

# Increasing access to lifesaving diarrhea treatment



Proposal for inclusion of co-packaged ORS and zinc on the World Health Organization Model List of Essential Medicines for Children

## Lifesaving benefits of ORS and zinc

Diarrhea remains the second leading infectious cause of childhood mortality, responsible for about nine percent, or an estimated half a million deaths in young children worldwide. An overwhelming majority of those deaths occur in South Asia and sub-Saharan Africa.

Low-osmolarity oral rehydration salts (ORS) and zinc sulfate tablets (zinc) are key to managing diarrheal disease and drastically reducing childhood mortality and morbidity. The use of both therapies has been demonstrated to significantly reduce the duration and severity of diarrheal episodes, and prevent future episodes. In a review of 157 studies, use of ORS had treatment failure rate of only 0.2%, and was found to have reduced diarrhea-specific mortality by 69%.<sup>1</sup> Zinc supplementation as an adjunct therapy has been shown to decrease mortality or treatment failure by 40% and the duration of diarrhea by 25%, as well as provide subsequent protection from recurrence in the two to three months following treatment.<sup>2,3,4</sup>



Mothers with children waiting to be seen at a diarrheal disease clinic in Dhaka, Bangladesh. Photo: Jonathan Torgovnik©

Access to ORS and zinc, however, remains a challenge in low-resource settings, and the rate of co-administration of both products is extremely low. Of 11 of the 15 highest-burden countries with available data, 6 (~55%) had ORS and zinc

coverage levels of 2% or less.<sup>5</sup> Globally, it is estimated that a median of 42% of children suffering from diarrhea are treated with ORS and a median of 7% with both ORS and zinc.<sup>6</sup>

## Increasing access through normative policy change

### Current global guidance

Both ORS and zinc are currently listed separately in the gastrointestinal medicines category on the World Health Organization (WHO) Model List of Essential Medicines (EML) and EML for Children (EMLc).<sup>i</sup>

Current WHO and United Nations Children's Fund (UNICEF) treatment guidelines for the management of childhood diarrhea, released in 2004, recommend the use of both ORS and zinc. There are numerous additional guidance documents from national and international associations that recommend or include the use of both ORS and zinc as co-therapy for diarrhea, particularly in children younger than five years of age.

To date, no formal normative guidance related to co-packaging of ORS and zinc exists, which leads to a number of barriers impeding access, including national-level policy and procurement challenges.

### Application to the WHO EML Secretariat

A listing for both products co-packaged as a single item would support the long-standing WHO/UNICEF recommendation for co-administration of ORS and zinc, and have a number of public health benefits.

In November 2018, PATH and other members of Diarrhea Innovations Group (DIG)—a global coalition of innovators committed to reducing global burden of diarrhea—submitted an application to the WHO EML Secretariat for the addition of co-packaged ORS and zinc, as an individual listing, on the core EMLc.<sup>ii</sup>

In addition to having ORS and zinc listed individually, the addition of a co-packaged listing has the potential to reinforce the lifesaving benefits of ORS and zinc in managing childhood

<sup>i</sup> The listing for zinc includes the following note: "In acute diarrhea, zinc sulfate should be used as an adjunct to oral rehydration salts".

<sup>ii</sup> This collaboration was initiated by a United Kingdom non-profit ColaLife under their Globalizer Programme.

diarrhea as a cornerstone for all health care systems involved in diarrhea management. This inclusion would also help achieve harmonization with the long-standing recommendation around the use of both therapies. Subsequently, it may clarify and stimulate country-level policy work to prioritize access to this treatment and lead to an increased coverage in regions where it is needed most.

Decisions related to the application will be made during the 22<sup>nd</sup> Expert Committee meeting in Geneva WHO Headquarters on 1-5 April 2019. Application, now open for public comment, can be accessed here:

[http://www.who.int/selection\\_medicines/committees/expert/22/or\\_s-zinc/en/](http://www.who.int/selection_medicines/committees/expert/22/or_s-zinc/en/).

**Table 1. Proposed listing for co-packaged oral rehydration salts and zinc sulfate.**

17.5 Medicines used in diarrhoea	
oral rehydration salts* – zinc sulfate* [c]	<p><b>Powder for dilution</b> (see section 17.5.1) – <b>Solid oral dosage form</b> (see section 17.5.2)</p> <p>* Co-packaged for treatment of acute diarrhoea.</p>

### Expected benefits

A number of significant public health benefits from introduction of co-packaged ORS and zinc have already been demonstrated, including:

- Increased uptake and coverage of ORS and zinc (as a combination therapy and as individual components).
- Improved adherence to the combined therapy of ORS and zinc.
- Improved adherence to/preparation of individual components as a result of improved packaging<sup>7</sup> (e.g. correct concentration of prepared ORS, completion of a full course of zinc).
- Improved dispensing practices by health care workers.

