Health Canada Santé Canada

NATURAL HEALTH PRODUCT

ORAL REHYDRATION SOLUTIONS

Oral rehydration salts generally consist of a mixture of electrolytes and glucose. When reconstituted in water to produce an oral rehydration solution (ORS), they are used for the treatment and/or prevention of mild-to-moderate dehydration caused by acute watery diarrhea. Severe dehydration constitutes a medical emergency requiring immediate intravenous rehydration, and clinical practice recommends health care practitioner supervision/monitoring in the treatment of mild-to-moderate dehydration (Buckingham 2020; Government of Canada 2015; Diggins 2008; CPS 2006; WHO 2006; WHO 2005; CDC 2003).

This monograph is therefore intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for market authorizations of natural health products recommended for the prevention of mild-to-moderate dehydration caused by acute watery diarrhea. These products are **not to be recommended** to maintain hydration during exercise or for rehydration after exercise, as according to the World Health Organization (WHO), a clear distinction should be made between products recommended for treating and/or preventing dehydration caused by diarrhea and preparations with compositions that are designed for replacing water and salt losses during exercise (WHO 2006).

Notes

- Text in parentheses is additional optional information which can be included on the label at the applicant's discretion.
- The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant on the label.
- **Brand name:** The term (re)hydration may be used provided the brand name does not imply a use beyond the approved claims.

Date February 28, 2025

This monograph cannot be combined with any other monograph at Class II. Products providing any medicinal ingredients outside this monograph will require Class III assessment. Note that ingredients which contribute to body water loss, such as diuretics and diaphoretics, are not allowed in Oral rehydration solutions.

Proper name(s), Common name(s), Source information

Table 1. Proper name(s), Common name(s), Source information

Proper name(s)	Common name(s)	Source ingredient(s)
Sodium	Sodium	• Sodium chloride • Sodium citrate[1] • Sodium citrate dihydrate
Potassium	Potassium	• Potassium chloride • Potassium citrate[1] • Potassium citrate, monohydrate
Chloride	Chloride	• Potassium chloride • Sodium chloride
Citrate	Citrate	• Citric acid • Potassium citrate • Sodium citrate[1] • Sodium citrate dihydrate
D-Glucose	• Dextrose • D-Glucose • Glucose	Glucose[2]

Reference: NHPID 2024.
[1]Anhydrous.
[2]Anhydrous or monohydrate.

Route of administration

Oral

Dosage form(s)

This monograph is not intended to include foods or food-like dosage forms such as ready-to-drink or powdered products if represented as beverages as per the principles outlined in the Guidance Document: Classification of products at the food-natural health product interface: products in food formats.

Acceptable dosage forms are: Powder, for solution; Solution; Solution, concentrated; Tablet, for solution; Tablet, effervescent (Buckingham 2020; Diggins 2008; CPS 2006; WHO 2006; WHO 2004).

Use(s) or Purpose(s)

All products

- Helps to prevent dehydration caused by (acute/watery) diarrhea and/or vomiting (due to acute gastroenteritis) (Buckingham 2020; Government of Canada 2015; Ciccarelli et al. 2013; Diggins 2008; CPS 2006; WHO 2006; WHO 2005; Bellemare et al. 2004; Fonseca et al. 2004; WHO 2004; CDC 2003; WHO 2001; WHO-ICDDR 1994).
- Helps to maintain hydration status/electrolytes and fluid balance in cases of (acute/watery) diarrhea and/or vomiting (due to acute gastroenteritis) (Buckingham 2020; Government of Canada 2015; Ciccarelli et al. 2013; Diggins 2008).
- (Source of electrolytes and glucose to) Help(s) (to) restore/replace water/fluid and electrolytes lost in cases of (acute/watery) diarrhea and/or vomiting (due to acute gastroenteritis) (Buckingham 2020; Government of Canada 2015; Ciccarelli et al. 2013; CPS 2006; WHO 2005; CDC 2003).

Products formulated as, or resulting in, the WHO formulation as outlined in Table 2

- Helps to reduce duration of diarrhea, stool output, and vomiting resulting from acute watery diarrhea in children (Musekiwa and Volmink 2011; CPS 2006; Pulungsih et al. 2006; WHO 2006; WHO 2005; CHOICE Study Group 2001; Hahn et al. 2001; WHO 2001; Alam et al. 1999; Santosham et al. 1996; WHO-ICDDR 1994).

Note: The terms ‘Helps’ or ‘Helps to’ can be used interchangeably on the label.

