Summary of Product Characteristics for Pharmaceutical Product

1. Name of the medicinal product

Tasaline 0.45% D5 - Sodium Chloride 0.45% and Glucose 5% Solution for Infusion

2. Qualitative and quantitative composition

Each 1ml solution for infusion contains 4.5mg Sodium Chloride and 50mg Glucose (as monohydrate)
This is equivalent to 154mmol/l of Sodium ions and 154mmo/l of chloride ions.
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Clear, colorless to straw colored Solution for infusion
Osmolarity: 432mOsm/l (approx.)
pH: 3.5 to 6.5

4. Clinical particulars

4.1 Therapeutic indications

Sodium Chloride 0.45 % w/v and Glucose 5% w/v solution is indicated for:
Treatment of dehydration or hypovolaemia in cases where supply of water, sodium chloride and carbohydrates is required due to restriction of the intake of fluids and electrolytes by normal routes.

4.2 Posology and method of administration

The choice of the specific sodium chloride and glucose concentration, dosage, volume, rate and duration of administration depends on the age, weight, clinical condition of the patient and concomitant therapy. It should be determined by a physician. For patients with electrolyte and glucose abnormalities and for paediatric patients, consult a physician experienced in intravenous fluid therapy.

Fluid balance, serum glucose, serum sodium and other electrolytes should be monitored before and during administration, especially 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 hyponatraemia. Monitoring of serum sodium is particularly important for physiologically hypotonic fluids. Sodium Chloride 0.45 % w/v and Glucose 5% w/v solution may become extremely hypotonic after administration due to glucose metabolization in the body (see sections 4.4, 4.5 and 4.8).

Rapid correction of hyponatraemia and hypernatremia is potentially dangerous (risk of serious neurologic complications). Electrolyte supplementation may be indicated according to the clinical needs of the patient
Adults, older patients and adolescents (age 12 years and over):
The recommended dosage is: 500ml to 3L/24h

<u>Administration rate:</u>

The infusion rate is usually 40 ml/kg/24h and should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycaemia. Therefore, the maximum acute administration rate is 5 mg/kg/min.

Paediatric population
The dosage and administration rate varies with weight

Paediatric population		
Body Weight	Dosage	Administration Rate
0-10 kg	100ml/kg/24h	6-8ml/kg/h
10-20 kg	1000ml + (50ml/kg over 10kg)/24h	4-6ml/kg/h
> 20 kg	1500ml + (20ml/kg over 20kg)/24h	2-4ml/kg/h

The infusion rate should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycaemia. Therefore, the maximum acute administration rate is 10-18 mg/kg/min depending on the total body mass.

For all patients, a gradual increase of flow rate should be considered when starting administration of glucose containing products.

Method of administration

The administration is performed by intravenous infusion.

Sodium chloride 0.45% w/v and Glucose 5% w/v solution is hypotonic and hyperosmolar, due to the glucose content. It has an approximate osmolarity of 432 mOsmol/l.

Precautions to be taken before manipulating or administering the product

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not administer unless the solution is clear and the seal is intact. Administer immediately following the insertion of infusion set. Do not remove unit from overwrap until ready for use. The inner bag maintains the sterility of the product.

The solution should be administered with sterile equipment using an aseptic technique.

The equipment should be primed with the solution in order to prevent air entering the system. Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

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 or during infusion through the resealable medication port. When additive is used, verify tonicity prior to parenteral administration. Hyperosmolar solutions may cause venous irritation and phlebitis. Thus, any hyperosmolar solution is recommended to be administered through a large central vein, for rapid dilution of the hyperosmotic solution

For further information on the product with additives, please see sections 6.2, 6.3 and 6.6.

4.3 Contraindications

The solution is contraindicated in patients presenting with:

- Known hypersensitivity to the product
- Extracellular hyperhydration or hypervolaemia
- Fluid and sodium retention
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac failure
- Hypernatremia or hyperchloremia
- General oedema and ascitic cirrhosis

Clinically significant hyperglycaemia. The solution is also contraindicated in case of uncompensated diabetes, other known glucose intolerances (such as metabolic stress situations), hyperosmolar coma or hyperlactataemia.

4.4 Special warnings and precautions for use

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization (see section 4.2).

Depending on the tonicity of the solution, the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolize glucose, intravenous administration of glucose can cause electrolyte disturbances most importantly hypo- or hyperosmotic hyponatraemia.

Hyponatraemia
The infusion of solutions with sodium concentrations <0.9% may result in hyponatraemia. Close clinical monitoring may be warranted.

