DIRECTIONS FOR USE

0084/12622546/0424

B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P.

1. NAME OF THE MEDICINAL PRODUCT

B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution for infusion contains:

Sodium chloride	4.5 g
Glucose monohydrate	55.00 g
equivalent to glucose	50.00 g

Electrolyte concentrations:

Sodium	77 mmol/l
Chloride	77 mmol/l

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion. A clear and colourless or faintly straw-coloured solution.

Energy	835 kJ/l ≙ 200 kcal/l
Theoretical osmolarity:	432 mOsm/l
Acidity (titration to pH 7.4):	< 0.5 mmol/l
pH:	3.5 – 5.5

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- Isotonic dehydration
- Hypertonic dehydration
- Vehicle solution for compatible medicinal products
- Partial coverage of energy requirements

4.2 Posology and Method of Administration

Posology

Adults

The dose is adjusted according to the individual requirements of fluid, electrolyte and energy. Thus the patients' age, weight, clinical and biological (acid-base balance) conditions and concomitant therapy should be taken into account. Fluid balance, serum glucose, serum sodium and other electrolytes may need to 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. B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P. may become hypotonic after administration due to glucose metabolisation in the body (see sections 4.4. 4.5 and 4.8).

Maximum daily dose:

Up to 40 ml/kg body weight per day

Any additional losses (due to e.g. fever, diarrhoea, vomiting, etc.) should be substituted according to the volume and composition of the lost fluids.

In case of dehydration the dose of 40 ml/kg body weight (BW) per day might need to be exceeded. The dose should be calculated based on the severity of the dehydration and the clinical condition of the patient.

Maximum infusion rate:

Up to 5 ml per kg body weight per hour.

In the treatment of hypertonic dehydration, the correction of sodium levels must not exceed 0.5 mmol/l/hour. Faster decrease of serum sodium level can cause brain oedema.

Paediatric population

The dosage depends on the age, weight, clinical and biological (acid-base balance) conditions of the patient, concomitant therapy and should be determined by the consulting specialist.

As children are at a higher risk of developing hyponatraemia, this solution should be used with caution and close monitoring of fluid balance and serum electrolytes (especially the serum sodium level) in paediatric patients.

Maximum daily dose

For routine maintenance the following daily doses should not be exceeded:

Age	Doses (ml/kg BW/d)
1st day of life *	120
2nd day of life *	120
3rd day of life *	130
4th day of life *	150
5th day of life *	160
6th day of life *	180
1st month of life	160
from 2nd month of life	150
1-2 years	120
3- 5 years	100
6-12 years	80
13-18 years	70

* for term neonates

Any additional losses (due to e.g. fever, diarrhoea, vomiting) should be substituted according to the volume and composition of the lost fluids.

The dose should be calculated based on the severity of the dehydration and the clinical condition of the patient.

Maximum infusion rate

For routine maintenance the following infusion rates should not be exceeded.

BW (kg)	ml/hour
0 - 10	4/kg
11 - 20	40 + 2/kg for each kg > 10
> 20	60 + 1/kg for each kg > 20

Elderly patients

Basically the same dosage as for adults applies, but caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that may frequently be associated with advanced age.

Other special patient groups

If the oxidative metabolism of glucose is impaired (e.g. in the early post-operative or posttraumatic period or in the presence of hypoxia or organ failure), the dosage should be adjusted to keep the blood glucose level close to normal values. Close monitoring of blood glucose levels is recommended in order to prevent hyperglycaemia. See also section 4.4.

Method of administration

Intravenous use.
This solution is not generally suitable for fluid and electrolyte supply over extended periods of time without additional administration of sodium containing medicinal products or infusions in the setting of the complete therapy scheme. Long-term administration of this solution alone may provoke disorders of fluid and electrolyte balance, dependent on kidney function.

4.3 Contraindications

- Hyperhydration
- Hypotonic dehydration
- Head trauma (first 24 hours)
- Persistent hyperglycaemia not responding to insulin doses of up to 6 units/hour.
- Hyponatraemia
- Severe renal insufficiency with oligo- or anuria
- Acute congestive heart failure

Due to the risk of hyponatraemia the product must not be used in paediatric patients with the non-osmotic secretion of ADH (in pain, anxiety, the post-operative state, nausea, vomiting, pyrexia, sepsis, reduced circulating volume, respiratory disorders, CNS infections, and metabolic and endocrine disorders).

