Desmopressin on the WHO Essential Medicines List

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Background

• The concept of essential medicines was pioneered by the World Health Organization (WHO) in 1977 with the introduction of the first essential medicines list (EML).

• Revised every 2 years since then.
THE WHO ESSENTIAL MEDICINES LIST

- In 1977, the WHO EML had 204 molecules.
- The 2013 list included 374 unique molecules. (431 molecules with duplications across indications including both core and complimentary medicines.)
- More than 130 countries have used the list to develop national EMLs.
Core and Complimentary medicines

- Core medicines are defined as efficacious, safe, and cost-effective medicines for priority conditions (based on current and future public-health relevance and potential for safe and effective treatment).
Core and Complimentary medicines

• The complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. In case of doubt, medicines may also be listed as complementary on the basis of consistent higher costs or less attractive cost-effectiveness in a variety of settings.
Changes to the process

• Before 1999, an experience-based approach was used for addition or deletion of molecules from the WHO EML.

• In 1999, the Expert Committee recommended moving from an experience-based approach to one that was evidence-based and modifications to the methodology were developed.
Changes to the process

• Since 2002, an evidence-based approach was adopted, including evidence for public-health relevance, efficacy, and cost-effectiveness.

• The guidelines are now prepared with input from different stakeholders present in the expert committee.
“...the public health relevance and/or efficacy and/or safety of this item has been questioned and its continued inclusion on the list will be reviewed at the next meeting of the Expert Committee. (rare disease)"
2003 – WFH response

A rare disease is defined by the following characteristics:

- Small numbers of affected persons
- Therefore not a public health problem
- Little is known about the disease
- Difficulty with diagnosis
- No effective treatment
- Expertise for treatment not available.
2003 – WFH response

Definition of a Rare Disease

In the case of hemophilia, although the first two characteristics do apply, the rest do not. Much is known about hemophilia, it is readily diagnosed, there is effective treatment and the availability of expertise is expanding. What rationale is there for excluding hemophilia?
2003 – WFH response

• Safety and efficacy of clotting factor concentrates versus alternatives – plasma, fresh frozen plasma, cryo

• Association with a healthy blood transfusion system
2005 – Factors VIII and IX retained on EML

• At the same meeting in 2005, the Expert Committee suggested that there was a need for WHO to establish a policy advisory group on rare diseases to study this issue in light of its increasing importance.
Exogenously administered desmopressin, a synthetic derivative of the antidiuretic hormone L-arginine vasopressin, raises plasma levels of factor VIII and von Willebrand factor. The ability of intravenously administered DDAVP to treat selected patients with haemophilia A and von Willebrand disease was first described by Mannucci in 1977.
DDAVP use has also been reported to successfully prevent or treat bleeding in patients with other bleeding disorders, including mild platelet function defects and vascular abnormalities such as Ehlers-Danlos syndrome.
### Treatment of Hemophilia No. 11

**TABLE 3. Indications for desmopressin in the treatment of bleeding disorders**

<table>
<thead>
<tr>
<th></th>
<th>Grading of recommendation</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Established</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild hemophilia A</td>
<td>B</td>
<td>III</td>
</tr>
<tr>
<td>WWD (see Table 2)</td>
<td>B</td>
<td>III</td>
</tr>
<tr>
<td><strong>Possible</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital defects of platelet function</td>
<td>C</td>
<td>IV</td>
</tr>
<tr>
<td>Uremia</td>
<td>C</td>
<td>IV</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>C</td>
<td>IV</td>
</tr>
<tr>
<td>Drug-induced bleeding (heparin, hirudin, antiplatelet agents, dextran, streptokinase)</td>
<td>C</td>
<td>IV</td>
</tr>
<tr>
<td><strong>Doubtful</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>A</td>
<td>I</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>A</td>
<td>I</td>
</tr>
</tbody>
</table>
Desmopressin was added to the EML in 1992 and deleted in 2003

Reviewers comments:

“Rare disorder: requires specialist supervision and facilities. Is this an essential medicine?”

“Agree. Probably not an essential drug.”

Reviewers comments in 2003
WFH applies to have desmopressin returned to the EML

- Efficacious treatment for rare diseases
- Affordable
- Safe
- Evidence-based – treatment guidelines, regulatory approval, multiple manufacturers, hemophilia treaters expertise
WFH application supported by multiple stakeholders

- CFC manufacturers
- International societies
- Individual hematologists
- Trade groups
- Charitable organizations
- National blood services
(9) Please comment briefly on issues regarding cost and affordability of this medicine.

D is a safe and affordable alternative to plasma products and fresh blood components for patients with moderate and mild hemophilia, vWD and other hereditary bleeding disorders in the developed world and particularly in developing countries.

(10) Any additional comments?

This reviewer could not find the reason why D was removed from the WHO EML in 2002 after being included in 1992.

Reviewer comments in 2014
(11) Please summarise the action you propose the Expert Committee takes.

It is the opinion of this reviewer that D should not be considered as an essential drug. However, it could be included in the Complementary List.

The reason for allowing D onto the Complementary List is that there is long-lasting experience in its use and empirical evidence of its efficacy, safety and cost-effectiveness in the prevention and treatment of bleeding in patients with mild hemophilia A and type 1 vWD. D could help avoid the potential danger and/or cost of blood derivatives and clotting factor concentrates or recombinant coagulation factors.
Desmopressin now added to the WHO Model List of Essential Medicines

Montreal, June 16, 2015 – In December 2014, the World Federation of Hemophilia (WFH) submitted an application to have desmopressin (DDAVP) added to the World Health Organization’s (WHO) Model List of Essential Medicines (EML). After public consultation and a review by the WHO Expert Committee on Selection and Use of Essential Medicines, desmopressin has now been officially added to the EML.

The global bleeding disorders community worked together to advocate for its inclusion.

Desmopressin is a critical addition to this list as it is a safe and affordable alternative to plasma products and fresh blood components for patients with moderate and mild hemophilia, VWD, and other hereditary bleeding disorders. Its acceptance by the WHO as an essential medicine will encourage lobbying for access to the medication in countries where it is not yet available and encourage regulatory approval in countries where it is not licensed.

According to the WHO, essential medicines satisfy the priority health care needs of the population. Public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness are all considered when essential medicines are included on this list. The Model List serves as a guide for the development of national and institutional essential medicine lists.

Increasingly, governments, and institutions around the world are using the WHO list to guide the
Desmopressin for hemophilia

- Available not used: 3
- Not used: 48
- Used: 31

Desmopressin for VWD

- Available not used: 45
- Not used: 33
- Used: 3

2014 WFH Annual Global Survey
THANK YOU