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 (brain oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain 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, and cerebral contusion) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia

Hypokalaemia
The infusion of Sodium chloride 0.45% w/v and Glucose 5% w/v solution may result in hypokalaemia. This medicine should be used with particular caution in patients with or at risk for hypokalemia. Close clinical monitoring may be warranted in patients with or at risk for hypokalaemia, for example:
Persons with metabolic alkalosis
Persons with thyrotoxic periodic paralysis. Administration of intravenous glucose

has been associated in aggravating hypokalaemia
Persons with increased gastrointestinal losses (e.g., diarrhoea, vomiting)
Prolonged low potassium diet
Persons with primary hyperaldosteronism
Patients treated with medications that increase the risk of hypokalaemia (e.g., diuretics, beta-2 agonists or insulin)

Sodium retention, fluid overload and oedema
Sodium Chloride 0.45 % w/v and Glucose 5.0 % w/v solution should be used with particular caution, in:

• Patients with conditions that may cause sodium retention, fluid overload and oedema (central and peripheral), such as
Primary hyperaldosteronism,
Secondary hyperaldosteronism associated with, for example,
hypertension,
congestive heart failure,
liver disease (including cirrhosis),
renal disease (including renal artery stenosis, nephrosclerosis)
Pre-eclampsia.

• Patients taking medications that may increase the risk of sodium and fluid retention, such as corticosteroids

Hypo- and Hyperosmolality, serum electrolytes and water imbalance
Depending on the volume, rate of infusion, the patient's underlying clinical condition and capability to metabolize glucose, administration of Sodium chloride 0.45% w/v and Glucose 5% w/v solution can cause:
Hypo-osmolality, Hyperosmolality, osmotic diuresis and dehydration
Electrolyte disturbances such as
hyponatraemia (see above)
hypokalaemia (see above)
hypophosphatemia,
hypomagnesaemia,
Overhydration/hypervolaemia and, for example, congested states, including central (e.g. pulmonary congestion) and peripheral oedema.

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.

Hyperglycaemia
Rapid administration of glucose solutions may produce substantial hyperglycaemia and hyperosmolar syndrome. In order to avoid hyperglycaemia, the infusion rate should not exceed the patient's ability to utilize glucose.

To reduce the risk of hyperglycaemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient

Intravenous glucose should be administered with caution in patients with, for example:
Impaired glucose tolerance (such as in diabetes mellitus, renal impairment, or in

the presence of sepsis, trauma, or shock),
Severe malnutrition (risk of precipitating a refeeding syndrome, see below),
Thiamine deficiency, e.g., in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolism of pyruvate),
Water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load

Other groups of patients in whom Sodium chloride 0.45% w/v and Glucose 5% w/v solution should be used with caution include:
Patients with ischemic stroke. Hyperglycaemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes.
Patients with severe traumatic brain injury (in particular during the first 24 hours following the trauma). Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury.
New-borns (See Paediatric glycaemia-related issues).

Prolonged intravenous administration of glucose and associated hyperglycaemia may result in decreased rates of glucose-stimulated insulin secretion.

Hypersensitivity Reactions
Hypersensitivity/infusion reactions, including anaphylaxis, have been reported (see section 4.8).
Stop the infusion immediately if signs or symptoms of hypersensitivity/infusion reactions develop

Appropriate therapeutic countermeasures must be instituted as clinically indicated.
Solutions containing glucose should be used with caution in patients with known allergy to corn or corn products

Refeeding syndrome
Refeeding severely undernourished patients may result in the refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intake while avoiding overfeeding can prevent these complications.

Severe renal impairment
Sodium chloride 0.45% w/v and Glucose 5% w/v solution should be administered with particular caution to patients at risk of (severe) renal impairment. In such patients, administration may result in sodium retention and/or fluid overload.

<u>Paediatric use</u>
The infusion rate and volume depend on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy, and should be determined by a physician experienced in paediatric intravenous fluid therapy.

Paediatric glycaemia-related issues
New-borns, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia. Close monitoring during treatment with intravenous glucose solutions is needed to ensure adequate glycaemic control, in order to avoid potential long term adverse effects.
Hypoglycaemia in the new-born can cause, e.g., prolonged seizures, coma, and cerebral injury

- Hyperglycaemia has been associated with cerebral injury, including intraventricular haemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotizing enterocolitis, increased oxygen requirements, prolonged length of hospital stay, and death.

Paediatric hyponatraemia-related issues
Children (including neonates and older children) are at increased risk of developing hyponatraemia as well as for developing hyponatraemic encephalopathy.
Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death; therefore, acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.
Plasma electrolyte concentrations should be closely monitored in the paediatric population
Rapid correction of hyponatraemia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in paediatric intravenous fluid therapy
Blood
Sodium chloride 0.45% w/v and Glucose 5% w/v solution should not be administered simultaneously with blood through the same administration set because of the possibility of pseudo-agglutination or haemolysis.

Geriatric use
When selecting 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.