Dose(s)

Subpopulation(s)

Infants 0-12 months; Children 1-11 years; Adolescents 12-17 years; Adults 18 years and older (Ciccarelli et al. 2013; CPS 2018; CPS 2006; WHO 2006; WHO 2005; WHO 2001; WHO-ICDDR 1994).

Quantity/Concentration

All medicinal ingredients must be present in the formulation (applies to Tables 2 and 3)**.**

Osmolarity must be indicated on the PLA form under ‘additional dosage information’ and on the product label.

Table 2. Medicinal ingredients and formulation characteristics – WHO formulation[1]

Medicinal ingredients	Concentration in prepared product[2]	Source ingredient(s)
Sodium	75 mmol/L (1.72 mg/mL or 75 mEq)	• Sodium chloride[3] • Sodium citrate[3] • Sodium citrate dihydrate
Potassium	20 mmol/L (0.78 mg/mL or 20 mEq)	Potassium chloride[3]
Chloride	65 mmol/L (2.3 mg/mL or 65 mEq)	• Potassium chloride[3] • Sodium chloride
Citrate	10 mmol/L (1.89 mg/mL or 30 mEq)	• Sodium citrate[3] • Sodium citrate dihydrate
D-Glucose	75 mmol/L (13.5 mg/mL)	Glucose[4]
Total osmolarity (mOsm/L) (See Appendix 1)	245 mOsm/L	

[1]References: WHO 2006; WHO 2005; WHO 2004; WHO 2001; WHO-ICDDR 1994.
[2]The unit 'mmol/L' should be used on the PLA form; however, the units 'mg/mL' or 'mEq' may also be used on the label.
[3]Anhydrous.
[4]Anhydrous or monohydrate.

Table 3. Medicinal ingredients and formulation characteristics – Other acceptable formulations[1]

Medicinal ingredients	Concentration in prepared product[2]	Source ingredient(s)
Electrolytes		
Sodium	45 – 75 mmol/L (1.035 – 1.725 mg/mL or 45 – 75 mEq)	• Sodium chloride[3] • Sodium citrate[3] • Sodium citrate dihydrate
Potassium	15 – 25 mmol/L (0.59 – 0.98 mg/mL or 15 – 25 mEq)	• Potassium chloride[3] • Potassium citrate[3] • Potassium citrate, monohydrate
Chloride	25 – 80 mmol/L (0.8875 – 2.84 mg/mL or 25 – 80 mEq)	• Potassium chloride[3] • Sodium chloride[3]
Base		
Citrate	Minimum 8 mmol/L (1.51 mg/mL or 24 mEq)	• Citric acid • Potassium citrate[3] • Sodium citrate[3] • Sodium citrate dihydrate
Carbohydrate		
D-Glucose	at least 1 time the quantity of sodium in mmol/L	Glucose[4]

Medicinal ingredients	Concentration in prepared product[2]	Source ingredient(s)
Total osmolarity (mOsm/L) (See Appendix 1)	Not to exceed 280 mOsm/L (i.e. hypotonic)	

[1]At least one of the following references was consulted per medicinal ingredient: Buckingham 2020; Government of Canada 2015; Binder et al. 2014; Ciccarelli et al. 2013; Mathew 2009; Diggins 2008; CPS 2006; WHO 2006; WHO 2005; WHO 2004; CDC 2003; CHOICE Study Group 2001; WHO 2001; WHO-ICDDR 1994.
[2]The unit 'mmol/L' should be used on the PLA form; however, the units 'mg/mL' or 'mEq' may also be used on the label.
[3]Anhydrous.
[4]Anhydrous or monohydrate.

Direction(s) for use

Infants under 12 months; Children under 2 years

Give as tolerated in small amount/sips, up to 100 mL per episode of diarrhea and/or vomiting.

Children 2 - 9 years

Take/give as tolerated in small amount/sips, up to 200 mL per episode of diarrhea and/or vomiting.

Children 10 - 11 years, Adolescents 12 - 17 years, Adults 18 years and older

Take/give as tolerated in small amount/sips, up to 400 mL per episode of diarrhea and/or vomiting.

Note: At least one of the following references was consulted per age group: Buckingham 2020; Government of Canada 2015; Ciccarelli et al. 2013; Diggins 2008; WHO 2006; WHO 2005; WHO 2004; CDC 2003.

All products

Attempt to take/give solution as soon as diarrhea begins (Government of Canada 2015; CDC 2003).

