A.42	Somatropin – hypoglycaemia secondary to growth hormone deficiency (GHD) – EMLc
Draft recommendation	☐ Recommended ☒ Not recommended Justification: Even when neonatal hypoglycemia can lead to severe neurological sequela, I do not think this is a medication that meets the criteria of "public health need". In many areas of the world, the diagnosis of GHD is hard or even impossible. Additionally, this medication is expensive while there are multiple requirements for its the appropriate administration and appropriate use (requires refrigeration, injectable, etc).
Does the proposed medicine address a relevant public health need?	☐ Yes ☒ No ☐ Not applicable Comments: The minimum prevalence rate of idiopathic GH deficiency in the USA and UK is between 1 in 3,400 and 4,000. It can be divided into congenital and acquired forms. There doesn't seem to be information available about the incidence or prevalence of the congenital form specifically. Even when the congenital form can present as hypoglycemia and persistent jaundice, the single most important clinical manifestation of GHD is growth failure (for both forms). Children who are diagnosed very early in life often suffer from a congenital disorder, such as anatomical defects in the hypothalamic-pituitary region. Hypoglycemia becomes more common and severe when GHD is combined with deficiency of adrenocorticotropic hormone.
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: Application reports that since it is ethically unreasonable to not treat patients diagnosed with GHD, there is a lack of RCTs trials to compare the effectiveness of rhGH therapy on hypoglycemia in neonates. However, clinical experience demonstrates that hypoglycemia in neonates and infants with GHD responds very well to rhGH. It is a correction of a deficiency.
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: Reports are based on the use of rGH in older population since there is not much information available in children <2y. Side effects reported in older patient do not seem to be concerning in newborns and infants.

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
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: Patients need to be managed by a pediatric endocrinologist (ideal) Patients required monitoring including physical examination and monitoring of other hormones
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable Comments: There is no data on cost-effectiveness of rhGH treatment in neonates and infants with hypoglycemia. It is readily available in all high-income countries and are usually covered by the government/ insurance for GHD. In LMICs, it is not readily available and is rarely funded by the health authorities.
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:
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:

1. Wit JM, van Unen H. Growth of infants with neonatal growth hormone deficiency. Arch Dis Child 1992; 67:920.
2. Gluckman PD, Gunn AJ, Wray A, et al. Congenital idiopathic growth hormone deficiency associated with prenatal and early postnatal growth failure. The International Board of the Kabi Pharmacia International Growth Study. J Pediatr 1992; 121:920.

3. De Luca F, Bernasconi S, Blandino A, et al. Auxological, clinical and neuroradiological findings in infants with early onset growth hormone deficiency. Acta Paediatr 1995; 84:561.
4. Pena-Almazan S, Buchlis J, Miller S, et al. Linear growth characteristics of congenitally GH-deficient infants from birth to one year of age. J Clin Endocrinol Metab 2001; 86:5691.