ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Neoatricon 1.5 mg/mL solution for infusion
Neoatricon 4.5 mg/mL solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Neoatricon 1.5 mg/mL solution for infusion

Each mL of solution contains 1.5 mg of dopamine hydrochloride.
Each vial contains 45 mg of dopamine hydrochloride in 30 mL.

Excipient with known effect
Each vial contains 9 mg sodium metabisulfite.

Neoatricon 4.5 mg/mL solution for infusion

Each mL of solution contains 4.5 mg of dopamine hydrochloride.
Each vial contains 225 mg of dopamine hydrochloride in 50 mL.

Excipient with known effect
Each vial contains 15 mg of sodium metabisulfite.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion

The solution is clear and colourless to pale yellow with a pH of 2.8 to 4.5.

Neoatricon 1.5 mg/ mL solution for infusion: Osmolarity is 20 mOsmol/kg
Neoatricon 4.5 mg/ mL solution for infusion: Osmolarity is 50 mOsmol/kg

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of hypotension in haemodynamically unstable neonates, infants and children < 18 years.

4.2 Posology and method of administration

Consideration should be given to the haemodynamic state of the patient and the pharmacodynamic profile of dopamine hydrochloride (see section 5.1) before deciding whether dopamine hydrochloride is appropriate.

Administration of dopamine hydrochloride should always be indicated/prescribed by a paediatric specialist or paediatric intensive care specialists to whom facilities are available for monitoring cardiovascular and renal indices, including blood volume, cardiac output, blood pressure, electrocardiography and urine flow.

Posology

Pressor therapy is not a substitute for replacement of blood, plasma, fluids, and/or electrolytes. Blood volume depletion should be corrected as fully as possible before dopamine hydrochloride therapy is instituted (see section 4.4). Because of variable, age-dependent clearance, the dose should be titrated slowly and deliberately, particularly in neonates.

Infusion of dopamine hydrochloride solution should begin at a rate of 5 µg/kg/min and increase gradually in 5 µg/kg/min increments. The recommended dose range is 5 – 10 µg/kg/min. Doses above 10 µg/kg/min up to a maximum of 20 µg/kg/min may be administered if considered justified.

Dose of dopamine hydrochloride should be adjusted according to the patient's response, with particular attention to diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias as indications for decreasing or temporarily suspending the dose (see section 4.4).

For ease of dosing there are two different strengths for patients of different weight categories.

Infusion rates may be calculated using the following formula:

$$\text{Infusion Rate (mL/hour)} = \frac{\text{[Dose (µg/kg/minute) x Weight (kg) x 60 (minutes/hour)]}}{\text{Concentration (µg/mL)}}$$

An example is provided for each concentration at a relevant weight below:

Example 1: for a 5 kg person at the recommended initial dose of 5 mcg/kg/minute using a 1.5 mg /mL concentration, the infusion rate would be as follows:

$$\text{Infusion Rate (mL/hour)} = \frac{\text{[5 (µg/kg/minute) x 5 (kg) x 60 (minutes/hour)]}}{\text{1.500 (µg/mL)}} = 1.00 \text{ (mL/hour)}$$

Example 2: for a 30 kg person at the recommended initial dose of 5 mcg/kg/minute using a 4.5 mg /mL concentration, the infusion rate would be as follows:

$$\text{Infusion Rate (mL/hour)} = \frac{\text{[5 (µg/kg/minute) x 30 (kg) x 60 (minutes/hour)]}}{\text{4.500 (µg/mL)}} = 2.00 \text{ (mL/hour)}$$

Weaning and discontinuation
Dopamine hydrochloride should be discontinued gradually and should not be stopped abruptly. Haemodynamic status should be continually assessed during the weaning phase (see section 4.4).

Special populations

Hepatic and renal impairment
Because of the low rate of clearance, especially in the neonate, low doses of dopamine hydrochloride and slow deliberate titration should be employed (see section 4.4).

MAO inhibitors
Patients who have been treated with MAO inhibitors prior to dopamine hydrochloride should be given reduced doses; the starting dose should be 10 % of the usual dose (see section 4.4 and 4.5).

Method of administration

For intravenous use. Dopamine hydrochloride should be administered via a central line [Umbilical venous catheter (UVC), Longline, or Surgical central venous line (CVL)]. If no central access is available, a cannula in large vein should be used.
A suitable metering device is required in the infusion system to control the rate and flow.

