SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

UNIDAR-F INFUSION (Full Strength Darrow's Solution)

Strength

Each 100ml contains:

Sodium Lactate BP	0.590g
Sodium Chloride BP	0.400g
Potassium Chloride BP	0.260g

Pharmaceutical/Dosage form

Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100ml contains:

Sodium Lactate BP	0.590g
Sodium Chloride BP	0.400g
Potassium Chloride BP	0.260g

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Infusion.

Clear and colorless solution, free from visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Unidar-F Infusion is used in the following indications:

- Restoration of extracellular fluid and electrolytes balances or replacement of extracellular fluid loss where isotonic concentrations of electrolytes are sufficient
- Short term volume replacement (alone or in association with colloid) in case of hypovolaemia or hypotension.
- Regulation or maintenance of metabolic acidosis balance and/or treatment of mild to moderate metabolic acidosis (except lactic acidosis)

4.2 Posology and method of administration Posology

Adults, the Elderly and Children:

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.

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

Recommended dosage:

The amount of **Unidar-F Infusion** needed to restore normal blood volume is 3 to 5 times the volume of lost blood.

The recommended dosage is:

- for adults: 500 ml to 3 L/24h
- for infants, toddlers and children: 20 ml to 100 ml/kg/24h *Administration rate:*

The infusion rate is usually 40 mL/kg/24h in adults.

Use in paediatric patients

The safety and efficacy of **Unidar-F Infusion** in children has not been established by adequate and well controlled trials; however, the use of electrolyte solutions in the paediatric population is referenced in the medical literature. Lactate-containing solutions should be administered with caution to neonates and infants less than 6 months of age.

Paediatric infusion rates is 5 ml/kg/h in average, but the value varies with age:

- infants: 6-8 mL/kg/h,
- toddlers: 4-6 mL/kg/h
- children: 2-4 mL/kg/h.

In children with burns, the dose is on average 3.4 mL/kg/per cent burn at 24 h post-burn and 6.3 mL/kg/per cent burn at 48 h.

In severely injured children the dose is on average 2850 mL/m^2.

Infusion rate and total volume can be higher in surgery or in case of need.

Note:

- infants and toddlers: aged from 28 days to 23 months (a toddler is an infant who can walk)
- children: age from 2 to 11 years

Use in geriatric patients

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.

Method of administration:

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

The solution should be inspected visually for particulate matter and discoloration prior to administration. Do not administer unless the solution is clear, free from visible particles and the seal is intact. Do not remove units from overwrap until ready for use. Administer immediately following the insertion of infusion set.

Do not connect flexible plastic containers in series 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. When making additions to

Unidar-F Infusion, aseptic technique must be used. Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives.

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

4.3 Contraindications

As for other calcium-containing infusion solutions, concomitant administration of ceftriaxone and
Unidar-F Infusion is contraindicated in newborns (≤28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream). For patients over 28 days of age please see section 4.4.

Unidar-F Infusion is also contraindicated in patients with

- A known hypersensitivity to sodium lactate.
- Extracellular hyperhydration or hypervolaemia
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac failure
- Hyperkalaemia
- Hypercalcaemia
- Metabolic alkalosis
- Ascitic cirrhosis
- Severe metabolic acidosis
- Conditions associated with increased lactate levels (hyperlactataemia) including lactic acidosis, or impaired lactate utilization, such as severe hepatic insufficiency.
- Concomitant digitalis therapy (see section 4.5 Interactions with other medicinal products and other forms of interaction)

4.4 Special warnings and precautions for use Hypersensitivity reactions

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.
Incompatibilities

Hypernatraemia

Unidar-F Infusion should only be administered to patients with hypernatraemia after careful consideration of the underlying cause and alternative intravenous fluids. Monitoring plasma sodium and volume status during treatment is recommended.

Unidar-F Infusion should be administered with caution in patients with conditions predisposing to hypernatraemia (such as adrenocortical insufficiency, diabetes insipidus or extensive tissue injury) and in patients with cardiac disease.

Hyperchloraemia
Unidar-F Infusion should only be administered to patients with hyperchloraemia after careful consideration of the underlying cause and alternative intravenous fluids. Monitoring plasma chloride and acid-based balance during treatment is recommended.

Unidar-F Infusion should be administered with caution to patients with conditions predisposing to hyperchloraemia (such as renal failure and renal tubular acidosis, diabetes insipidus), and patients with urinary diversion or patients taking certain diuretics (carbonic anhydrase inhibitors eg acetazolamide) or steroids (androgens, estrogens corticosteroids) and in patients with severe dehydration.

Use in patients with potassium deficiency

Although **Unidar-F Infusion** has a potassium concentration similar to the concentration in plasma, it is insufficient to produce a useful effect in case of severe potassium insufficiency and therefore it should not be used for this purpose.

