1. Name of the finished pharmaceutical product

Chlorure De Sodium 0.9 % Unimed

2. Qualitative and quantitative composition

Sodium chloride: 9.0 g/l

Each ml contains 9 mg sodium chloride.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

CHLORURE DE SODIUM 0.9 % UNIMED® is an injectable isotonic solution for infusion based on sodium chloride and is presented under the following form:

Sterile clear and colorless solution ready for use, packaged in multilayered bags of 500 ml.

4. Clinical particulars

4.1 Therapeutic indications

- Ionic equilibration through intake of chloride and sodium.
- Extra cellular dehydration.
- Vehicle for therapeutic intake.
- Hypovolemia.

4.2 Posology and method of administration

Adults, older people and children:

Doses may be expressed in terms of mEq or mmol of sodium, mass of sodium, or mass of sodium salt (1 g NaCl = 394 mg, 17.1 mEq or 17.1 mmol of Na and Cl).

Fluid balance, serum electrolytes and acid-base balance should be monitored before and during administration, with particular attention to serum sodium in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist drugs, due to the risk of hospital acquired hyponatraemia (see sections 4.4, 4.5 and 4.8). Monitoring of serum sodium is particularly important for hypotonic fluids.

Sodium Chloride 0.9% intravenous infusion has a tonicity of 308 mOsm/l (approx.)

The infusion rate and volume depend on age, weight, clinical condition condition (e.g. burns, surgery, head-injury, infections), and concomitant therapy should be determined by the consulting physician experienced in paediatric intravenous fluid therapy (see sections 4.4. and 4.8).

<u>Recommended dosage</u>

The recommended dosage for treatment of isotonic extracellular dehydration and sodium depletion is:

- For adults: 500 ml to 3 litres/24h
- For babies and children: 20 to 100 ml per 24h and per kg of body weight, depending of the age and the total body mass.

The recommended dosage when used as a vehicle or diluent ranges from 50 to 250 ml per dose of medicinal product to be administered.

dosage and the infusion rate will also be dictated by the nature and the dose regimen of the prescribed drug

Method of administration

The solution is for administration by intravenous infusion through a sterile and non-pyrogenic administration set, using aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

The product should be inspected visually for particulate matter and discoloration prior to administration. Do not administer unless solution is clear, free from visible particles and the seal is intact.

Do not remove unit from overwrap until ready for use. The inner bag maintains the sterility of the solution. Administer immediately following the insertion of infusion set.

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container. Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration. Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

Additives may be introduced before infusion or during infusion through the injection site.

For information on incompatibilities and preparation of the product (with additives), please see sections 6.2 and 6.6.

4.3 Contra-indications

This product must be used with caution in patients with an impaired ability to handle sodium such as organic heart disease especially with a history of congestive heart failure, patients with renal insufficiency, cirrhosis of the liver, cardiopulmonary diseases or patients receiving salt retaining steroids.

When used in conjunction with cell separator procedures, the solution is contraindicated in those patients where adequate anticoagulation cannot be achieved.

4.4 Special warnings and precautions for use

Fluid balance/renal function

Use in patients with (severe) renal impairment

Sodium Chloride 0.9% should be administered with particular caution to patients with or at risk of severe renal impairment. In such patients administration of Sodium Chloride 0.9% may result in sodium retention. (See “Use in patients at risk for sodium retention, fluid overload and oedema” below, for additional considerations.)

Risk of fluid and/or solute overload and electrolyte disturbances

Depending on the volume and rate of infusion, intravenous administration of Sodium Chloride 0.9% can cause:

- Fluid and/or solute overload resulting in overhydration/hypervolemia and, for example, congested states, including central and peripheral oedema.
- Clinically relevant electrolyte disturbances and acid-base imbalance.

In general, the risk of dilutional states (retention of water relative to sodium) is inversely proportional to the electrolyte concentrations of Sodium Chloride 0.9% and its additions. Conversely, the risk of solute overload causing congested states (retention of solute relative to water) is directly proportional to the electrolyte concentrations of Sodium Chloride 0.9% and its additions.

evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia (see below).