Other infusions should not be co-infused into the dopamine hydrochloride line. Administration into a second injection site should be used to avoid mixing of potent medicinal products with dopamine hydrochloride (see sections 4.4 and 6.2).

Single use only. For instructions on handling of the medicinal product before administration see section 6.6.

4.3 Contraindications

- Patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients with phaeochromocytoma or hyperthyroidism.
- Presence of uncorrected atrial or ventricular tachyarrhythmias or ventricular fibrillation.
- Combination with cyclopropane and halogenated hydrocarbon anaesthetics (see section 4.5).

4.4 Special warnings and precautions for use

Avoid co-infusion with other medicinal products.

Mono-amine oxidase (MAO) inhibitors

To avoid potentiation patients who have been treated with MAO inhibitors prior to dopamine hydrochloride should be given reduced doses of dopamine hydrochloride (see sections 4.2, 4.5 and 5.2).

Monitoring of volume, electrolyte and diastolic blood pressure

Vasopressors, including dopamine hydrochloride, are generally not indicated in hypovolemic shock. Once adequate fluid resuscitation has been initiated, vasopressor therapy may be considered in specific cases where blood pressure remains severely low despite adequate fluid resuscitation. Dopamine hydrochloride should be chosen if inotropic, chronotropic, vasoconstrictive effects and an increase in peripheral venous resistance is required. However, the use of vasopressors in haemorrhagic or hypovolemic shock should be approached cautiously and under close monitoring.

Excess administration of potassium-free solutions may result in significant hypokalaemia.

If a disproportionate rise in diastolic pressure (i.e. a marked decrease in pulse pressure) is observed, the infusion rate should be decreased and the patients observed carefully for further evidence of predominant vasoconstriction activity, unless such an effect is desired.

Constant evaluation of therapy in terms of blood volume, augmentation of cardiac contractility, and distribution of peripheral perfusion and urinary output is required for patients of any age.

Monitoring of potential cardiac adverse reactions

Careful monitoring should be performed for dysrhythmia and tachycardia and if present consideration should be given to reducing the infusion rate or discontinuing dopamine hydrochloride if clinically appropriate. Any reversible causes of tachycardia such as volume depletion, hypoxia or pain should be corrected and tachycardia should be controlled.

Peripheral vascular disease

Patients should be closely monitored for any changes in colour or temperature of the skin of the extremities. If change of skin colour or temperature occurs and is thought to be the result of compromised circulation to the extremities, the benefits of continued dopamine hydrochloride infusion should be weighed against the risk of possible necrosis. These changes may be reversed by decreasing the rate or discontinuing the infusion. Even at low doses, dopamine hydrochloride can cause skin necrosis; the risk is particularly high in patients with disorders of acral circulation and when higher doses are administered (≥ 10 µg/kg/min).

Because of variable, age-dependent clearance, titrate dose slowly and deliberately, particularly in neonates. Neonates may be more sensitive to vasoconstrictive effects.

Subcutaneous, intramuscular or intra-arterial administration must be avoided, as the vasoconstrictor effect may result in tissue damage.

Extravasation

Dopamine hydrochloride should be infused into a large vein whenever possible to prevent the possibility of infiltration of perivascular tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of the surrounding tissue. Ischaemia can be reversed by infiltration of the affected area with a vasodilator. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischaemic area as soon as extravasation is noted.

Renal and hepatic impairment

The clearance of dopamine hydrochloride is affected by renal and hepatic dysfunction - decreasing by 2-fold in the presence of either. In younger children, particularly neonates, clearance is highly variable, close monitoring is advised.

Withdrawal effect

Dopamine hydrochloride infusion should be withdrawn gradually, to avoid unnecessary hypotension. It may be necessary to decrease the dose of dopamine hydrochloride gradually while expanding blood volume with IV fluids to prevent a recurrence of hypotension. Sudden cessation of dopamine hydrochloride infusion may result in marked hypotension. See also weaning instructions in section 4.2.

Septic shock

Based on signals of an increased mortality with the first line use of dopamine in paediatric and adult patients with septic shock, first line administration of dopamine in paediatric patients with sepsis is not recommended.

