




		EMLc	ATC codes: L04AX03
Indication	Rheumatoid arthritis, serology unspecified	ICD11 code: FA20.Z	
INN	Methotrexate		
Medicine type	Chemical agent		
List type	Complementary		
Formulations	Oral > Solid: 2.5 mg (as sodium salt)		
EML status history	First added in 1997 (TRS 882) Changed in 2003 (TRS 920) Changed in 2011 (TRS 965)		
Sex	All		
Age	Also recommended for children		
Therapeutic alternatives	The recommendation is for this specific medicine		
Patent information	Patents have expired in most jurisdictions Read more about patents . 		
Wikipedia	Methotrexate 		
DrugBank	Methotrexate 		

Summary of evidence and Expert Committee recommendations

At its 2009 meeting, the Committee had requested a review of the medicines needed for the treatment of juvenile idiopathic arthritis (JIA) in children, as it did not endorse any of the medicines currently listed. A review was prepared by P Gowdie (Royal Children’s Hospital, Melbourne, Australia) to identify priority rheumatic conditions in children, treatment options, evidence for efficacy and safety, and to make recommendations for the inclusion of medicines. The Committee noted that the most frequent condition in children is JIA, with three main forms: systemic onset, polyarticular, and oligo-monoarticular. Other conditions of interest are juvenile dermatomyositis/polymyositis (JDM), and systemic lupus erythematosus (SLE), but these are infrequent in children. Other chronic arthritic diseases affecting children such as acute rheumatic fever, Lyme disease, post-streptococcal reactive arthritis, Kawasaki disease, and other vasculitides were not discussed in the application. The Committee noted that the following pharmacological classes were used: NSAIDs for the management of symptoms; corticosteroids at immunosuppressive doses (especially for paediatric SLE and JDM); and DMARDs which include methotrexate, cyclophosphamide, azathioprine, cyclosporine, mycophenolate, leflunomide, sulfasalazine, and chloroquine or hydroxychloroquine. DMARDs aim to control disease activity, prevent irreversible organ damage, and decrease the burden of the disease or steroid treatment. The Committee first considered whether these conditions represent a priority health problem for the population. Estimates of prevalence are available for JIA in developed countries (from 7 to 401 per 100 000 children) and this condition can produce a high burden of disease if it continues into adulthood with severe disability or the need for joint replacement. Juvenile dermatomyositis, on the other hand, is a rare disease and if treated appropriately with high doses of steroids, immunosuppressants and supportive care, can result in little disability. The prevalence of paediatric SLE, a chronic, life-threatening disease, ranges between 0.36 and 0.9 per 100 000 children. The Committee noted the lack of specific data in children affected by chronic arthritis or inflammatory systemic diseases in developing countries. The Committee evaluated the evidence provided in the review for each of the medicines. A summary of the considerations is provided in Table 1 (page 14, TRS 965) and full details of the clinical evidence are in the application. The Committee noted that the use of methotrexate (MTX) in children requires monitoring, in particular of liver enzymes, on a regular

basis. The Committee noted the risk of serious adverse effects associated with inadvertent daily dosing of MTX instead of weekly. Such mistakes can be due to prescribing errors (commonly seen at transfers between sites of care), dispensing errors, and patient errors. The Committee concluded that methotrexate should be included in the Complementary List of the EMLc, based on the evidence of efficacy and safety available in children.

