<thead>
<tr>
<th>1st line drug</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>Sandoz; Sanofi Aventis</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Laphal</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Sanofi Aventis</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>GenoPharm; SERP; GSK</td>
</tr>
<tr>
<td>Rifampicin+Isoniazid</td>
<td>Sanofi Aventis</td>
</tr>
<tr>
<td>Rifampicin+Isoniazid+Pyrazinamide</td>
<td>Sanofi Aventis</td>
</tr>
</tbody>
</table>

Source: IMS MIDAS
## Manufacturers of 2nd line drugs in France

<table>
<thead>
<tr>
<th>2nd line drug</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin</td>
<td>Sanofi Aventis</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>Sanofi Aventis, Sandoz</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Sandoz</td>
</tr>
<tr>
<td>Clavulanic acid</td>
<td>Sandoz</td>
</tr>
</tbody>
</table>

Source: IMS MIDAS
Method of calculating cost of treating 1st line TB patients

- Patient numbers were sourced from the EuroTB website
- Cost of the regimen (for a 70kg patient) was calculated using prices of the most popular brand and pack size (by units sold) for each of the 1st line drugs
- Patient population was split into active, drug resistant, latent and retreated
- The size of each subpopulation of TB patients was then multiplied by the cost of the regimen they receive
- These figures were then summed to give a top-line value
- The low end estimate was derived by summing the lowest cost regimen to treat each of these subpopulations of patients
- The high end estimate was derived by summing the highest cost regimen to treat each of these subpopulations of patients
# Method of calculating cost of treating 1st line TB patients (USD)

<table>
<thead>
<tr>
<th></th>
<th>Active</th>
<th>Latent</th>
<th>Retreated</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>receiving treatment in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patients per category</strong></td>
<td>5,252</td>
<td>236</td>
<td>452</td>
<td>276</td>
</tr>
<tr>
<td><strong>Average cost of</strong></td>
<td>270.92</td>
<td>69.27</td>
<td>270.92</td>
<td>349.05</td>
</tr>
<tr>
<td>treatment</td>
<td></td>
<td></td>
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<tr>
<td><strong>First Line</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>estimate</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adjusted Second</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Line estimate*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

|                          |         |        |           |           |
| **Total patients**       |         |        |           |           |
| receiving treatment in   |         |        |           |           |
| 2004                     | 6,216   |        |           |           |

*Source: IMS MIDAS, IMS Expertise

*A number of studies have suggested that only 50% of cases are reported in France – hence we can increase the estimate by a factor of 2*
### Method of calculating cost of treating 2nd line TB patients

#### Hospital

<table>
<thead>
<tr>
<th>Drug</th>
<th>Price per day</th>
<th>Price for one year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cipro</td>
<td>3.65</td>
<td>1335.17</td>
</tr>
<tr>
<td>Ofx</td>
<td>4.04</td>
<td>1476.04</td>
</tr>
<tr>
<td>Moxi</td>
<td>3.26</td>
<td>1189.87</td>
</tr>
<tr>
<td>Clav</td>
<td>6.72</td>
<td>2453.89</td>
</tr>
<tr>
<td>Clarith</td>
<td>1.67</td>
<td>611.01</td>
</tr>
</tbody>
</table>

#### Retail

<table>
<thead>
<tr>
<th>Drug</th>
<th>Price per day</th>
<th>Price for one year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cipro</td>
<td>3.26</td>
<td>1189.90</td>
</tr>
<tr>
<td>Ofx</td>
<td>3.30</td>
<td>1205.11</td>
</tr>
<tr>
<td>Moxi</td>
<td>1.67</td>
<td>611.01</td>
</tr>
<tr>
<td>Clav</td>
<td>3.80</td>
<td>1387.00</td>
</tr>
<tr>
<td>Clarith</td>
<td>5.23</td>
<td>1909.41</td>
</tr>
</tbody>
</table>

#### Total cost of treatment

- **USD**: 14,683
- **Euros**: 11,466

- **Initial Phase**: 9049
- **Continuation Phase**: 5635

**Source**: IMS MIDAS, IMS Expertise
MIDAS data in France is collected in government funded hospitals and retail pharmacies