Use in patients at risk for hyperkalemia

Unidar-F Infusion should be administered with caution to patients with conditions predisposing to hyperkalemia (such as severe renal impairment or adrenocortical insufficiency, acute dehydration, or extensive tissue injury or burns) and in patients with cardiac disease. The plasma potassium level of the patient must be particularly closely monitored in patients at risk of hyperkalaemia.

Use in patients with renal impairment

Unidar-F Infusion should be administered with caution to patients with renal impairment. In such patient's administration of Unidar-F Infusion may result in sodium and/or potassium retention.

Risk of Fluid and/or Solute Overload and Electrolyte Disturbances

Depending on the volume and rate of infusion, intravenous administration of Unidar-F Infusion can cause

- fluid and/or solute overload resulting in overhydration and, for example, congested states, including pulmonary congestion and oedema.
- clinically relevant electrolyte disturbances and acid-base imbalance.

Clinical 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 with hypervolaemia, overhydration or conditions causing sodium retention and oedema

Unidar-F Infusion should be administered with caution to hypervolaemic or overhydrated patients.

Due to the sodium chloride content Unidar-F Infusion should be administered with caution to patients with conditions that may cause sodium retention, fluid overload and oedema, such as patients with primary hyperaldosteronism, secondary hyperaldosteronism (associated with, e.g., hypertension, congestive heart failure, renal artery stenosis, or nephrosclerosis), or preeclampsia. (See also Section 4.5)

Acid-base balance

Use in patients at risk for alkalosis

Unidar-F Infusion should be administered with caution to patients at risk for alkalosis. Because lactate is metabolized to bicarbonate, administration may result in, or worsen, metabolic alkalosis. Seizure may be precipitated by the alkalosis induced by lactate, but this is uncommon.

Other warnings

Use in patients with type 2 diabetes

Lactate is a substrate for gluconeogenesis. Therefore, glucose levels should be carefully monitored in patients receiving Unidar-F Infusion.

Administration

Adding other medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In such cases the infusion must be stopped immediately.

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

During long term parenteral treatment, a convenient nutritive supply must be given to the patient.

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.

Interaction related to the presence of sodium:
Caution is advised when administering Unidar-F Infusion to patients treated with drugs that may increase the risk of sodium and fluid retention (with oedema and hypertension), such as corticosteroids.

Interaction related to the presence of potassium:

Because of its potassium content, Unidar-F Infusion should be administered with caution in patients treated with agents or products that can cause hyperkalaemia or increase the risk of hyperkalaemia, such as -
Potassium-sparing diuretics (amiloride, spironolactone, triamterene, alone or in association).

- Angiotensin converting enzyme inhibitors (ACEi) and angiotensin II receptor antagonists
- Tacrolimus, cyclosporine

Administration of potassium in patients treated with such medications can produce severe and potentially fatal hyperkalaemia, particularly in patients with severe renal insufficiency.

Interaction related to the presence of lactate (which is metabolized into bicarbonate):

Caution is advised when administering Unidar-F Infusion to patients treated with drugs for which renal elimination is pH dependent. Due to the alkalinizing action of lactate (formation of bicarbonate), Unidar-F Infusion may interfere with the elimination of such drugs.

- Renal clearance of acidic drugs such as salicylates, barbiturates, and lithium may be increased because of the alkalinisation of urine by the bicarbonate resulting from lactate metabolism.

- Renal clearance of alkaline drugs, such as sympathomimetics (e.g. ephedrine, pseudoephedrine) and stimulants (e.g. dexamphetamine sulfate, phenfluramine hydrochloride) may be decreased

4.6 Fertility, pregnancy and lactation
Unidar-F Infusion can be used safely during pregnancy and lactation as long as the electrolyte- and fluid balance is controlled.

It is reminded that calcium crosses the placenta and is distributed into breast milk.

Unidar-F Infusion should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see section 4.4, 4.5 and 4.8).

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

4.7 Effects on ability to drive and use machines
There is no information of the effects of Unidar-F Infusion on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects
The following adverse reactions (listed by MedDRA System Organ Class) have been reported spontaneously during the post-market experience.
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Immune System Disorders	Hypersensitivity/Infusion reactions including Anaphylactic/Anaphylactoid reaction, possibly manifested by one or more of the following symptoms: Angioedema, Chest pain, Chest discomfort, decreased heart rate, Tachycardia, Blood pressure decreased, Respiratory distress, Bronchospasm, Dyspnea, Cough, Urticaria, Rash, Pruritus, Erythema, Flushing, Throat irritation, Paresthesias, Hypoesthesia oral, Dysgeusia, Nausea, Anxiety, Pyrexia, Headache
Metabolism and Nutrition Disorders	Hyperkalaemia Hospital acquired hyponatraemia*
Nervous system disorders	Acute hyponatraemic encephalopathy*
General Disorders and Administration Site Conditions	Infusion Site Reactions manifested by one or more of the following symptoms: Phlebitis, Infusion site inflammation, Infusion site swelling, Infusion site rash, Infusion site pruritus, Infusion site erythema, Infusion site pain, Infusion site burning