<sup>1</sup> Munos MK, Walker CL, Black RE. The effect of oral rehydration solution and recommended home fluids on diarrhoea mortality. *International Journal of Epidemiology*. 2010;39(Suppl 1):i75–i87. doi:10.1093/ije/dyq025.

<sup>2</sup> Bhutta ZA, Bird SM, Black RE, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *American Journal of Clinical Nutrition*. 2000;72(6):1516–1522. doi:10.1093/ajcn/72.6.1516.

<sup>3</sup> Strand TA, Chandyo RK, Bahl R, et al. Effectiveness and efficacy of zinc for the treatment of acute diarrhea in young children. *Pediatrics*. 2002;109(5):898–903.

<sup>4</sup> Lazzarini M, Ronfani L. Oral zinc for treating diarrhoea in children. *Cochrane Database of Systematic Reviews*. 2012;(6):CD005436. doi:10.1002/14651858.CD005436.pub3.

- Reduced hospitalization due to diarrhea.
- Reductions in inappropriate antibiotic prescribing and use.
- Enhanced satisfaction levels by caregivers of 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.

Additional benefits of EML listing would include:

**A cascade effect.** Global treatment guidelines and the essential medicines listings serve as important guides for countries in their development of national EMLs (NEMLS) and procurement and supply of medicines for donation and local medicine production, as well as training of health care providers. Listing of co-packaged ORS and zinc has the potential to foster an enabling environment for country-level policy work to prioritize access to treatment and incorporate ORS and zinc co-therapy into national health programs.

**An awareness effect.** WHO EML listing stands to increase recognition and reinforcement among policymakers and health care professionals of co-administered ORS and zinc as a cornerstone of childhood diarrheal treatment worldwide.

**Availability effect.** Listing of a co-packaged product can guide the selection, procurement, and supply of medicines in the public sector, schemes that reimburse medicine costs, and medicine donations, from the national level down to provincial/regional and district levels within countries.

**A manufacturer effect.** The listing may catalyze increased demand and spur local medicine production, with manufacturers responding and creating more market competition.

For more information on this initiative, or to learn how you can support this effort, please contact Elena Pantjushenko [epantjushenko@path.org](mailto:epantjushenko@path.org) or [drugdev@path.org](mailto:drugdev@path.org).

Learn more about DIG -

<https://www.defeatdd.org/other/diarrhea-innovations-group>.

<sup>5</sup> International Vaccine Access Center, The Johns Hopkins University Bloomberg School of Public Health. *Pneumonia & Diarrhea Progress Report 2017: Driving Progress through Equitable Investment and Action*. Baltimore MD, USA: The Johns Hopkins University; 2017.

<https://www.jhsph.edu/ivac/wp-content/uploads/2018/04/IVAC-2017-Pneumonia-Diarrhea-Progress-Report-2.pdf>.

<sup>6</sup> Countdown to 2030 Collaboration. Countdown to 2030: tracking progress towards universal coverage for reproductive, maternal, newborn, and child health. *Lancet*. 2018;391(10129):1538–1548. [https://doi.org/10.1016/S0140-6736\(18\)30104-1](https://doi.org/10.1016/S0140-6736(18)30104-1).

<sup>7</sup> Ramchandani, R., "Emulating Commercial Private-Sector Value-Chains to Improve Access to ORS and Zinc in Rural Zambia: Evaluation of the ColaLife Trial (Doctoral Dissertation)," Johns Hopkins Bloomberg School of Public Health, Baltimore, 2016.



path.org

PATH is a global organization that works to accelerate health equity by bringing together public institutions, businesses, social enterprises, and investors to solve the world's most pressing health challenges. With expertise in science, health, economics, technology, advocacy, and dozens of other specialties, PATH develops and scales solutions—including vaccines, drugs, devices, diagnostics, and innovative approaches to strengthening health systems worldwide.

**Mailing Address**  
PO Box 900922  
Seattle, WA 98109 USA

**Street Address**  
2201 Westlake Avenue  
Suite 200  
Seattle, WA 98121 USA

**Date Published**  
November 2018