Cardiac surgery

Dopamine hydrochloride is selectively used in paediatric patients with low cardiac output syndrome (LCOS) and low systemic vascular resistance (SVR) to improve cardiac output. Its use in patients with elevated SVR or elevated pulmonary vascular resistance (PVR) is generally limited due to the potential to worsen vascular resistance abnormalities. The decision to administer dopamine hydrochloride in cardiac surgery should always be made based on the patient's specific clinical condition.

Instances of increased pulmonary arterial pressure

Dopamine hydrochloride can increase pulmonary vascular resistance, particularly at higher doses. When administering dopamine hydrochloride in patients with increased pulmonary arterial pressure,

close haemodynamic monitoring is recommended and doses above 10 µg/kg/min should be avoided. In acute pulmonary hypertension dopamine hydrochloride should only be administered if considered necessary based on an individual assessment of the haemodynamic and clinical state of the patient.

Risk of intraventricular haemorrhage (IVH) /subependymal bleed

To mitigate the risk of IVH/subependymal bleed, blood pressure and hemodynamic status of infants receiving dopamine hydrochloride should be closely monitored by healthcare professionals in the neonatal intensive care unit (NICU). Dose adjustments should be made as needed to maintain stable blood pressure and minimize the risk of adverse reactions such as tachycardia, extravasation at injection site, disproportionate rise in diastolic pressure, chest pain, palpitations, hypotension. The overall management of IVH/subependymal bleed should involve supportive care and measures to address potential risk factors beyond vasoactive medicinal products.

Risk of infection

The potential unfavourable effects of dopamine hydrochloride on the risk of infection should be considered, particularly when used in high doses or for prolonged periods. The decision to use dopamine hydrochloride or any vasoactive medicinal product should be individualized, taking into account the patient's clinical condition, infection risk, and potential benefits of treatment. Close monitoring and infection prevention measures are essential in managing patients receiving dopamine hydrochloride.

Narrow angle glaucoma

Dopamine is not recommended in patients with narrow angle glaucoma.

Alkalizing substances

If sodium bicarbonate is simultaneously indicated to treat acidosis, it should be given through a separate infusion line from a separate container or administration set.

Laboratory test interferences

Infusion of dopamine hydrochloride suppresses pituitary secretion of thyroid stimulating hormone (TSH), and prolactin (see section 4.8). Dopamine hydrochloride-induced decrease of TSH may interfere with early diagnosis of congenital hypothyroidism, which is characterized by high TSH levels in connection with low T4. It is therefore recommended to test all new-borns for TSH and T4 values not only at primary screening, but also after dopamine hydrochloride discontinuation.

Dopamine hydrochloride may lead to false positive results when urinary catecholamine excretion is determined.

Prolactin

Dopamine hydrochloride is known to reduce serum prolactin (see section 4.6).

Excipients with known effect

Contains sodium metabisulfite which may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicinal product contains less than 1 mmol of sodium (23 mg) per dose, and therefore is essentially sodium free.

4.5 Interaction with other medicinal products and other forms of interaction

Anaesthetics

The myocardium is sensitised by cyclopropane or halogenated hydrocarbon anaesthetics, and these medicinal products are contraindicated with dopamine hydrochloride (see section 4.3). This interaction applies both to pressor activity and cardiac beta adrenergic stimulation.

Alpha and beta blockers

It is not recommended to use dopamine with alpha and beta blockers. The cardiac effects of dopamine hydrochloride are antagonised by β-adrenergic blocking agents such as propranolol acebutolol, atenolol, bisoprolol, nadolol, nebivolol, and metoprolol, and the peripheral vasoconstriction caused by high doses of dopamine hydrochloride is antagonised by α adrenergic blocking agents (e.g. doxazosin, prazosin, terazosin).

MAO inhibitors

It is not recommended to use dopamine with MAO inhibitors. MAO inhibitors (e.g. isocarboxazid, phenelzine, tranylcypromine, rasagiline, selegiline, linezolid) potentiate the effect of dopamine hydrochloride and its duration of action. Patients who have been treated with MAO inhibitors prior to administration of dopamine hydrochloride will therefore require a substantially reduced dose (see sections 4.2, 4.4 and 5.2).

Phenytoin

Administration of IV phenytoin to patients receiving dopamine hydrochloride has resulted in hypotension, bradycardia and cardiac arrest; it is recommended that phenytoin should be used with extreme caution, if at all, in patients receiving dopamine hydrochloride.