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 metabolisation (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 metabolise glucose, intravenous administration of glucose can cause electrolyte disturbances most importantly hypo- or hyperosmotic hyponatraemia.

Hyponatraemia:

Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, bums, 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.

Due to the risk of developing a severe lactic acidosis and/or a Wernicke encephalopathy a preexisting thiamin (Vitamin B1) deficiency must be corrected before infusion of glucose containing solutions.

Compared to metabolically healthy persons, glucose tolerance is reduced in patients with metabolic alterations being characteristic for the post-operative/post-traumatic phase (post-aggression metabolism). The older the patient and the more severe his/her underlying disease, operation or injury, the more frequently metabolic disorders may develop as a part of the post-aggression metabolism that are similar to diabetes.

Administration in post-operative and post-traumatic patients and patients suffering from other causes of glucose intolerance is recommended only if blood glucose levels are adequately monitored (see also section 4.2). B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P. is indicated in clinical situations where glucose utilisation disorders frequently occur. For this reason, administration of insulin may be required.

B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P. should only be administered with caution and with careful monitoring in patients with renal insufficiency.

Caution should be taken in patients with hypokalaemia as this solution may aggravate the condition.

Administration of glucose solutions is not recommended after acute ischaemic strokes as hyperglycaemia was reported to worsen ischaemic brain damage and impair recovery.

Clinical monitoring should include checks of the serum electrolytes (especially potassium and sodium), glucose level, the acid-base and water balance.

The solution should not be administered through the same infusion equipment simultaneously, before or after an administration of blood because of the possibility of pseudo-agglutination see section 6.2.

Use as vehicle solution

Please note: If this solution is used as vehicle solution the safety information of the additive provided by the respective manufacturer have to be taken into account.

Paediatric population

Intravenous fluid therapy should be closely monitored in the paediatric population as they may have impaired ability to regulate fluids and electrolytes. Children are at an especially high risk of developing hyponatraemia following the administration of hypotonic solutions. Adequate urine flow must be ensured and careful monitoring of fluid balance, plasma and urinary electrolyte concentrations are essential.

Newborns and preterm neonates with low birth weight have an increased risk of hypo- or hyperglycaemia. Close monitoring of the blood glucose level is mandatory during administration of glucose containing infusions, to avoid long-term undesirable effects.

Elderly patients:

Elderly patients are more likely to suffer from cardiac insufficiency and renal impairment, and therefore should be closely monitored during treatment, and the dosage should be carefully adjusted, in order to avoid cardiocirculatory and renal complications resulting from fluid overload.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Medicinal products causing sodium retention

The concomitant use of sodium-retaining drugs (e.g. corticosteroids, non-steroidal anti-inflammatory agents) may lead to oedema.

Medicinal products influencing the glucose metabolism

Interactions with medicinal products influencing the glucose metabolism e.g. corticosteroids should be considered.

Medicinal products 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 i. v. 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, vasopressin, terlipressin

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

4.6 Fertility, Pregnancy and Lactation

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of sodium chloride and glucose in pregnant women. Animal studies relating to physiological amounts of glucose and sodium chloride do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3).

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Approval for Printing

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As all components of the solution are naturally present in the body the product can be used if indicated.

However, B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P. 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).

Caution should be exercised when prescribing to pregnant women especially in the presence of pre-eclampsia.
Careful monitoring of blood glucose is necessary.

Breast-feeding

As all components of this solution are naturally present in the body the product can be used if indicated. However, it is known that glucose/metabolites are excreted in human milk, but at therapeutic doses of B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P. no effects on the breastfed newborns/infants are anticipated.

Fertility

No data available.

4.7 Effects on Ability to Drive and Use Machines

This medicinal product has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable Effects

Undesirable effects are listed according to their frequencies as follows:

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)

Metabolism and nutrition disorders:

Not known: Hospital Acquired Hyponatraemia

Neurological disorders:

Not known: Hyponatraemic encephalopathy

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

Local reactions at injection/infusion site may be associated to the technique of administration.

4.9 Overdose

Symptoms

Overdose or too fast administration of this solution may result in hypotonic hyperhydration, increased skin tension, venous congestion and oedema possibly leading to lung or brain oedema. Disturbances of electrolyte balances and acid-base imbalances may occur. Furthermore, overdose can lead to hyperglycaemia, glucosuria, dehydration, serum hyperosmolarity and hyperglycaemic-hyperosmolar coma.

