TENDERS AND PROCUREMENT OF COAGULATION FACTOR CONCENTRATES: A EUROPEAN SURVEY OF 38 COUNTRIES

Clinical involvement in alternative processes

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## Disclosures

<table>
<thead>
<tr>
<th>Category</th>
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<tr>
<td>Shareholder</td>
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<tr>
<td>Grant / Research Support</td>
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<td>Employee</td>
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<tr>
<td>Paid Instructor</td>
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<td>Speaker bureau</td>
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HAEMOPHILIA IN BELGIUM

- Haemophilia A 800*
- Haemophilia B 200*
- Medical doctors 40,000

Population: 10,600,000 inhabitants
FVIII annual consumption: 80 Millions units/year

* Association des Hémophiles AH-VH.
## Cost of Clotting Factor Concentrates to Treat Patients with Haemophilia in Belgium

<table>
<thead>
<tr>
<th>Therapeutic agent</th>
<th>Cost in € 2002</th>
<th>Cost in € 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII</td>
<td>27,839,925</td>
<td>61,670,978</td>
</tr>
<tr>
<td>Factor IX</td>
<td>2,139,053</td>
<td>5,883,035</td>
</tr>
<tr>
<td>Novoseven</td>
<td>3,054,971</td>
<td>2,583,762</td>
</tr>
<tr>
<td>FEIBA</td>
<td>150,084</td>
<td>570,127</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>33,184,033 €</strong></td>
<td><strong>70,707,902 €</strong></td>
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</table>
Estimated lifetime cost of haemophilia in Belgium

Total costs: €97.3 million (for 14 new cases)
€7.8 million/incident case

94.3%
5.7%

Direct costs (€91.8 million)
- > 4/5 Treatment
- 7% Hospitalisations

Indirect costs (€5.6 million)
- 2/3 Transport
- 1/3 Absence from work

## Cost of concentrates available in Belgium

<table>
<thead>
<tr>
<th>Concentrate (FVIII-VWF)</th>
<th>Name</th>
<th>Dosing</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVIII</td>
<td>Advate (Baxter)</td>
<td>250-500-1000-1500 units</td>
<td>253-1481 euros</td>
</tr>
<tr>
<td></td>
<td>Kogenate (Bayer)</td>
<td>250-500-1000 units</td>
<td>258-987 euros</td>
</tr>
<tr>
<td></td>
<td>Refacto (Pfizer)</td>
<td>250-500-1000-2000 units</td>
<td>212-1631 euros</td>
</tr>
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<td></td>
<td>Factane (CAF-DCF)</td>
<td>1000 units</td>
<td>894 euros</td>
</tr>
<tr>
<td></td>
<td>Octanate (Octapharma)</td>
<td>250-500-1000 units</td>
<td>223-867 euros</td>
</tr>
<tr>
<td>FIX</td>
<td>Benefix (Pfizer)</td>
<td>500-1000-2000 units</td>
<td>387-1521 euros</td>
</tr>
<tr>
<td></td>
<td>Nonafact (CAF-DCF)</td>
<td>500-1000 units</td>
<td>273-537 euros</td>
</tr>
<tr>
<td></td>
<td>Octanine (Octapharma)</td>
<td>500-1000 units</td>
<td>249-489 euros</td>
</tr>
<tr>
<td>FVIII-VWF</td>
<td>Wilate (octapharma)</td>
<td>450-900 units (FVIII)</td>
<td>420-832 euros</td>
</tr>
<tr>
<td></td>
<td>Haemate-P (ZLB)</td>
<td>500-1000 units (FVIII)</td>
<td>273-537 euros</td>
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<tr>
<td>VWF</td>
<td>Wilfactin (LFB)</td>
<td>1000 units (VWF)</td>
<td>894 euros</td>
</tr>
<tr>
<td>FVIIa</td>
<td>NovoSeven</td>
<td>50-100-250 x 103</td>
<td>592-2967 euros</td>
</tr>
<tr>
<td>FII,VII,IX,Xa</td>
<td>FEIBA (Baxter)</td>
<td>250-500-1000 units</td>
<td>792 euros</td>
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</table>
The 10 European Principles of Hemophilia Care

1. A central hemophilia organisation with supporting local groups
2. National hemophilia patient registries
3. Comprehensive care centres and hemophilia treatment centres
4. Partnership in the delivery of hemophilia care
5. Safe and effective concentrates at optimum treatment levels
6. Home treatment and delivery
7. Prophylaxis treatment
8. Specialist services and emergency care
9. Management of inhibitors
10. Education and research
### Summary of adherence to Principles 1, 2 and 3 and 7 according to country