Diuretic agents

It is not recommended to use dopamine with diuretic agents (e.g. bumetanide, torsemide, and furosemide). Dopamine hydrochloride may increase the effect of diuretic agents.

Ergot alkaloids

The combination of dopamine hydrochloride with ergot alkaloids (e.g., ergotamine) should be avoided because of the possibility of excessive peripheral vasoconstriction, increasing the risk of gangrene.

Tricyclic antidepressants and guanethidine

Tricyclic antidepressants (e.g. amitriptyline, desipramine, doxepin, imipramine, nortriptyline) and guanethidine may potentiate the pressor response to dopamine hydrochloride.

Inactivation of dopamine hydrochloride by addition of alkalizing substances

Dopamine hydrochloride is inactivated in alkaline solution please refer to section 4.4 and section 6.2.

Metoclopramide

It is not recommended to use dopamine with metoclopramide as metoclopramide can impair the dopamine hydrochloride effect.

Blood glucose levels

Dopamine hydrochloride may increase the blood glucose level and may therefore interfere with antidiabetic medicinal products (e.g. meglitinides – repaglinide etc.; sulfonylureas – glipizide etc.).

The metabolism of neonates can be very fragile; therefore, hypo- or hyperglycaemia is more common in this group. Metabolic parameters should be monitored during dopamine hydrochloride infusion, e.g. blood pressure and blood glucose.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited amount of data from the use of dopamine hydrochloride in pregnant woman. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Neoatricon is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

It is not known if dopamine hydrochloride is excreted in human milk. However, because of the short plasma half-life of dopamine hydrochloride at therapeutic doses no effects on the breastfed infants are anticipated. Therefore, Neoatricon can be used during breast-feeding. See section 4.4 for information on prolactin.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Summary of the safety profile

Except for vasoconstrictive effects caused by inadvertent infusion of dopamine hydrochloride into the umbilical artery, adverse reactions unique to the paediatric population have not been identified.

Tabulated list of adverse reactions

The data in the following table is extracted from clinical studies and post-marketing experience pertaining to the adult population. The frequency of adverse events cannot be estimated in the paediatric population. The adverse reactions are listed below by SOC (System Organ Class) and by frequency, most frequent reactions first, with the following guidelines: 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) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 1: Adverse reactions identified in clinical studies and post-marketing

System organ class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Gangrene
	Not known	Infection
Immune system disorders	Unknown	Anaphylactic reactions*
Endocrine disorders	Not known	Suppression of pituitary function
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Mydriasis
Cardiac disorders	Common	Ectopic heart beats
		Sinus tachycardia
		Anginal pain
		Palpitation

	Uncommon	Aberrant conduction
		Bradycardia
		Widened QRS complex
		Supraventricular tachycardia
		Ventricular tachycardia up to ventricular fibrillation
	Not known	Severe palpitations
Vascular disorders	Common	Hypotension
		Vasoconstriction
	Uncommon	Hypertension
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea
	Not known	Increase in hypoxemia
Gastrointestinal disorders	Common	Nausea
		Vomiting
	Not known	Gastrointestinal bleeding
Skin and subcutaneous tissue disorders	Uncommon	Piloerection
		Skin necrosis
	Not known	Local necrosis due to extravasation
Renal and urinary disorders	Uncommon	Azotaemia
	Not known	Changes in urinary output

* Anaphylactic reactions and severe life-threatening asthmatic episodes may be due to Sodium metabisulphite sensitivity (see section 4.4).

Description of selected adverse reactions

Suppression of pituitary function
Due to activation of D2 receptors in the pituitary gland, dopamine suppresses the release of prolactin and thyroid-stimulating hormone (TSH), the latter resulting in a decrease of T4 release from the thyroid gland. Conversely, dopamine discontinuation may lead to a rebound effect with overshooting release of prolactin, TSH and T4.

Increase in hypoxemia
Dopamine may contribute to hypoxemia by several mechanisms, e.g. by ventilation-perfusion mismatch, i.e., increased blood flow even to hypoventilated alveolar areas (pulmonary "shunt" formation), specifically in ventilator-dependent patients. Moreover, dopamine may increase systemic oxygen consumption (VO2).

