**Acute Myelogenous Leukemia (AML) (including Acute Promyelocytic Leukemia (APML))**

Proposed medicines(s) for treatment of AML and APML (refer to application for specific protocols):

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Currently on EML</th>
<th>Addition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine (AML, APML)</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Daunorubicin (AML, APML)</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>ATRA (all-trans retinoic acid) (APML)</td>
<td></td>
<td>✗</td>
</tr>
<tr>
<td>Arsenic trioxide (APML)</td>
<td></td>
<td>✗</td>
</tr>
<tr>
<td>6-mercaptopurine (APML)</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Methotrexate (APML)</td>
<td>✗</td>
<td></td>
</tr>
</tbody>
</table>

(1) Does the application adequately address the issue of the public health need for the treatment of the disease?  

Yes (X)  

No □

Comments: The classification part should be revised. The FAB classification is no longer used and instead of the WHO classification 2001 there should be the WHO classification 2008, which has made some important changes. In the classification based on cytogenetics and novel molecular parameters the monosomal cariotype is lacking, since it emerged later than the classification used here, which was published by Döhner.

(2) Have all important studies that you are aware of been included in the application?  

Yes (X)  

No □

Comments: Since the study by Mayer et al. (6) published in 1994 is still the basis for structuring the treatment, it should be stated that only less than 30% of elderly patients were able to receive the 4 cycles of maintenance because of toxicity. This is important, since age is one of the discriminatory issues in choosing the treatment.

(3) Does the application provide adequate evidence of efficacy/effectiveness of the proposed treatment regimen(s)?

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**20th Expert Committee on Selection and Use of Essential Medicines**

**Peer Review Report #1**

Acute Myelogenous Leukemia (AML) (including Acute Promyelocytic Leukemia (APML))
Comments: It is correct to state that allogeneic transplantation should not be included in this discussion, so perhaps on page 8 (***) should be dropped, since it is misleading.

(4) Does the application provide adequate evidence of safety for the proposed treatment regimen(s)? Are there any adverse effects of concern, or that may require special monitoring?

Comments:

ADDITIONAL CONSIDERATIONS:

(5) Are there special requirements or training needed for the safe, effective and/or appropriate use of the proposed treatment(s)?

Comments: As rightly stated in the summary, the decision whether AML can be treated in a centre or even in a country, depends on the availability of many structures and products (e.g. safe blood products). So a lot of care has to be used to decide whether a patient can be treated locally or has to be referred to more competent centres or even abroad. Since referring patients abroad if often impossible or too costly, perhaps there should be a discussion about the possibility of reducing further the dosage of the treatment (e.g. adapting it to the local situation and to the general status of the population and of the patients) as it has been done for some paediatric projects in developing countries. Of course this would decrease the CR-rate, but between no treatment at all or a lower CR-rate, the latter is better!

(6) Are there any issues regarding the registration of the proposed medicines by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Comments: While ATRA and arsenic trioxide are today considered to be necessary for the treatment of APML, there are problems in their availability (ATRA) in many developing countries and even more for the incredibly high price of arsenic trioxide. The latter (20'000 USD in Switzerland!) is absolutely out of reach for the vast majority of the low resource countries. This should be discussed intensively at the meeting.
(7) **Comment briefly on issues regarding cost and affordability of treatment.**

See point 6.

(8) **Any additional comments on the application?**

- As regards age: today in developing countries the limit for declaring patients being “older” for AML treatment has been moved to 65 years.
- On page 6, when discussing peripheral blood, in the second paragraph Coulter should be replaced by haematology counter, there must not be a Coulter.

(9) **Please summarise the action(s) you propose the Expert Committee take.**

Add ATRA and possible also arsenic trioxide, but only after intensive discussion about the cost.