Products to be dissolved/diluted (powder, for solution; solution, concentrated; tablet, for solution; tablet, effervescent)

- Dissolve/Dilute (e.g., 1 effervescent tablet; entire content of packet, etc.) in XX mL of potable water (Buckingham 2020; WHO 2006).
- If potable water is not available, use boiled water (Buckingham 2020; Government of Canada 2015).
- Stir the product before taking/giving (WHO 2006).

- Do not boil the product after it is prepared (Buckingham 2020; Government of Canada 2015).

Duration(s) of use

For occasional use only (Health Canada 2022).

Risk information

Caution(s) and warning(s)

All products

- **Get medical help right away for** infants under 1 year of age as dehydration may be a medical emergency.
- **Ask a health care practitioner/health care provider/health care professional/doctor/ physician before use if** you have a gastrointestinal obstruction, cardiovascular or kidney disease (Buckingham 2020; CPS 2006; WHO 2004; CDC 2003).
- **Ask a health care practitioner/health care provider/health care professional/doctor/ physician if** diarrhea/vomiting worsen or persist for more than 24 hours (WHO 2006; WHO 2005).
- **Ask a health care practitioner/health care provider/health care professional/doctor/ physician if** diarrhea contains blood or mucus, if vomit is green or contains blood, if diarrhea/vomiting are accompanied by a high fever, yellowing of eye or skin, severe abdominal pain, or if a bowel obstruction is suspected (Buckingham 2020; Government of Canada 2015; CPS 2006; CDC 2003).
- **Ask a health care practitioner/health care provider/health care professional/doctor/ physician if** you experience irritability, confusion, tiredness/weakness, reduced urine output, dry mouth, increased heart and/or breathing rate, decreased tears and/or sunken eyes , disproportionate thirst, or swelling of the hands, face and/or feet (Diggins 2008; CPS 2006; WHO 2005; CDC 2003).

Contraindication(s)

Do not use for (re)hydration associated with exercise (WHO 2006; CPA 2001; IOM 1994).

Known adverse reaction(s)

No statement required.

Non-medicinal ingredients

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database.

Storage conditions

Must be established in accordance with the requirements described in the *Natural Health Products Regulations*.

Ready-to-drink products

Store opened product in the refrigerator, discard remaining product after XX hours.

Note: XX to be replaced with the storage time established based on stability data for the product once opened.

Products to be dissolved/diluted

Store reconstituted solution in the refrigerator, discard remaining solution after 24 hours (Buckingham 2020; Government of Canada 2015; WHO 2006).

Specifications

- The finished product specifications must be established in accordance with the requirements described in the Natural and Non-Prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide
- The medicinal ingredient must comply with the requirements outlined in the NHPID.
- Osmolarity must be measured for the finished product, including non-medicinal ingredients.

EXAMPLE OF PRODUCT FACTS:

Consult the Guidance Document, Labelling of Natural Health Products for more details.

Product Facts

Medicinal ingredients in each serving*

Sodium (Sodium chloride)	XX mmol/L
Potassium (Potassium chloride)	XX mmol/L
Chloride (Sodium chloride)	XX mmol/L
Citrate (Sodium citrate dihydrate)	XX mmol/L
D-Glucose (Glucose)	XX mmol/L

Total osmolarity: XX mOsm/L; *once prepared after mixing with water

Uses

• Helps to prevent dehydration caused by acute diarrhea and/or vomiting due to acute gastroenteritis • Source of electrolytes and glucose to help restore fluid and electrolytes lost in cases of diarrhea and/or vomiting.

Warnings

If applicable[1]:
Allergens: food allergen, gluten (gluten source), sulphites
Contains aspartame

Do not use for (re)hydration associated with exercise.

Get medical help right away for infants under 1 year of age as dehydration may be a medical emergency.

Ask a health care practitioner before use if you have a gastrointestinal obstruction, cardiovascular or kidney disease.

Ask a health care practitioner if • diarrhea or vomiting worsen or persist for more than 24 hours • diarrhea contains blood or mucus, if vomit is green or contains blood, if diarrhea or vomiting are accompanied by a high fever, yellowing of eye or skin, severe abdominal pain, or if a bowel obstruction is suspected • you experience irritability, confusion, tiredness, reduced urine output, dry mouth, increased heart and/or breathing rate, decreased tears and/or sunken eyes, disproportionate thirst, or swelling of the hands, face and/or feet.

Directions

Take/Give as tolerated in small amount, up to 100 mL (infants/children up to 2 years), 200 mL (children 2-9 years), 400 mL (adults, adolescents, children 10 years and older) per episode of diarrhea and/or vomiting.