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Possible symptoms of overdose include: severe increase in blood pressure, tachycardia, tachycardic arrhythmias, increase in left ventricular end-diastolic pressure with consequent pulmonary congestion to pulmonary oedema, angina pectoris-attacks (especially in patients with known coronary artery disease), nonspecific chest pain, palpitations, nausea, vomiting, sensation of coldness in the extremities and cyanosis. These conditions can be rapidly reversed by dose reduction or discontinuing the infusion, since dopamine hydrochloride has a half-life of less than 2 minutes in the body.

Should these measures fail, an infusion of an alpha-adrenergic blocking agent, should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cardiac therapy, adrenergic and dopaminergic agents, ATC code: C01CA04

Mechanism of action

Dopamine hydrochloride stimulates adrenergic receptors of the sympathetic nervous system. Dopamine hydrochloride has principally a direct stimulatory effect on β1-adrenergic receptors, but also appears to have an indirect effect by releasing norepinephrine from its storage sites. Dopamine hydrochloride also appears to act on specific dopaminergic receptors in the renal, mesenteric, coronary, and intracerebral vascular beds to cause vasodilation. Dopamine hydrochloride has little or no effect on β2-adrenergic receptors.

At higher doses (10 to 20 μg/kg/min), dopamine hydrochloride can also stimulate alpha-1 receptors, resulting in vasoconstriction and increased peripheral vascular resistance.

Pharmacodynamic effects

The main effects of dopamine hydrochloride depend on the dose administered.

In IV doses of 0.5-2 μg/kg/min, dopamine hydrochloride acts predominantly on dopaminergic receptors; in IV doses of 2-10 μg/kg/min, dopamine hydrochloride also stimulates β1-adrenergic receptors, resulting in an increase of cardiac output.
At higher doses, dopamine hydrochloride also stimulates alpha-1 adrenergic receptors. This results in vasoconstriction, increased peripheral vascular resistance, and an increase in blood pressure. The pressor effect of dopamine hydrochloride can be used to raise blood pressure in cases of hypotension or shock.

Vasoconstriction induced by dopamine hydrochloride, or any other vasoactive agent, can affect both the peripheral vascular system and the pulmonary vascular system. This can lead to changes in peripheral vascular resistance and blood pressure, as well as pulmonary vascular resistance (PVR).

Premature infants often have physiological differences compared to full-term infants and older children. One significant difference is the maturation of adrenergic receptors, including beta-1 receptors and these receptors may not be fully developed and may exhibit a variable response to dopamine hydrochloride, which may have a more or less pronounced effect on cardiac contractility compared to older infants or adults.

Some premature infants may show a robust positive inotropic response, while others may have a more limited response.

These differences in receptor maturation and individual variability require careful monitoring and titration of dopamine hydrochloride to optimise cardiac function while minimizing the risk of adverse effects.

5.2 Pharmacokinetic properties

Absorption

Orally administered dopamine hydrochloride is rapidly metabolised in the gastrointestinal tract. Following IV administration, the onset of action of dopamine hydrochloride occurs within 5 minutes, and dopamine hydrochloride has duration of action of less than 10 minutes.

Distribution

Dopamine is widely distributed in the body but does not cross the blood-brain barrier to a substantial extent. It is not known if dopamine crosses the placenta.

Biotransformation

Dopamine hydrochloride has a plasma half-life of about 2 minutes. Dopamine hydrochloride is metabolised in the liver, kidneys, and plasma by MAO and catechol-O-methyltransferase to the inactive compounds homovanillic acid (HVA) and 3, 4- dihydroxyphenylacetic acid. In patients receiving MAO inhibitors, the duration of action of dopamine hydrochloride may be as long as 1 hour. About 25 % of a dose of dopamine hydrochloride is metabolised to norepinephrine within the adrenergic nerve terminals.

Elimination

Dopamine hydrochloride is excreted in urine principally as HVA and its sulfate and glucuronide conjugates and as 3, 4-dihydroxyphenylacetic acid. A very small fraction of a dose is excreted unchanged. Following administration of radio labelled dopamine hydrochloride, approximately 80 % of the radioactivity reportedly is excreted in urine within 24 hours.

Paediatric population
Elimination half-life in neonates is between 5 and 11 minutes. In critically ill infants and children clearance reportedly ranges from 48 to 168 mL/kg/min with the higher values reportedly in younger patients.
Clearance of dopamine hydrochloride is unpredictable in infants, particularly neonates. Clearance may be as much as 2-fold greater in those < 2 years of age.

