



EMLc
ATC codes: A07CA

Indication	Diarrhoea <span>ICD11 code: MG31</span>
Medicine type	Chemical agent
List type	Core
Formulations	Oral > Other: ORS powder for dilution and zinc sulfate solid oral dosage form 20 mg (co-packaged) (EMLc)
EML status history	First added in 2019 (TRS 1021)
Sex	All
Age	Children (1 month - 12 years)
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more <a href="#">about patents</a> . 
Wikipedia	<a href="#">Oral rehydration salts - zinc sulfate</a> 

## Expert Committee recommendation

The Committee recommended the inclusion of co-packaged oral rehydration salts (ORS) and zinc sulfate tablets on the core list of the EMLc. The Committee considered that since these products are recommended to be administered together in the management of diarrhoea, the availability of the co-packaged product will be practical and support better adherence to treatment. Countries may also realize cost savings with the co-packaged product.

## Background

The application requested inclusion of co-packaged oral rehydration salts (ORS) and zinc sulfate tablets on the core list of the EMLc. Oral rehydration salts and zinc sulfate 20 mg solid oral dosage form are currently both listed individually on the EML and EMLc for use in the treatment of diarrhoea.

## Public health relevance

Diarrhoea is present globally, in all regions and among all populations. However, an inequitable proportion of diarrhoea morbidity and mortality occurs in low-income countries, which in turn have fewer resources and less robust infrastructure to manage the burden (1). The Global Burden of Disease Study 2016 (GBD) estimated diarrhoea as the eighth leading cause of death, responsible for well more than 1.6 million deaths and the fifth leading cause of death among children younger than 5 years (446 000 deaths). Approximately 90% (89.37%) of diarrhoeal deaths occurred in South Asia and sub-Saharan Africa (2).

## Benefits

The benefits associated with ORS and zinc have been previously considered and accepted at the time of the original listings. The current application identified a number of studies (3–8) that provide supporting evidence for the benefits of co-packaged ORS and zinc, including: ■ Increased uptake and coverage of ORS and zinc (as a combination therapy, and as individual components), reducing the risk of severe health consequences of chronic diarrhoea and stunting, acute diarrhoea, and zinc deficiency among children. ■ Improved adherence to the combined therapy of ORS and zinc. ■ Improved adherence to/preparation of individual

components (e.g. correct concentration of prepared ORS and completion of a full course of zinc). ■ Improved dispensing practices by health care workers. ■ Reduced hospitalizations due to diarrhoea. ■ Reductions in inappropriate antibiotic prescription and use. ■ Enhanced satisfaction levels by caregivers with ORS and zinc relative to status quo products. ■ Enhanced opportunities for developing private sector models and leveraging value chains to improve availability and access closer to the household level.

## Harms

Overall, ORS is safe, with few reports of adverse events. Additional adverse events that occur with ORS administration include oedematous (puffy) eyelids, which are a sign of over hydration, and vomiting. Zinc supplementation has been utilized extensively with demonstrated safety in the treatment of diarrhoea. To date, there have been no reports of severe adverse reactions from any form of zinc treatment for diarrhoea, alone or in combination with ORS.

## Cost / cost effectiveness

The application presented the comparative costs of co-packaged and individually packaged ORS and zinc from five African countries. In each case, the co-packaged product was less expensive than the combined cost of the individual products.

## WHO guidelines

The current WHO recommendations for ORS and zinc use in the management of diarrhoea in children with no signs of dehydration (Plan A) are: Low-osmolarity ORS (containing 75 mEq/L of sodium and 75 mmol/L of glucose) after each loose motion: ■ In a child younger than 2 years of age, provide 50 mL to 100 mL of ORS solution. ■ In a child 2 to 10 years of age, provide 100 mL to 200 mL of ORS solution. ■ In a child older than 10 years of age, provide ORS ad libitum (i.e. to drink freely). Zinc sulfate from the start of the diarrhoea: ■ In a child younger than six months, provide one half of a 20 mg tablet (i.e. 10 mg) once a day for 10 to 14 days. ■ In a child older than six months, provide one whole 20 mg tablet once a day for 10 to 14 days. The current WHO recommendations for ORS and zinc use in the management of diarrhoea in children with some dehydration (Plan B) are: Low-osmolarity ORS (containing 75 mEq/L of sodium and 75 mmol/L of glucose): ■ ORS in the first four hours is administered according to the weight of the child (or the child's age if the weight is not known). Zinc sulfate from the start of the diarrhoea: ■ As per Plan A

## Availability

Co-packaged ORS and zinc is available from multiple suppliers.

## Other considerations

The Committee noted the multiple letters of support received in relation to this application.

1. Mills A. Health care systems in low- and middle-income countries. *N Engl J Med.* 2014;370(6):552-7.
2. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet.* 2017;390(10100):1151-210.
3. Borapich D, Warsh M. Improving Child Health in Cambodia: Social Marketing of Diarrhea Treatment Kit, Results of a Pilot Project. *Cases in Public Health Communication & Marketing.* 2010;4:4-22.
4. Gebremedhin S, Mamo G, Gezahign H, Kung'u J, Adish A. The effectiveness bundling of zinc with Oral Rehydration Salts (ORS) for improving adherence to acute watery diarrhea treatment in Ethiopia: cluster randomised controlled trial. *BMC Public Health.* 2016;16:457.
5. Roche M, Meza RG, Vossenaar M. An Intervention to Co-package Zinc and Oral Rehydration Salts (ORS) Improves Health Provider Prescription and Maternal Adherence to WHO-recommended Diarrhea Treatment in Western Guatemala. *The FASEB Journal.* 2015;29(1\_supplement):902.23.
6. Habib MA, Soofi S, Sadiq K, Samejo T, Hussain M, Mirani M et al. A study to evaluate the acceptability, feasibility and impact of packaged interventions ("Diarrhea Pack") for prevention and treatment of childhood diarrhea in rural Pakistan. *BMC Public Health.* 2013;13:922.
7. Ramchandani R. Emulating Commercial, Private-Sector Value-Chains to Improve Access to ORS and Zinc in Rural Zambia: Evaluation of the Colalife Trial. Dissertation submitted to The Johns Hopkins University in conformity with the requirements for the degree of Doctor of Public Health. Available from <https://jscholarship.library.jhu.edu/handle/1774.2/39229>, accessed 29 September 2019.
8. Goh N, Pollak K. Progress over a Decade of Zinc and ORS Scale-up: Best Practices and Lessons Learned. Boston MA, USA: Clinton Health Access Initiative; 2016. Available from <https://clintonhealthaccess.org/content/uploads/2016/02/Progress-over-a-Decade-of-Zinc-and-ORSScale-Up.pdf>, accessed 29 September 2019.