<table>
<thead>
<tr>
<th>Country</th>
<th>No of Centres</th>
<th>Principle 1 Central Organisation</th>
<th>Principle 2 Patient Registry</th>
<th>Principle 3 All patients treated in CCC/HTC</th>
<th>No of CCC/HTC per Million inhabitants</th>
<th>Principle 7 % of Children on prophylaxis</th>
<th>Principle 7 % of Adults on prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>1</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>0.83</td>
<td>75-100</td>
<td>50-75</td>
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<tr>
<td>France</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>0.71</td>
<td>75-100</td>
<td>1-25</td>
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<tr>
<td>Germany</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>0.89</td>
<td>75-100</td>
<td>50-75</td>
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<td>Greece</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>0.37</td>
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<td>Italy</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>0.81</td>
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<td>Netherlands</td>
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<td>No</td>
<td>Yes</td>
<td>0.78</td>
<td>75-100</td>
<td>50-75</td>
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<tr>
<td>Norway</td>
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<td>Yes</td>
<td>No</td>
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<td>0.40</td>
<td>75-100</td>
<td>50-75</td>
</tr>
<tr>
<td>Poland</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>0.84</td>
<td>75-100</td>
<td>1-25</td>
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<tr>
<td>Portugal</td>
<td>1</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3.77</td>
<td>75-100</td>
<td>1-25</td>
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<td>Slovakia</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>7.78</td>
<td>75-100</td>
<td>1-25</td>
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<tr>
<td>Spain</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>0.91</td>
<td>75-100</td>
<td>1-25</td>
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<tr>
<td>Sweden</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>0.32</td>
<td>75-100</td>
<td>75-100</td>
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<tr>
<td>Switzerland</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>1.27</td>
<td>75-100</td>
<td>1-25</td>
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<tr>
<td>United Kingdom</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1.06</td>
<td>75-100</td>
<td>50-75</td>
</tr>
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</table>

**Total 21** 79% Yes 57% Yes 64% Yes  Median 0.84  IQR 0.62-1.11
KEY STAKEHOLDER INTERACTIONS ON PRICING, MARKET ACCESS AND PRESCRIBING

Ministry of Economic Affairs
Ministère des Affaires Économiques (MAE)

Price Department
Service des Prix

Medicines Pricing Commission
Commission des Prix des Spécialités Pharmaceutiques (CPSP)

Federal government
Minister of Social Affairs and Public Health

Federal Public Service for Social Security

Federal Agency for Medicines and Health Products (AFMPS)

Belgian Health Knowledge Centre, KCE
Centre Fédéral d’expertise des soins de santé

National Office for Social Security
Office National de la Sécurité Sociale, ONSS

Sickness Funds

Belgian Haemophilia Society

National Office for Sickness and Invalidity Insurance
Institut National d’Assurance Maladie-Invalidité, INAMI

Medicines Reimbursement Commission
Commission de Remboursement des Médicaments (CRM)

National Office for Social Security
Office National de la Sécurité Sociale, ONSS

Hospital sector

HTCs
May negotiate price directly with manufacturer

Regional/local

Communities and regions

Regions only provide subsidies for preventative medicine (i.e. HPV vaccines, breast exams)

Funding bodies

Influencers for reimbursement decisions

Bodies to increase buying power

Influencers for usage/purchase

Other body

Influence

HTC, Haemophilia Treatment Centre

Key stakeholders
# Reimbursement of Medicines in Belgium

## Federal Government

<table>
<thead>
<tr>
<th></th>
<th>Minister of Public Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketing authorization</td>
<td></td>
</tr>
<tr>
<td>Price setting</td>
<td>Minister of Economy</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>Minister of Social affairs</td>
</tr>
</tbody>
</table>
COMMISSION OF MEDICINES
REIMBURSEMENT

30 members

• 22 voting members:
  7 academics
  8 insurers
  4 physicians association
  3 pharmacists association

• 8 non voting members:
  4 representative Minister (Social affairs, Budget, Economy and Public Health)
  1 INAMI / RIZIV
  3 industry
PRINCIPLES - CRITERIA FOR EVALUATION AND ASSESSMENT

1. THERAPEUTIC VALUE – ADDED VALUE
   = efficacy + safety + effectiveness + applicability + convenience
   as determined by
   MORBIDITY – MORTALITY – QUALITY OF LIFE
   class 1 added value
   class 2 comparable value
   class 3 generics copies

1. PRICE and LEVEL OF REIMBURSEMENT

2. IMPORTANCE IN CLINICAL PRACTICE (social and/or therapeutic needs)

3. BUDGETARY IMPACT

4. ratio COST / THERAPEUTIC VALUE
**PRICE AND LEVEL OF REIMBURSEMENT**

**Public Price** = Ex Factory Price + Margin Wholesale + Margin Pharmacist + (margin finance) + Tax

Margin Wholesale = 13,1% of (Ex Factory price + margin wholesale) = « ceiling » (maximum) at 2,18 €

