Direction for Use

B. Braun Medical Industries Sdn. Bhd. 11900 Bayan Lepas, Penang, Malaysia.

B. Braun 0.45% Sodium Chloride Intravenous Infusion B.P.

1. NAME OF THE MEDICINAL PRODUCT

B.Braun 0.45% Sodium Chloride Intravenous Infusion B.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contains

Sodium Chloride	4.5g

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 solution.

Theoretical osmolarity:	154 mOsm/l
pH	4.5 – 7.0

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Hypertonic dehydration,
- Vehicle solution for compatible medicinal products

4.2 Posology and method of administration

Posology

Adults

The dose is adjusted according to the actual requirements of water and electrolytes. Fluid balance, serum electrolytes and acid-base balance may need to 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 4.5 mg/ml B. Braun Solution for Infusion osmolarity: 154 mOsm/l

Maximum daily dose:

Up to 40 ml per kg body weight per day, corresponding to 3 mmol of sodium per kg body weight.

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

Infusion rate:

The infusion rate will depend on the conditions of the individual patient (see section 4.4) but should not exceed 5 ml/kg bw per hour corresponding to 1.7 drops/kg body weight per min.

In patients with chronic hypernatraemia the serum sodium concentration should not be lowered faster than 0.5 mmol/l/h.

Vehicle solution

When Sodium Chloride 4.5 mg/ml is used as vehicle solution, the dosage and the infusion rate will be principally guided by the nature and the dosage regimen of the additive.

Elderly population

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.

Paediatric population

The dose has to be adjusted according to the individual need of water and electrolytes as well as the patient`s age, weight and clinical condition.

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

Method of administration

Intravenous use

4.3 Contraindications

Sodium Chloride 4.5 mg/ml must not be administered to patients in states of

- hyperhydration or hypervolaemia
- hypotonic dehydration
- acute congestive heart failure,
- severe renal insufficiency (with oligo or anuria)
- ascetic cirrhosis and generalised oedema
- hyponatraemia
- hypochloraemia

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

Special warnings

0.45 % w/v Sodium Chloride Intravenous Infusion should only be administered with caution in cases of

- disorders where restriction of sodium intake is indicated, such as cardiac insufficiency, generalized oedema, pulmonary oedema, hypertension, pre-eclampsia, renal insufficiency.
- hypokalaemia,
- cortical adrenal hyperfunction,

High volume infusions must only be used under specific monitoring and caution in patients with cardiac, renal or pulmonary failure, lung or brain oedema, 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.

In patients with chronic hypernatraemia the serum sodium concentration should not be lowered faster than 0.5 mmol/l/h.

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

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

Paediatric population

Premature or term infants may retain an excess of sodium due to immature renal function. In premature or term infants, repeated infusion of sodium chloride should therefore only be given after determination of the serum sodium level. Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes. The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death, therefore acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

4.5 Interactions 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.

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

4.6 Pregnancy and lactation

Pregnancy

There are limited or no data regarding the use of Sodium Chloride 4.5 mg/ml in pregnant women. These data do not indicate direct or indirect harmful effects of Sodium Chloride 4.5 mg/ml with respect to reproductive toxicity (see section 5.3).

As the concentrations of sodium and chloride are half of that in human body no harmful effects are to be expected if the product is used as indicated.

Therefore, Sodium Chloride 4.5 mg/ml can be used if indicated.

Sodium Chloride 4.5 mg/ml B. Braun Solution for 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).

Caution has to be exercised in the presence of pre-eclampsia (see section 4.4).

Breast-feeding

As the concentration of sodium and chloride are half of that in human body no harmful effects are to be expected if the product is used as indicated.

Sodium Chloride 4.5 mg/ml can be used during breast-feeding, if required.

Fertility

No data available

4.7 Effects on ability to drive and use machines

Sodium Chloride 4.5 mg/ml 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).

Due to the low pH of the solution, local reactions at the infusion site including local pain and venous irritation may occur.

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4.9 Overdose

Symptoms

Overdose of Sodium Chloride 4.5 mg/ml may result in dilution of serum electrolytes, hyperhydration, electrolyte disturbances and acid-base imbalances. Further, retention of excess sodium, when renal disorder is present, may result in pulmonary and peripheral oedema and excessive administration of chloride salts may cause a loss of bicarbonate with an acidifying effect.

Signs of overdose can be due to resulting hyponatraemia e.g. headache, lethargy, dizziness, ataxia, confusion, psychosis, seizures or coma. Furthermore, symptoms can be directly related to fluid overload e.g. pulmonary oedema, pleural effusion, shortness of breath or peripheral oedema.

Treatment

The infusion must be stopped immediately. Further treatment depends on the nature and severity of symptoms and may include administration of diuretics. Serum electrolytes should be continuously monitored. Measures must be taken to correct any acid-base then electrolyte imbalances.

In severe cases of overdose or in case of oligo- or anuria dialysis may become necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions affecting the electrolyte balance, electrolytes
ATC- code: B05B B01

Mechanism of action

Sodium is the primary cation of the extracellular space and together with various anions, regulates the size of this. Sodium is one of the major mediators of bioelectric processes within the body.
Chloride is the principal osmotic active anion in the extracellular space.

Pharmacodynamic effects

0.45% NaCl is intended to be used as a parenteral fluid and for electrolyte restoration in patients with hypertonic dehydration. The solution contains equimolar proportions of sodium and chloride corresponding to half the physiological concentration in the plasma in order to replace free-water loss.

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 ca. 80 mmol/kg of which ca. 97 % is extracellular and ca. 3% intracellular. The daily turnover is ca. 100 - 180 mmol (corresponding to 1.5 - 2.5 mmol/kg body weight

The total body chloride in adults is about 33 mmol/kg body weight. Serum chloride is maintained at 98 – 108 mmol/l.

Biotransformation

Although sodium and chloride is absorbed, distributed, and excreted, there is no metabolism in the strict sense.

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.

Elimination

Sodium and chloride ions are excreted via sweat, urine and gastrointestinal tract.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Water for injections

6.2 Incompatibilities

When mixing with other medicinal products, possible incompatibilities should be considered.

6.3 Shelf Life

Unopened:

3 years

– after first opening

Not applicable, see also section 6.6.

– after dilution or addition of additives

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special Precautions for Storage

Do not store above 30 °C.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and Contents of Container

The product is supplied in

- polyethylene bottles,
  containing: 500 ml, 1000 ml available in sets of 10 x 500 ml, 10 x 1000 ml

6.6 Special precautions for disposal and other handling

Containers are for single use only. Discard container and any unused content after use.
Do not use if the solution is not clear, colourless or the container or its closure show visible signs of damage.

7 DATE OF REVISION OF THE TEXT

11.2022

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Product registration holder and
manufactured by:
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