Substantial interindividual variation was seen in dopamine hydrochloride pharmacokinetics in seriously ill infants, and plasma concentrations could not be predicted accurately from its infusion rate. Marked variation in clearance explains in part, the wide dose requirements of dopamine hydrochloride.

Available data suggest that dopamine hydrochloride and pharmacokinetics are similar to those in adults. Wide interindividual variability has been noted. A consistent relationship between clearance and age has not been demonstrated.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of this summary of product characteristics.
Standardized reproductive toxicity studies were not performed for dopamine hydrochloride. Studies available show conflicting results.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulfite (E223)
Dilute hydrochloric acid (for pH-adjustment)
Sodium hydroxide (for pH-adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. Avoid mixing with alkalis (including sodium bicarbonate), oxidizing agents or iron salts.

Do NOT add dopamine hydrochloride to sodium bicarbonate solution for injection, or other alkaline I.V. solutions.

Admixtures of ampicillin and dopamine in 5% glucose solution are alkaline and incompatible and result in decomposition of both drugs. They should not be admixed.

It is suggested that admixtures containing gentamicin sulphate, cephalothin sodium, cephalothin sodium neutral or oxacillin sodium should be avoided unless all other viable alternatives have been exhausted.

Admixtures of dopamine, amphotericin B in 5% glucose solution are incompatible as a precipitate forms immediately on mixing.

6.3 Shelf life

3 years.
After first opening, the medicinal product should be used immediately; any unused contents should be discarded after 24 hours.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Type I clear glass vial with bromobutyl rubber stopper, sealed with flip-off aluminium seal.

Pack size:
Neoatricon 1.5 mg/mL solution for infusion: single carton containing 30 mL vial.
Neoatricon 4.5 mg/mL solution for infusion: single carton containing 50 mL vial.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Do not use this medicinal product if you notice an opaque, cloudy or discoloured solution

This medicinal product does not require dilution prior to administration.

This medicinal product is for single use only. Any unused solution should be discarded.

Discard vial and any unused contents after 24 hours (see section 6.3).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

BrePco Biopharma Ltd.,
Suite One, The Avenue,
Beacon Court, Sandyford,
Dublin D18HX31.
Ireland.

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1804/001 – 1.5 mg / ml 1 vial
EU/1/24/1804/002 – 4.5 mg / ml 1 vial

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27-05-2024

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency: http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Pharmadox Healthcare Ltd.
KW20A Kordin Industrial Park,
Paola PLA3000,
Malta.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of product characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON-1.5 mg/ml (30ml vial)

1. NAME OF THE MEDICINAL PRODUCT

neoatricon 1.5 mg/mL solution for infusion
DOPamine hydrochloride
For neonates and children up to 9 kg.

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution contains 1.5 mg of DOPamine hydrochloride.
Each vial contains 45 mg of DOPamine hydrochloride in 30 mL.

3. LIST OF EXCIPIENTS

Also contains:
Sodium metabisulfite (E223)
Dilute hydrochloric acid for pH adjustment
Sodium hydroxide for pH adjustment
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion
45 mg/30 mL
1 x 30 mL vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.
Single use only.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

BrePco Biopharma Limited
Suite One, The Avenue,
Beacon Court, Sandyford.
Dublin D18HX31
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1804/001

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

Vial label-1.5 mg/mL (30mL vial)

1. NAME OF THE MEDICINAL PRODUCT

neoatricon 1.5 mg/mL solution for infusion
DOPamine hydrochloride.

For neonates and children up to 9 kg

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution contains 1.5 mg of dopamine hydrochloride.

3. LIST OF EXCIPIENTS

Also contains:
E 223
Dilute hydrochloric acid
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion,
30 mL
45 mg/30 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.
Single use only.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

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BrePco Biopharma Limited.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1804/001

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON-4.5 mg/ml (50ml vial)

1. NAME OF THE MEDICINAL PRODUCT

neoatricon 4.5 mg/mL solution for infusion
DOPamine hydrochloride

For children 10 kg and over.

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution contains 4.5 mg of DOPamine hydrochloride.
Each vial contains 225 mg of DOPamine hydrochloride in 50 mL.

