A.37	Intra-articular Triamcinolone Hexacetonide (TH)– Juvenile Idiopathic Arthritis (JIA)
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: JIA is the most common rheumatic disease of childhood. Currently, it is estimated that there are >2 million children with JIA around the world. Most of then in Africa and Asia. Many of these children have little or no access to specialist care and appropriate treatment leading to poor outcomes.
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	The only medication listed specifically for juvenile joint disorders is acetylsalicylic acid. It is not indicated in JIA Disease modifying agents (DMARDs), mainly methotrexate can also be used in JIA. They are included in the EML. They are recommended once patients failed intra-articular asteroids and NSAIDs or as initial therapy in patients with poor prognosis. NSAIDs (Ibuprofen is included in the EML) are an important part of the treatment of JIA but usually not used as single therapy anymore.
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included:
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes ☐ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). Currently, intra-articular steroids are considered first line therapy for JIA. Single arm cohort studies (2) have shown good response and sustained effect to intra-articular TH. There seems to be a dose response correlation Two observational studies with small sample sizes compared TH vs. triamcinolone acetate (TA). They showed a statistically significant difference favouring TH. They showed higher response rate in the TH group, lower relapse rate and longer time until relapse compared to TA. A double blind RCT with a small sample size showed similar results. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or

	populations (e.g. children, the elderly, pregnant patients)? No. Studies included mostly oligoarticular cases of JIA. None of them were conducted in the developing world.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: Side effects are not reported based on study results, incidence is not mentioned. Serious adverse events seem to be uncommon: • Systemic side effects from TH seem be to be very rare due to low solubility and no affinity for the mineralocorticoid receptor. • Avascular necrosis of femoral is usually limited to patients who require systemic and intra-articular steroids
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Even when the evidence to support the superiority of TH over TA is limited, TH seems to be superior and a safe option for the treatment for JIA. I consider it shows a favourable benefit risk ratio.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Intra-articular steroids are considered an important tool in the treatment of JIA. Low to moderate quality of evidence shows superiority of TA over TH.
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: The process of administering intra-articular medications requires special training. Laboratory tests are needed to determine disease activity and risk of progression in order to establish the most appropriate therapeutic regime. JIA should be managed, ideally, by a paediatric rheumatologist.

Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☒ Yes ☐ No ☐ Not applicable Comments: TH is approved for use in the Canada, UK and many countries in the EU. Due to short supply the FDA has discontinued it. It can be imported for specific patients There is no information about the situation in Latin America, Africa or Asia.
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☒ No ☐ Not applicable Comments: As far as I could find WHO has not developed guidelines for joint pathology or paediatric autoimmune pathologies.
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Access is limited due to short supply worldwide. Manufacturers are currently working to resolve the problem. Cost is really variable since dosing is based on weight. Administrations costs should also be considered. Taking into account that TH is administered every few moths costs might be reasonable.
Any additional comments	
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	Include. Considering how important intra-articular steroid are in the treatment of JIA and the evidence suggesting benefits I consider TH should be included in the complementary EML and EMLc. Inclusion may be helpful in improving access and resolving shortage.
References (if required)	