Hyponatraemia

Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and brain oedema) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.

Use in patients at risk for sodium retention, fluid overload and oedema

Sodium Chloride 0.9% should be used with particular caution, if at all, in patients with or at risk for:

- Hypernatraemia. Rapidly correcting hypernatraemia once adaptation has occurred may lead to cerebral oedema, potentially resulting in seizures, permanent brain damage, or death.
- Hyperchloraemia
- Metabolic acidosis, which may be worsened by prolonged use of this product, especially in patients with renal impairment.
- Hypervolaemia such as congestive heart failure and pulmonary oedema may be precipitated, particularly in patients with cardiovascular disease.
- Iatrogenic hyperchloraemic metabolic acidosis (e.g., during intravenous volume resuscitation)
- Conditions that may cause sodium retention, fluid overload and oedema (central and peripheral), such as patients with

primary hyperaldosteronism,

secondary hyperaldosteronism, associated with, for example:

- hypertension,
- congestive heart failure,
- liver disease (including cirrhosis),
- renal disease (including renal artery stenosis, nephrosclerosis) or pre-eclampsia.

Medications that may increase the risk of sodium and fluid retention, such as corticosteroids

Infusion reactions

Symptoms of unknown aetiology which can appear to be hypersensitivity reactions have been reported very rarely in association with infusion of Sodium Chloride 0.9 %. These have been characterized as hypotension, pyrexia, tremor, chills, urticaria, rash and pruritus. Stop the infusion immediately if signs or symptoms of these reactions develop. Appropriate therapeutic countermeasures should be instituted as clinically indicated.

Specific patient groups

populations that are especially sensitive to rapid changes in serum sodium levels.

Rapid correction of hyponatraemia and hypernatremia is potentially dangerous (risk of serious neurologic complications). See section “Hyponatraemia/hypernatraemia” above.

Paediatric population

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes. Repeated infusions of sodium chloride should therefore only be given after determination of the serum sodium level.

Geriatric population

When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, consider that geriatric patients are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant drug therapy.

For information on preparation of the product and additives, please see section 6.6.

As with any prolonged intravenous infusion, venous irritation and thrombophlebitis may occur at the injection site.

When used in conjunction with cell separator procedures, there is a risk of air embolism or haemolysis. A donor should not be subjected to this procedure more frequently than once in a 48 hour period, twice in 7 days or 24 times a year.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs leading to an increased vasopressin effect

The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

Drugs stimulating vasopressin release include: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics

Drugs potentiating vasopressin action include: Chlorpropamide, NSAIDs, cyclophosphamide

Vasopressin analogues include: Desmopressin, oxytocin, terlipressin

Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be increased during administration of Sodium Chloride 0.9%. Administration of Sodium Chloride 0.9% may result in decreased lithium levels.

Corticoids/Steroids and carbenoxolone, are associated with the retention of sodium and water (with oedema and hypertension). See Section 4.4 Special warnings and precautions for use.

4.6 Fertility, pregnancy and lactation

There are no adequate data from the use of Sodium Chloride 0.9% in pregnant or lactating women. The physician should carefully consider the potential risks and benefits for each specific patient before administering Sodium Chloride 0.9%.

Sodium Chloride 0.9% should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see sections 4.4, 4.5 and 4.8).

Caution is advised with patients with pre-eclampsia (See Section 4.4. Special warnings and precautions for use).

When a medicinal product is added, the nature of the drug and its use during pregnancy and lactation has to be considered separately.

4.7 Effects on ability to drive and use machines

No studies have been conducted on the influence of Sodium Chloride on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects

of the adverse drug reactions listed in this section cannot be estimated from the available data.

System Organ Class (SOC)	Adverse reactions (Preferred Term)	Frequency
Nervous system disorders	Tremor Acute hyponatraemic encephalopathy*	Not known
Metabolism and nutrition disorders	Hospital acquired hyponatraemia*	Not known
Vascular disorders	Hypotension	Not known
Skin and subcutaneous tissue disorders	Urticaria Rash Pruritus	Not known
General disorders and administration site conditions:	Infusion site reactions, such as Infusion site erythema, Injection site streaking, Burning sensation, Infusion site urticaria Pyrexia Chills	Not known

*Hospital acquired hyponatraemia may cause irreversible brain injury and death, due to development of acute hyponatraemic encephalopathy, frequency unknown (see sections 4.2. 4.4, 4.5).

