A.50	Triamcinolone hexacetonide (TH) – juvenile idiopathic arthritis (JIA) – EML and EMLc
Draft recommendation	☒ Recommended ☐ Not recommended Justification: Considering how important intra-articular steroids 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. Currently, 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 have failed intra-articular asteroids and NSAIDs or as initial therapy in patients with poor prognosis. NSAIDs (Ibuprofen is included in the EML/ EMLc) are an important part of the treatment of JIA but not recommended to be used as single therapy anymore.
Does the proposed medicine address a relevant public health need?	☒ 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 them in Africa and Asia. Many of these children have little or no access to specialist care and appropriate treatment leading to poor outcomes.
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes. ☐ No ☐ Not applicable Comments: 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.

Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☐ 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 head is usually limited to patients who require systemic and intra-articular steroids at the same time.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: If the medication is used appropriately. Adverse effects related to systemic absorption are unlikely but must be considered.
Are there any special requirements for the safe, effective and appropriate use of the medicines? (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 to establish the most appropriate therapeutic regimen. JIA should be managed, ideally, by a paediatric rheumatologist.
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable Comments: Access is limited due to short supply worldwide. Manufacturers are currently working to resolve the problem. Cost is variable since dosing is based on weight. Administrations costs should also be considered. Considering that TH is administered every few months costs might be reasonable.
Are there 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 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? (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 disorders or paediatric autoimmune diseases.