Reviewer No.1 checklist for application of:

Artesiane 20 (20mg/ml) imi

In the WHO Essential Medicines List for Children

(1) Have all important studies that you are aware of been included?

Yes ☐ No ☒

(2) Is there adequate evidence of efficacy for the proposed use?

Yes ☐ No ☒

Standard therapy for severe malaria- monotherapy IVI initial followed by ACT. Alternative existing parental products artemether 80 mg/ml (arachis oil based), artesunate (60 mg/ml) & quinine (300 mg/ml -2 ml vial). Other alternatives to oral and parental medications were rectal artesunate100mg and 400mg Arachis oil (variable & very slowly absorbed)versus miglyol (coconut oil claimed to more rapidly absorbed) 3.2 mg/kg initial dose followed by 1.6 mg/kg body weight for 5-7 days (prevent recrudescences)

Children studies – Papua New Guinea suppository ARTESUNATE 9N-=41) Artemether IMI n=38 showed equivalency for effect and adverse effect African studies – single agent imi artemether good efficacy and safety Gambia, Malawi, eastern Sudan–artemether 3.2 mg/kg loading and 1.6 mg/kg body weight follow up vs imi/ivi quinine 20 mg/kg followed by 10 mg/kg body weight-faster parasite clearance with artemether but overall outcome same. Therefore current data supports use of IMI artemether as monotherapy initially followed by ACT.

Overall data suggest equivalent cure rates, coma recovery or hospital stay or mortality with quinine based, artesunate based artemether based, dihydroartemisinin based therapies given parentally or rectally for severe malaria. Some minor differences in terms of reduction in parasite loads were noted with artesunate/ artemether.

Artesunate(ivi) first option/artemether IMI(2nd option) drugs of choice for malaria in pregnancy especially 2nd and 3rd trimester because quinine may be associated with hypoglycaemia, vertigo AND CARDIAC TOXICITY-no evidence for safe use in first trimester – COCHRANE insufficient reliable research on subject. Rectal artesunate only for preferal cases. However major limitation with this motivation of artemether 20mg/ml is lack of comparison with existing artemether 80 mg/ml of equivalent especially that carrier medium is different.

(3) Is there evidence of efficacy in diverse settings and/or populations?

Yes ☐ No ☒

The majority of studies identified were in adults with small numbers with scant methodological details. Children were not included.

(4) Are there adverse effects of concern?

Yes ☐ No ☒

(5) Are there special requirements or training needed for safe/effective use?

Yes ☐ No ☒

(6) Is this product needed to meet the majority health needs of the population?

Yes ☒ No ☐

(7) Is the proposed dosage form registered by a stringent regulatory authority?

Yes ☐ No ☒

(8) What action do you propose for the Committee to take?

Not approved for inclusion onto the essential drug list for children until data on pharmocockinetics, pharmodynamics, clinical efficacy and safety of miglyol based artemether 20 mg/ml in children is available.

(9) Additional comment, if any.

Cost per treatment of new agent is twice that parental quinine.