Margin Pharmacist = 31% of (Ex Factory price + margin wholesale + Margin pharmacist) = « ceiling » (maximum) at 7,44 €

Margin finance = « extra » (pre-financing) margin for pharmacist and wholesale for « expensive drugs »
= 3% of Ex Factory price minus 0,4314 € (if the ex factory price is higher then 29,35 €)
= 3,38% of Ex Factory price minus 0,48604 € (if the ex factory price is higher then 53,36 €)

Tax = 6% on (Ex Factory price + Margin Wholesale + Margin Pharmacist + margin finance)
## European Strategies to Optimise Haemophilia Funding

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Country</th>
<th>Principle</th>
<th>Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Tenders for Coagulation Factors</td>
<td>UK, Ireland</td>
<td>Create competition between concentrates</td>
<td>Ensure safe reliable supply of FVIII</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Involvement of all partners in a rigorous decision-making process: patients, doctors, health authorities,…</td>
<td>Manage usage of clotting factors (consumption per centre)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reduce product prices by leveraging economies of scale</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Impact on physicians and patients depends upon the aim and methods of the tender</td>
</tr>
<tr>
<td>Haemophilia Budget Capitation</td>
<td>Germany</td>
<td>Fixed reimbursement per patient e.g., tariff of €60,000 per patient per year</td>
<td>Reduction of costs</td>
</tr>
<tr>
<td>Centralisation of Haemophilia Care</td>
<td>UK, Spain</td>
<td>Limited number of specialised centres (2–3 per country)</td>
<td>Better control of FVIII consumption / use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Care provided exclusively in these centres</td>
<td>Tender business to reduce cost of concentrates</td>
</tr>
<tr>
<td>Health Technology Assessment</td>
<td>Sweden</td>
<td>To assess the clinical and cost effectiveness of pharmaceutical products</td>
<td>To decide which products will be reimbursed by society</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Will the Swedish HTA set the precedent for future reviews across Europe?</td>
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BELGIAN MEDICAL SURREALISM
The ambiguity and paradox of haemophilia care in Belgium

- Availability of plasma-derived and recombinant FVIII or FIX concentrates
  - No prescription restriction
  - No limitations of use of concentrates
  - Home treatment and prophylaxis widely available
  - Cost per FVIII unit: 0.7-0.9 Euro

- Process of setting official treatment centres just initiated
- Limited funding for haemophilia care (excluding replacement)
- No national registry
- No formal national certification
- No auditing
More on Haemophilia care in Belgium

- F8 and F9 concentrates can be prescribed by GPs

- Patients can select the hospital of their choice, even if not hosting an HTC

- Immunotolerance can be initiated in hospitals with no HCCC

- Vague definition of haemophilia specialists
Negative aspects of haemophilia funding in Belgium

- Public price of F8 is high - close to 0.8-0.9 euros/FVIII unit
- 90 % of haemophilia funding for replacement therapy
- No initiative (that I know) to reduce the price
- Limited funding for haemophilia centers (1500 euros expected per severe patient)
- No national registry and no comprehensive view of concentrates prescription and use
- No reliable tracing of concentrates use
- Prescribing policy heterogenous and not driven by economical constraints
Haemophilia Multidisciplinary Team

- Adult haemophilia specialist
- Paediatric haemophilia specialist
- Haemostasis laboratory
- Physiotherapist
- Liver diseases specialist
- Infectious diseases specialist
- Orthopaedic surgeons
- Geneticist
- Psychologist
- Social worker
- Clinical research unit
- Patients association (AHVH / WFH)
- Pharmacy
- Pharmaceutical companies
Rebalancing cost of haemophilia care

Cost of replacement therapy

Other costs

Today

Cost of replacement therapy

Other costs

Investments

Tomorrow
How to invest in a more sustainable haemophilia care beyond replacement therapy

• National interactive registry
• Traceability of concentrates
• Standardised clinical follow-up
• Standardised outcome collection

• Patients education to new concepts - modalities of haemophilia care (PK, individualised therapy, optimised replacement according to lifestyle, recognition of bleeds)

• Management, care and prevention of co-morbidities
• Treatment of all HCV+ patients with new treatments

• Promotion of social and professional insertion
• Psychological follow-up,…
• …
Rebalancing cost of haemophilia care

- Cost of replacement therapy
- Other costs

- Cost of replacement therapy
  - Other costs
  - Investments
  - Extra-funding
Concluding remarks

• Access and reimbursement of concentrates are critical for haemophilia care

• Cost of concentrates should not impact negatively on the multidisciplinary and complex care of haemophilia and implementation of new treatment options

• Validity of current cost estimate of replacement therapy should be revisited (cost per unit versus cost of annual-treatment)

• Financing of haemophilia should be cost-effectively rebalanced between replacement therapy and global care

• Global modalities of haemophilia funding should ideally be discussed and agreed between all stakeholders, including treaters, patients’ association.