Treatment

Depending on the severity of the disorders immediate stop of infusion, administration of diuretics with continuous monitoring of serum electrolytes, correction of electrolyte and acid-base imbalances, administration of insulin if necessary.

In severe cases of overdose dialysis may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Solutions affecting the electrolyte balance
ATC code: B05B B02 (Electrolytes with carbohydrates)

Mechanism of action

The solution contains equimolar proportions of sodium and chloride corresponding to half the physiological concentration in the plasma.

In addition the solution also contains 5 % (w/v) of carbohydrate in the form of glucose.

Sodium is the primary cation of the extracellular space and together with various anions, regulates the size of this. Sodium and potassium are the major mediators of bioelectric processes within the body.

Pharmacodynamic effect

The sodium content and the liquid metabolism of the body are closely coupled to each other. Each deviation of the plasma sodium concentration from the physiological one simultaneously affects the fluid status of the body.

Glucose is metabolized ubiquitously as the natural substrate of the cells of the body. Under physiological conditions glucose is the most important energy-supplying carbohydrate with a caloric value of ca. 17 kJ or 4 kcal/g. Nervous tissue, erythrocytes and medulla of the kidneys are amongst the tissues with an obligate requirement for glucose.

Glucose serves for the synthesis of glycogen as the storage form of carbohydrates. It is subject to glycolysis to pyruvate and lactate for energy production in the cells.

Glucose also serves to maintain the blood glucose level and for the synthesis of important body components such as glycoproteins and DNA. It is primarily insulin, glucagon, glucocorticoids and catecholamines that are involved in the regulation of the blood glucose concentration.

A normal electrolyte and acid-base status is a prerequisite for the optimal utilization of administered glucose. So an acidosis, in particular, can indicate impairment of the oxidative glucose metabolism.

There are close metabolic relationships between the electrolytes and carbohydrate metabolism; potassium, in particular, is affected. The utilization of glucose is associated with an increased potassium requirement. Not taking this relationship into account can lead to considerable disturbances of potassium metabolism, which can, amongst other things, lead to massive cardiac arrhythmia.

5.2 Pharmacokinetic Properties

Absorption

As the solution is administered by intravenous infusion the bioavailability of the solution is 100%.

Distribution

The total sodium content of the body is approx. 80 mmol per kg body weight, of which approx. 95% is extracellular.

In adults, the concentration of glucose in the blood is 70 – 100 mg/100 ml, or 3.9 – 5.6 mmol/l (fasting).

On infusion glucose is first distributed in the intravascular space and then is taken up into the intracellular space.

Biotransformation

In glycolysis, glucose is metabolized to pyruvate. Under aerobic conditions pyruvate is completely oxidized to carbon dioxide and water. In case of hypoxia pyruvate is converted to lactate. Lactate can be partially re-introduced into the glucose metabolism (Cori cycle).

Elimination

The kidneys are the major regulator of the sodium and water balances. In co-operation with the hormonal control mechanisms (renin-angiotensin-aldosterone system, antidiuretic hormone) and the hypothetical natriuretic hormone they are primarily responsible for keeping the volume of the extracellular space constant and regulating its fluid composition.

Chloride is exchanged for hydrogen carbonate in the tubule system and is, thus, involved in the regulation of the acid base balance.

The final products of the complete oxidation of glucose are eliminated via the lungs (carbon dioxide) and the kidneys (water).

Practically no glucose is excreted renally in normoglycaemic conditions. If blood glucose concentration exceeds the maximum tubular resorption capacity (approximately 200 mg/dl) glucose is also excreted via the kidneys (glucosuria).

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.The solution should not be administered through the same infusion equipment simultaneously, before or after an administration of blood because of the possibility of pseudo-agglutination.

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

- Polyethylene (LDPE) bottles, contents: 500 ml, 1000 ml
  available in packs of 10 x 500 ml, 10 x 1000 ml

6.6 Special Precautions for Disposal, Other Instructions for Use and Handling

No special requirements for disposal

The container is for single use only. After use discard container and any remaining contents.

Do not re-connect partially used containers.

Only to be used if solution is clear and colourless or faintly straw-coloured and the container and its closure are undamaged

Before mixing any additive, the compatibility with B. Braun 0.45% Sodium Chloride & 5% Glucose IV Infusion B.P. must be confirmed. See also section 6.2.

7. DATE OF REVISION OF THE TEXT

04.2024

B BRAUN

Product registration holder and
manufactured by:
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