4.5 Interaction with other medicinal products and other forms of interaction

Both the glycaemic and effects on water and electrolyte balance should be taken into account when administering Sodium chloride 0.45% w/v and Glucose 5% w/v solution to patients treated with other substances that affect glycaemic control, or fluid and/or electrolyte balance.

Drugs leading to an increased vasopressin effect
The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with IV fluids (see sections 4.2, 4.4 and 4.8).
Drugs stimulating vasopressin release, e.g.: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics
Drugs potentiating vasopressin action, e.g.: Chlorpropamide, NSAIDs, cyclophosphamide
Vasopressin analogues, e.g.: 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 and can result in decreased lithium levels.
corticosteroids, which are associated with the retention of sodium and water (with oedema and hypertension).
diuretics, beta-2 agonists or insulin, whom increase the risk of hypokalaemia

certain antiepileptic and psychotropic medications that increase the risk of hyponatraemia

4.6 Fertility, pregnancy and lactation

Pregnancy
Intrapartum maternal intravenous glucose infusion may result in foetal hyperglycaemia and metabolic acidosis as well as rebound neonatal hypoglycaemia due to foetal insulin production.

Sodium Chloride 0.45 % w/v and Glucose 5.0 % w/v solution should be administrated with special caution for pregnant women during labour particularly if administered in combination with oxytocin due to the risk of hyponatraemia (see sections 4.4, 4.5 and 4.8).

Fertility
There is no information on the effects of Sodium chloride 0.45% w/v and Glucose 5% w/v solution on fertility

Lactation
Sodium chloride 0.45% w/v and Glucose 5% w/v solution can be used during breast-feeding.
The potential risks and benefits for each specific patient should be carefully considered before administration.

Sodium chloride 0.45% w/v and Glucose 5% w/v solution should be administrated with special caution for pregnant women during labour particularly if administered in combination with oxytocin due to the risk of hyponatraemia (see section 4.4, 4.5 and 4.8).

4.7 Effects on ability to drive and use machines

There is no information on the effects of Sodium chloride 0.45% w/v and Glucose 5% w/v solution on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects

Tabulated summary of adverse reactions
Adverse events are listed below by system organ class and frequency. The following adverse reactions have been reported in post-marketing experience.

Term	**Frequency of occurrence**
Very common	(≥1/10)
Common	(≥1/100 to <1/10)
Uncommon	(≥1/1 000 to <1/100)
Rare	(≥1/10 000 to <1/1 000)
Very rare	(<1/10 000)
Not known	(Cannot be estimated from the available data)

System Organ Class	**Frequency**	**Undesirable effects**
Immune system disorders	Not Known	Anaphylactic reaction, * hypersensitivity*

Metabolism and nutrition disorders	Not Known	Hypernatremia, hyperglycaemia, Hospital acquired hyponatraemia**
Nervous system disorders	Not Known	Hyponatraemic encephalopathy**
Vascular disorders	Not Known	Phlebitis
Skin and subcutaneous tissue disorders	Not Known	Rash, Pruritus
General disorders and administration site conditions	Not Known	Infusion site reactions, including • Pyrexia • Chills • Infusion site pain • Infusion site vesicles
Potential manifestation in patients with allergy to corn, see section 4.4** * Hospital acquired hyponatraemia may cause irreversible brain injury and death due to development of acute hyponatraemic encephalopathy (see sections 4.2 and 4.4).**		

Other adverse reactions reported with isotonic saline and glucose infusions include:

- Hyponatraemia, which may be symptomatic
- Hyperchloremic acidosis

Adverse reactions may be associated to the medicinal product(s) added to the solution; the nature of the additive will determine the likelihood of any other adverse reactions.

4.9 Overdose

Excess administration of Sodium chloride 0.45% w/v and Glucose 5% w/v solution can cause:

- Hyperglycaemia, adverse effects on water and electrolyte balance and corresponding complications. For example, severe hyperglycaemia and severe dilutional hyponatraemia and their complications, can be fatal.
- Hyponatraemia (which can lead to CNS manifestations, including seizures, coma, cerebral oedema and death).
- Hypernatremia especially in patients with renal impairment.
- Fluid overload (which can lead to central and/or peripheral oedema).
- See also sections 4.4 and 4.8

A clinically significant overdose of Sodium chloride 0.45% w/v and Glucose 5% w/v solution may, therefore, constitute a medical emergency

When assessing an overdose, any additives in the solution must also be considered.

Interventions include discontinuation of Sodium chloride 0.45% w/v and Glucose 5% w/v solution administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group “Electrolytes with Carbohydrates”,

ATC code: “B05BB02”.

Sodium Chloride 0.45% w/v and Glucose 5% w/v is an isotonic and hyperosmolar solution.
The pharmacodynamic properties of this solution are those of its components (glucose, sodium and chloride).