• Dissolve 1 effervescent tablet in XX mL of potable water[2] • If potable water is not available, use boiled water • Do not boil the solution after it is prepared • Attempt to take/give solution as soon as diarrhea begins • Stir the solution before taking/giving • For occasional use only.

Other information

Store reconstituted solution in the refrigerator, discard remaining solution after 24 hours
(Add any other storage information)

Non-medicinal ingredients

List all NMIs

Questions? (Call) 1-XXX-XXX-XXXX

[1]This section can be removed from the table if the product contains no allergen or aspartame.
[2]Include the dosage unit and the volume required to achieve appropriate concentration of medicinal ingredients.

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Appendix 1

Osmolarity

Osmotic concentration (osmolarity), is the measure of solute concentration, defined as the number of osmoles (Osm) of solute per litre (L) of solution (osmol/L or Osm/L). The osmolarity of a solution is usually expressed as Osm/L. Osmolarity measures the number of *osmoles of solute particles* per unit volume of solution. This value allows the measurement of the osmotic pressure of a solution and the determination of how the solvent will diffuse across a semipermeable membrane (osmosis) separating two solutions of different osmotic concentration.

To obtain the best medical outcome, the osmolarity of the Oral Rehydration Solution should be hypotonic [less than 280 mOsm/L], and ideally in the range of [225-250 mOsm/L].
An isotonic solution [280-295 mOsm/L] will have slightly delayed absorption because there is no osmotic concentration gradient present to accelerate absorption from the intestine to the bloodstream (Wesley 2004).

How to calculate Osmolarity

Ionic compounds, such as salts, can dissociate in solution into their constituent ions, so there is not a one-to-one relationship between the molarity and the osmolarity of a solution. For example, sodium chloride (NaCl) dissociates into Na+ and Cl− ions. Thus, for every 1 mole of NaCl in solution, there are 2 osmoles of solute particles (i.e., a 1 mol/L NaCl solution is a 2 osmol/L NaCl solution). Both sodium and chloride ions affect the osmotic pressure of the solution.

Nonionic compounds do not dissociate, and form only 1 osmole of solute per 1 mole of solute. For example, a 1 mol/L solution of glucose is 1 osmol/L.
Multiple compounds may contribute to the osmolarity of a solution. For example, a 3 Osm solution might consist of: 3 moles glucose, or 1.5 moles NaCl, or 1 mole glucose + 1 mole NaCl, or 2 moles glucose + 0.5 mole NaCl, or any other such combination.

For the WHO formulation *which does not have any non-medicinal ingredients*, osmolarity may be calculated rather than tested (addition of the concentrations of solutes, i.e. 75 + 20 + 65 + 10 + 75 = 245). If the formulation includes any non-medicinal ingredients, osmolarity may be affected so applicant must test their product to determine osmolarity.

- 1 mole of sodium chloride (58.44 g/mol) dissociates in 1 mole of sodium (22.98977 g/mol) and 1 mole of chloride (35.4527 g/mol).
- 1 mole of potassium chloride (74.55 g/mol) dissociates in 1 mole of potassium (39.0983 g/mol) and 1 mole of chloride (35.4527 g/mol).
- 1 mole of trisodium citrate dihydrate (294.10 g/mol) dissociates in 3 moles of sodium (22.98977 g/mol) and 1 mole of citrate (189.1 g/mol).

- 2.6 g of sodium chloride = 0.045 mole = 45 mmol or mOsm of sodium and 45 mmol or mOsm of chloride

- 1.5 g of potassium chloride = 0.020 mole = **20 mmol or mOsm of potassium** and 20 mmol or mOsm of chloride
- 2.9 g trisodium citrate dihydrate = 0.0097 mol = 9.86 mmol or **10 mmol or mOsm of citrate** and (3 x 9.86) = 29.58 mmol or mOsm of sodium
- 13.5 g of glucose (180.16 g/mol = 0.075 mol = **75 mmol or mOsm of glucose**.

- 45 mmol or mOsm of sodium (from sodium chloride) + 29.58 mmol or mOsm of sodium (from trisodium citrate dihydrate) = 74.58 mmol or **75 mmol or mOsm of sodium**.
- 45 mmol or mOsm of chloride (from sodium chloride) + 20 mmol or mOsm of chloride (from potassium chloride) = **65 mmol or mOsm of chloride**

Osmolarity = 20 + 10 + 75 + 75 + 65 = 245 mmol/L or mOsm/L