3. LIST OF EXCIPIENTS

Also contains:
Sodium metabisulfite (E223)
Dilute hydrochloric acid for pH adjustment
Sodium hydroxide for pH adjustment
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion
225 mg/50 mL
1 x 50 mL vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.
Single use only.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

BrePco Biopharma Limited
Suite One, The Avenue,
Beacon Court, Sandyford.
Dublin D18HX31
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1804/002

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

Vial label-4.5 mg/ml (50ml vial)

1. NAME OF THE MEDICINAL PRODUCT

neoatricon 4.5 mg/mL solution for infusion
DOPamine hydrochloride.
For children 10 kg and over

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 50 mL vial contains 225 mg of dopamine hydrochloride.

3. LIST OF EXCIPIENTS

Also contains:
E223
Dilute hydrochloric acid
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion,
50 mL
225 mg/50 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.
Single use only.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

BrePco Biopharma Limited.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1804/002

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Neoatricon 1.5 mg/mL solution for infusion
dopamine hydrochloride

Read all of this leaflet carefully before your child starts using this medicine because it contains important information for your child.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you are concerned about any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Neoatricon is and what it is used for

Neoatricon contains the active substance dopamine hydrochloride. Dopamine is a substance that occurs naturally in the body. It increases blood pressure by activating specific receptors (targets), which causes narrowing of the blood vessels.

Neoatricon is used to treat hypotension (low blood pressure) in newborn babies, infants and children less than 18 years of age.

2. What you need to know before your child uses Neoatricon

Your child should not be given Neoatricon
- If your child is allergic to dopamine hydrochloride or any of the other ingredients of this medicine (listed in section 6).
- If your child has phaeochromocytoma (a tumour of the adrenal gland).
- If your child has an uncorrected atrial or ventricular tachyarrhythmia (abnormal or irregular heartbeats in the upper or lower chambers of the heart) or ventricular fibrillation (dangerous, irregular and uncoordinated contractions of the lower chambers of the heart)
- If your child has an overactive thyroid gland.
- If your child is receiving cyclopropane or halogenated hydrocarbon anaesthetics.

Talk to your doctor if you are not sure if any of the above apply to your child.

Warnings and precautions
Talk to your doctor or nurse before using Neoatricon if:

- your child has any heart-related problems
- your child uses or has recently used monoamine oxidase inhibitors (MAOIs), which are for example used to treat depression; (see section 'Other medicines and Neoatricon').
- your child is suffering or has suffered from peripheral vascular disease (problems related to blood circulation in their hands and feet)
- your child has any kidney or liver diseases

- your child has low blood volume. Your child's doctor will take steps to get their blood volume up to normal before giving them dopamine hydrochloride
- your child has sepsis (a serious bacterial infection)
- your child has diseases associated with an increased pressure in the arteries of the lungs.
- your child suffers from a certain form of glaucoma (narrow-angle glaucoma)

Your doctor will monitor your child for any side-effects affecting the heart or kidneys while your child is receiving dopamine hydrochloride.

Your doctor will monitor your child's blood pressure and blood flow to reduce the risk of bleeding in the brain.

Neoatricon may increase the risk of infection, so your doctor will closely monitor your child and infection prevention measures will be put in place.

Your doctor will reduce the use of Neoatricon gradually to avoid low blood pressure.

Dopamine hydrochloride may lead to changes in your child's blood test. Your doctor may take blood samples to monitor for these.

Other medicines and Neoatricon
Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines, including those obtained without prescription.

Special care is needed if your child is using other medicines as some could interact with Neoatricon, for example:
- anaesthetics.
- certain medicines used to treat diabetes (e.g. repaglinide, sulfonylureas etc.) Dopamine hydrochloride may increase blood glucose levels may interfere with antidiabetic medicines.
- certain medicines used to treat depression (tricyclic antidepressants), such as amitriptyline , desipramine, doxepin, imipramine, nortriptyline.
- Monoamine-oxidase inhibitors (MAOI), a type of medicine used to treat depression, such as selegiline, isocarboxazid, phenelzine, tranylcypromine, rasagiline, linezolid.
- phenytoin, a medicine used to treat epilepsy.
- alpha- and beta-blockers (medicines which are often used for treating blood pressure and heart disorders), such as doxazosin, prazosin, terazosin, acebutolol, atenolol, bisoprolol, metoprolol, nadolol, nebivolol, propranolol.
- ergotamine, a medicine used to treat headaches.
- metoclopramide a medicine used to treat feeling sick (nausea) and being sick (vomiting)
- guanethidine, a medicine used to treat high blood pressure.
- diuretics (medicines that increase urine production), such as bumetanide, torsemide, and furosemide.

