Reviewer No.1 checklist, section reviews
EML

Section: 2.4 DISEASE MODIFYING AGENTS USED IN RHEUMATOID DISORDERS

<table>
<thead>
<tr>
<th>Proposed 'Green' medicines</th>
<th>Proposed 'yellow' medicines</th>
<th>Proposed 'red' medicines</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td><strong>methotrexate</strong></td>
</tr>
</tbody>
</table>

For ‘reds’ medicines: are these potentially essential medicines for children?

Do these medicines meet a public health need? Yes ☒ No ☐

*If no, no further comments needed.*

If they meet a public health need, what is needed?

- Product development of an appropriate dosage form? Yes ☒ No ☐

  *If yes, please suggest what might be needed:*

- Regulatory approval (i.e. clinical trials exist)? Yes ☒ No ☐

- Clinical trials of efficacy and safety in children? Yes ☒ No ☐

*Additional comments if any:*
US, UK licensed
No oral liquid formulation

*Action proposed for the Committee to take:*
To approve
Additional comments if any:

Methotrexate

Indications and dose

Juvenile idiopathic arthritis, juvenile dermatomyositis, vasculitis, uveitis, systemic lupus erythematosis, localised scleroderma, sarcoidosis

By mouth, subcutaneous injection, or intramuscular injection

Child 1 month–18 years

10–15 mg/m² once weekly initially, increased if necessary to max. 25 mg/m² once weekly

Important

Note that the above dose is a weekly dose. The CSM has received reports of prescription and dispensing errors including fatalities. Attention should be paid to the strength of methotrexate tablets prescribed and the frequency of dosing.


Oral, I. M., S.C.: 5-15 mg/m²/week as a single dose or in 3 divided doses given 12 hours apart; folic acid 1mg daily or folinic acid ≤5 mg weekly are often to prevent folate depletion from methotrexate.


- Clinical trials of efficacy and safety in children? Yes


Z Rheumatol;63(2):147-58, 2004 Apr. Evidence-based use of methotrexate in children with rheumatic disorders. Consensus statement of the Working Group for Children and Adolescents with Rheumatic Diseases in Germany (AGKJR) and the Working Group Pediatric Rheumatology Austria


Registro Cochrane de Ensaios Controlados (CENTRAL/CCTR) (3 de 489167) Comparative efficacy and safety of advanced drug therapy in children with juvenile rheumatoid arthritis.

A randomized trial of parenteral methotrexate comparing an intermediate dose with a higher dose in children with juvenile idiopathic arthritis who failed to respond to standard doses of methotrexate.


Additional comments if any:


Arthritis Rheum;52(4):1338-9; author reply 1339-40, 2005 Apr. Folic acid and folinic acid supplements and methotrexate therapy: comment on the article by Morgan et al.


Rheumatology (Oxford);39(10):1102-9, 2000 Oct. Do patients with rheumatoid arthritis established on methotrexate and folic acid 5 mg daily need to continue folic acid supplements long term?

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For 'reds' medicines: are these potentially essential medicines for children?

Do these medicines meet a public health need?  
Yes □ No ☒

*If no, no further comments needed.*

If they meet a public health need, what is needed?

- Product development of an appropriate dosage form?  
  Yes □ No □

  *If yes, please suggest what might be needed:*

- Regulatory approval (i.e. clinical trials exist)?  
  Yes □ No □

- Clinical trials of efficacy and safety in children?  
  Yes □ No □

*Additional comments if any:*

*Action proposed for the Committee to take:*