A.37	Ready-to-use therapeutic food – severe acute malnutrition – EML and EMLc
Draft recommendation	☒ Recommended ☐ Not recommended Justification: The evidence for the efficacy suggests that RUTF increases recovery and weight gain with low costs overall and little risks of harms. However, more adequate data are needed on long-term effects and reduction of mortality.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable Comments: Severe acute malnutrition (SAM) is still a global health burden that affects 13.6 million children every year. SAM is associated with metabolic dysregulations such as hypoglycaemia, impaired gluconeogenesis, disrupted amino acid or lipid metabolism that are responsible for the different clinical manifestations of SAM and lead to the children suffering from it to be more susceptible to illness. Children with moderate to severe acute malnutrition have three to nine times higher mortality than well-nourished children. Undernutrition contributes to nearly 45% of all deaths in children under 5 years old globally. Low- and middle-income countries are worst affected. Treatment services are estimated to reach less than 15% of undernourished children.
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: One systematic review from 2019 with 15 randomized studies concludes that RUTF likely contributed to improved recovery of malnutrition (moderate certainty) and weight gain (low certainty), however the effects on relapse and mortality remain unknown (very low certainty). Different formulations of RUTF were compared with different benefits of a particular formulation over another.
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: There was no difference in mortality between the children who received RUTF and those who received standard diets (RR 0.97; 95% CI 0.46 to 2.05; n = 599). Similarly, there was no difference in the frequency of diarrhea (number of days of diarrhea in the first two weeks of treatment) between the children who received RUTF and those who received the standard diets (MD -0.6; 95% CI -1.30 to 0.10; n=352).

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: Other than diarrhoea and allergic reactions, there are no concerns on the possible harms from the formulation. These events are rare, although the evidence is still uncertain (low certainty).
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 formulations are easy to use, transport, and prepare.
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☐ Yes ☒ No ☐ Not applicable Comments: SAM treatment costs $262 per child with a median cost of $196. Total costs for the treatment service per child admitted range from $76 in Niger to $805 in Ghana. However, the absolute cost of RUTF is more consistent across programs. The cost per DALY averted ranges from $26 in Bangladesh to $ 53 in Zambia. Given that these estimates fall below the GDP per capita in the countries where implemented, the intervention was considered cost effective.
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: As of November 2021, 25 countries (36%) with programmes to treat SAM with RUTF had included RUTF in their country's national EML. The percentage of countries with RUTF in the national EML is considerably higher in the Africa Region (63%). Only 18% countries in the Region of the Americas and one in ten of the countries in West Pacific had included RUTF in the national EML, and none in the Eastern Mediterranean Region, Europe Region, or Southeast Asia Region, but some countries are in the process to request for its inclusion.

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: RUTF is currently recommended for use in the following guidelines: • WHO. Community-based management of severe acute malnutrition, A Joint Statement, World Health Organization, World Food Programme, United Nations System Standing Committee on Nutrition and United Nations Children's Fund, 2007 • WHO. Guideline: Updates on the management of severe acute malnutrition in infants and children. 2013 • WHO guideline on the dairy protein content in ready-to-use therapeutic foods for treatment of uncomplicated severe acute malnutrition. Geneva: World Health Organization; 2021.