*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 been reported spontaneously during the use of other sodium-lactate containing solutions:

- Hypersensitivity: Laryngeal oedema (Quincke's oedema), skin swelling, Nasal congestion, Sneezing
- Electrolyte disturbances
- Hypervolaemia
- Panic Attack
- Other infusion site reactions: Infection at the site of injection, Extravasation, Infusion site anesthesia (numbness)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose
An excessive volume or too high a rate of administration of Unidar-F Infusion may lead to fluid and sodium overload with a risk of oedema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired. In this case extra renal dialysis may be necessary.

Excessive administration of potassium may lead to the development of hypercalcaemia, especially in patients with renal impairment. Symptoms include paresthesia of extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and mental confusion.

Excessive administration of calcium salts may lead to hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi, and, in severe cases, cardiac arrhythmia and coma. Too rapid intravenous injection of calcium salts may also lead to many of the symptoms of hypercalcaemia as well as to chalky taste, hot flushes, and peripheral vasodilatation. Mild asymptomatic hypercalcaemia will usually resolve on stopping administration of calcium and other contributory drugs such as vitamin D. If hypercalcaemia is severe, urgent treatment (such as loop diuretics, haemodialysis, calcitonin, bisphosphonates, trisodium edetate) is required.
Excessive administration of lactate may lead to metabolic alkalosis. Metabolic alkalosis may be accompanied by hypokalaemia, Symptoms may include mood changes, tiredness, shortness of breath, muscle weakness, and irregular heartbeat. Muscle hypertonicity, twitching, and tetany may develop especially in hypocalcaemic patients. The treatment of metabolic alkalosis due to bicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance. Replacement of calcium, chloride, and potassium may be of particular importance.

When overdose is related to medications added to the solution infused, the signs and symptoms of over infusion will be related to the nature of the additive 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 symptomatic and supportive measures should be provided as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

5.2 Pharmacokinetic properties

The pharmacokinetic properties of the Unidar-F Infusion are those of the ions whose composition includes (sodium, potassium and chloride).

Infusion of Unidar-F Infusion in normal hemodynamically stable adults does not increase circulating lactate concentrations.

The pharmacokinetics of D-lactate and L-lactate are similar. The lactate in Unidar-F Infusion is metabolized by both oxidation and gluconeogenesis, predominantly in the liver, and bicarbonate is generated by both processes over 1-2 h.

5.3 Preclinical safety data

Preclinical safety data of Unidar-F Infusion in animals are not relevant since its constituents are physiological components in animal and human plasma.

Toxic effects are not to be expected under the condition of clinical application.

The safety of potential additives should be considered separately

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections

6.2 Incompatibilities

As with all parenteral solutions additives may be incompatible. Compatibility of the additives with the Unidar-F Infusion and LDP container must be assessed before addition. After the addition of the additive, incompatibility may become visible by a possible colour change and/or the appearance of precipitates, insoluble complexes or crystals.

The Instructions for the Use of Medication to be added and other relevant literature must be consulted.

When making additions to the solution, aseptic technique must be used. Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives.

Additives known or determined to be incompatible should not be used.

6.3 Shelf life:

3 years

6.4 Special precautions for storage:

Do not store above 30°C

6.5 Nature and contents of container

LDPE (Low-density polyethylene) bottle.

Pack sizes: 500ml.

The bottle is overwrapped with nylon wrapper composed of Plain Biaxially Oriented Polypropylene (Plain BOPP). The bottles are packed into cardboard cartons containing 20 x 500ml bottles per carton.

6.6 Special precautions for disposal and other handling

After opening the container, the contents should be used immediately and should not be stored for a subsequent infusion.

Discard after single use.

Discard any unused portion.

Opening

- Remove the LDPE bottle from the nylon wrapper just before use.
- Check for minute leaks by squeezing inner bottle firmly. If leaks are found, discard solution, as sterility may be impaired
- Check the solution for clarity and absence of foreign matter. If the solution is not clear or contains foreign matter, discard the solution.

Preparation for administration

Use sterile material for preparation and administration.

- Use an aseptic method to set up the infusion.

Techniques for injection of additive medications

Warning: Some additives may be incompatible. Check additive compatibility with both the solution and container prior to use. When additive is used, verify isotonicity prior to parenteral administration. Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored.

7. APPLICANT/HOLDER OF CERTIFICATE PRODUCT REGISTRATION.

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8. DRUG PRODUCT MANUFACTURER

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9. NAFDAC REGISTRATION NUMBER(S)

04-0336

10. DATE OF REVISION OF THE TEXT

22/02/2028