The following adverse reactions have not been reported with this product but may occur:

• Hypernatraemia (eg. when administered to patients with nephrogenic diabetes insipidus or high nasogastric output)

• Hyperchloremic metabolic acidosis

• Hyponatraemia, which may be symptomatic. Hyponatraemia may occur when normal free water excretion is impaired. (eg SIADH or postoperative)

General adverse effects of sodium excess are described in section 4.9 Overdose.

Additives

When Sodium Chloride 0.9% is used as a diluent for injectable preparations of other drugs, the nature of additives will determine the likelihood of any other undesirable effect.

If an adverse event occurs the patient should be evaluated and appropriate counter measures be started, if needed the infusion should be stopped. The remaining part of the solution should be kept for investigation if deemed necessary.

When used in conjunction with cell separator procedures, reactions commonly experienced in routine blood collection such as syncope, vomiting and hyperventilation may occur. Individuals donating for the first time may be predisposed to these symptoms due to psychological factors. Reactions unique to apheresis collection procedures may also occur.

4.9 Overdose

General adverse effects of sodium excess in the body include nausea, vomiting, diarrhea, abdominal cramps, thirst, reduced salivation and lacrimation, sweating, fever, tachycardia, hypertension, renal failure, peripheral and pulmonary oedema, respiratory arrest, headache, dizziness, restlessness, irritability, weakness, muscular twitching and rigidity, convulsions, coma, and death.

An excessive volume of Sodium Chloride 0.9% may lead to hypernatraemia (which can lead to CNS manifestations, including seizures, coma, cerebral oedema and death) and sodium overload (which can lead to central and/or peripheral oedema) and should be treated by an attending specialized physician.

Excess chloride in the body may cause a loss of bicarbonate with an acidifying effect.

When Sodium Chloride 0.9% is used as a diluent for injectable preparations of other drugs, the signs and symptoms of over infusion will be related to the nature of the additives being used. In the event of accidental over infusion, treatment should be discontinued and the patient should be observed for the appropriate signs and symptoms related to the drug administered. The relevant and supportive measures should be provided as necessary.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic class: Product of isotonic sodium intake (B : blood and hematopoietic organs. ATC code: B05CB01).

Parenteral solution for ionic equilibration.

The properties are those of the sodium and chloride ions.

5.2. Pharmacokinetic Properties

Nothingness

5.3. Preclinical safety data

Nothingness

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Check an eventual change in colour and/or an eventual formation of precipitate, of insoluble complex or of crystals.

Before adjunction of any medicine, check whether the pH zone for which it is efficient corresponds to that of the solution of chlorure de sodium at 0.9%.

When a medicine is added to that solution, the mixture should be administered immediately.

6.3 Shelf life

Validity period: 24 months.

6.4 Storage condition and special precautions for manipulatio

Do not store above 30°C.Protect from light.

Remove the bag from the over package, check the limpidity of the solution and the integrity of the container.

For the medicinal additions, inject to the syringe through the site of injection.

For the reconstitution of powders, use a transfer device with double syringes.

Release the trocardable access.

Place the necessary adapted for infusion through perforating the trocardable access, purge the infusion line. Set the infusion flow.

6.5 Nature and contents of container

Multilayered bag of 500ml made of multilayered film that is a Polyolefin/Styrene-block copolymer, based film.

Any unused or waste medicine must be disposed of in accordance with applicable regulations.

7. Marketing authorization holder and manufacturing site addresses

Unimed Laboratories
P.O box n° 38, I.Z 4060 Kalaa Kebira,
TUNISA

8. Marketing authorization number

Will be allocated

9. Date of first authorization/de renewal of the authorization

10. Date of revision of the text

April, 2022
Distribution category; Prescription Only Medicine (POM).