- MIDAS data in France is collected for government funded hospitals and retail pharmacies – drugs dispensed by private hospitals are not included
  - All prescriptions dispensed by pharmacies in public and semi-private hospitals and retail pharmacies are captured in the data
  - Hospital data includes prescriptions dispensed by both hospital inpatient and outpatient pharmacies

- The value data we have used is collected at an ex-manufacturer price and so represents the value of drug sales when sold by the manufacturer (not the value of sales to the end user)

- The volume data we have used collects units sold. The figure given covers the number of individual units sold. In most cases a unit is a single tablet. For injectables it is a single pre-filled syringe

Source: IMS MIDAS
PharmaQuery Systems is IMS’s unique online database of Pricing and Reimbursement regulations in 22 key world markets

- PQ Systems provides detailed coverage, on a country by country basis, of 22 key pharmaceutical markets
  - Argentina, Australia, Belgium, Brazil, Canada, Chile, China, Denmark, France, Germany, Hungary, Italy, Japan, Mexico, Netherlands, South Korea, Spain, Sweden, Switzerland, UK and the USA

- It contains detailed information about pricing and reimbursement regulations in each country
  - This information is divided into 4 areas; facts and figures, healthcare system, pharmaceutical market and useful information

- Information is updated daily by a network of multilingual pricing analysts
Manufacturers with new drugs are able to obtain market authorisation through one of three routes:

In order to obtain permission to sell a drug in France (marketing authorisation) the manufacturer may apply through one of three routes:

**Centralised procedure**
- The European Medicines Agency (EMEA) reviews applications and then is able to grant access throughout all EU member states

**National procedure**
- AFFSAPS is responsible for granting marketing authorisation for drugs in France only
- This would result in access also being granted in all EU member states via mutual recognition

**Mutual recognition procedure**
- Certain countries within the EU have an agreement in which when a drug is authorised through one of their national schemes it is automatically approved in all EU member states

Once access is granted the manufacturer is immediately free to market their drug in France.

Source: PQ Systems
Following marketing authorisation, products are assessed for clinical value by the Transparency Commission (CT)

CT issues an ASMR rating...

... that corresponds to a reimbursement recommendation

In addition, CT decides whether to issue a hospital authorisation

- The CT also grants Agrément aux Collectivités Publiques (hospital supply authorizations)
- Obtaining this entitles manufacturers to market their drugs to hospitals

### ASMR RATING CRITERIA

1. Major therapeutic advance
2. Important improvement
3. Moderate improvement
4. Minor improvements
5. No improvement, but may be reimbursed
6. No improvement, should not be reimbursed

### BENEFIT

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td>65% 35%</td>
</tr>
<tr>
<td>Moderate</td>
<td>35% 35%</td>
</tr>
<tr>
<td>Modest but reimbursed</td>
<td>35% 35%</td>
</tr>
<tr>
<td>Insufficient</td>
<td>0% 0%</td>
</tr>
<tr>
<td>Hospital products</td>
<td>100% 100%</td>
</tr>
<tr>
<td>Affections de longue durée</td>
<td>100% 100%</td>
</tr>
</tbody>
</table>

### CLINICAL VALUE ADDED

<table>
<thead>
<tr>
<th>Affections de longue durée</th>
<th>Serious</th>
<th>Not</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

Source: PQ Systems
Finally the actual price and level of reimbursement are determined by CEPs and UNCAM

**TRANSPARENCY COMMISSION (CT)**

**COMITE ECONOMIQUE DES PRODUITS DE SANTE (CEPS)**
- A *rapporteur* (external expert) cites the price decided by the manufacturer and the arguments developed to support this proposition
- CEPS compares the price to price in other countries’ prices
- If CEPS is not happy with the price then it uses price volume agreements to limit the sales in France
- Manufacturers exceeding the agreed sales are forced to pay back part of their profits

**UNION NATIONALE DES CASSIES D’ASSURANCE MALADIE (UNCAM)**
- UNCAM use the CT’s advice, in particular the SMR rating, to determine the exact rate of reimbursement
- UNCAM is free to place the reimbursement rate anywhere within the range defined by the SMR however to date they have only used 35% or 65%
- The reimbursement rate is published in the *Journal Officiel*

*Source: PQ Systems*