Ions, such as sodium, circulate through the cell membrane, using various

mechanisms of transport, among which is the sodium pump (Na+/K+-ATPase). Sodium plays an important role in neurotransmission and cardiac electrophysiology, and also in renal metabolism.

Chloride is mainly an extracellular anion. Intracellular chloride is in high concentration in red blood cells and gastric mucosa. Reabsorption of chloride follows reabsorption of sodium.

Glucose is the principal source of energy in cellular metabolism. The glucose in this solution provides a caloric intake of 200kcal/l.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of this solution are those of its components (glucose, sodium and chloride).

After injection of radio sodium (24Na), the half-life is 11 to 13 days for 99% of the injected Na and one year for the remaining 1%. The distribution varies according to tissues: it is fast in muscles, liver, kidney, cartilage and skin; it is slow in erythrocytes and neurones; it is very slow in the bone. Sodium is predominantly excreted by the kidneys, but (as described earlier) there is extensive renal reabsorption. Small amounts of sodium are lost in the faeces and sweat.

The two main metabolic pathways of glucose are gluconeogenesis (energy storage) and glycogenolysis (energy release). Glucose metabolism is regulated by insulin.

5.3 Preclinical safety data

Preclinical safety data of this solution for infusion in animals are not relevant since its constituents are physiological components of 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

Sodium hydroxide
Hydrochloric acid
Water for Injections.

6.2 Incompatibilities

As with all parenteral solutions compatibility of the additives with the solution must be assessed before addition. In the absence of compatibility studies, this solution must not be mixed with other medicinal products. Those additives known to be incompatible should not be used.

The instructions for use of the medicinal product to be added must be consulted.

Before adding a drug, verify it is soluble and stable in water at the pH of Sodium Chloride 0.45% w/v and Glucose 5% w/v solution (see section 3).

As guidance, the following medications are incompatible with the Sodium Chloride 0.45 % w/v & Glucose 5% w/v solution (non-exhaustive listing):

- Ampicillin sodium
- Mitomycin
- Amphotericin B

- Erythromycin lactobionate
- Human Insulin

Those additives known to be incompatible should not be used.

Because of the presence of glucose, Sodium chloride 0.45% w/v and Glucose 5% w/v solution should not be administered simultaneously with blood through the same administration set because of the possibility of pseudo-agglutination or haemolysis

6.3 Shelf life

Shelf life unopened 2 years
It is recommended that the product is used immediately once opened (see section 4.2).

In-use shelf life: Additives
From a physico-chemical viewpoint, solution containing additives should be used immediately unless chemical and physical in-use stability has been established.

From a microbiological point of view, solutions containing additives should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Bag sizes: 250ml, 500ml or 1000 ml
The bags are composed of polyolefin/polyamide co-extruded plastic.
The bags are overwrapped with a protective tri-laminate pouch.

6.6 Special precautions for disposal and other handling

Please see section 4.2 for information regarding the method of administration.
Discard after single use.
Discard any unused portion.
Do not reconnect partially used bags.
Do not remove unit from overwrap until ready for use. The inner bag maintains the sterility of the product.

Instructions for use

Opening

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

Preparation for administration
Use sterile material for preparation and administration.

- Suspend container from eyelet support.
- Remove plastic protector from outlet port at bottom of container:
- Use an aseptic method to set up the infusion.

- Attach administration set. Refer to directions of the accompanying set for connection, priming of the set and administration of the solution.

Techniques for injection of additive medications
Warning: Additives may be incompatible.
To add medication before administration

- Disinfect medication site.
- Using syringe with 19-gauge (1.10 mm) to 22-gauge (0.70 mm) needle, puncture resealable medication port and inject.
- Mix solution and medication thoroughly. For high-density medication such as potassium chloride, tap the ports gently while ports are upright and mix.

Caution: Do not store bags containing added medications.
To add medication during administration

- Close clamp on the set
- Disinfect medication site.
- Using syringe with 19-gauge (1.10 mm) to 22-gauge (0.70 mm) needle, puncture resealable medication port and inject.
- Remove container from IV pole and/or turn to an upright position.
- Evacuate both ports by tapping gently while the container is in an upright position.
- Mix solution and medication thoroughly.
- Return container to in use position, re-open the clamp and continue administration.
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7. **Marketing authorization holder and manufacturing site addresses**

Marketing authorisation holder
Tasa Pharma Limited
Unit C1-C3
Kay complex
Nairobi
Kenya

Manufacturing site address:
Tasa Pharma Limited
Unit C1-C3
Kay complex
Nairobi

8. **Marketing authorization number**
CTD10272

9. **Date of first registration**
20/06/2023

10. **Date of revision of the text:**
11/2024