If your child is taking any of the medicines listed above, please ask your doctor for further information about the possible consequences of these interactions.

Pregnancy and breast-feeding
Neoatricon is intended for use in children. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

If you are a woman of child-bearing age, you should practise effective contraception during treatment with Neoatricon. Neoatricon is not recommended during pregnancy.
However, your doctor will only use this medicine if the expected benefits outweigh any potential risk to your baby.

It is not known whether Neoatricon is excreted into human-milk. However, since Neoatricon is quickly eliminated from your body, you can use Neoatricon during breast-feeding.

Driving and using machines
Do not drive or operate machinery if taking this product.

Neoatricon contains sodium metabisulfite
This excipient may rarely cause severe hypersensitivity (severe allergy) reactions and bronchospasm (excessive and prolonged contraction of the airway muscles causing breathing difficulty).

This medicinal product contains less than 23 mg of sodium in each dose and therefore is essentially 'sodium-free'.

3. How to use Neoatricon

Dose and method of administration
Your doctor will decide on the most suitable dose for your child. The dose will depend on your child's medical condition and body weight. The rate of administration will be carefully controlled and adjusted according to your child's response.

This medicine will be given by infusion (drip) in a large vein under the supervision of a doctor. In newborns, the medicine may also be given into the umbilical cord.

Your child's breathing, blood pressure, oxygen levels, kidney function and other vital signs will be watched closely while they are receiving Neoatricon.

If your child's blood volume is low, your child may be given a transfusion of blood or a plasma expander (fluids that increase the volume of circulating blood) before this medicine is given.

Tell your doctor or nurse if your child feels any burning, pain or swelling around the intravenous needle when dopamine hydrochloride is given. If the medicine infusion escapes from the vein into the surrounding tissues, it may damage (e.g. blister; tissue death) the surrounding tissues. Tell your doctor if you or your child notice any pain or swelling at the injection site so that the appropriate treatment may be given.

If you are given too much or too little dopamine hydrochloride
This medicine will be given to your child in a hospital, under the supervision of a doctor. It is unlikely that your child will be given too much or too little. However, tell your doctor or nurse if you have any concerns.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious adverse reactions
If you notice any changes in the way your child feels during or after the treatment, tell your doctor immediately:

- severe allergic reaction – your child may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and your child may feel they are going to faint (frequency unknown)
- gangrene (decay and death of tissue; you may notice a change in skin colour even to black) (frequency uncommon).
- severe palpitations (frequency unknown); ventricular tachycardia up to ventricular fibrillation (uncommon).

These are serious side effects. Your child may need urgent medical attention.

Other adverse reactions
If any of the following happens, tell your doctor as soon as possible:

Common side effects (may affect up to 1 in 10 people)
- sinus tachycardia (rapid heartbeat)
- palpitation (a forceful heartbeat that may be rapid or irregular)
- anginal pain (a type of chest pain caused by reduced blood flow to the heart)
- ectopic heartbeat (change in a heartbeat that is otherwise normal)
- dyspnoea (shortness of breath)
- hypotension (low blood pressure)
- vasoconstriction (narrowing of blood vessels)
- nausea (feeling sick)
- vomiting
- headache

Uncommon side effects (may affect up to 1 in 100 people)
- hypertension (high blood pressure)
- abnormalities in the electrocardiogram (a tracing of electrical currents in the heart – aberrant conduction)
- mydriasis (dilation of the pupil of the eye)
- bradycardia (slow heart rate)
- azotaemia (abnormally high levels of nitrogen-containing compounds, such as urea, in the blood)
- episodes of abnormally fast heart rate (supraventricular tachycardia and ventricular tachycardia)
- very fast contractions of the lower heart chambers, rendering the heart unable to pump blood effectively (ventricular fibrillation)
- piloerection (goose bumps)
- gangrene (decay and death of tissue; you may notice a change in skin colour even to black)
- skin necrosis (death of tissue)

Not known (cannot be estimated from the available data)
- increased risk of bleeding after operations in the abdominal (belly) region or in patients with a tendency to bleed in the gastrointestinal tract (stomach and gut)
- an increase in hypoxemia (a low level of oxygen in the blood) in ventilator-dependent patients
- decrease in renal (kidney) blood flow at higher doses, due to narrowing of blood vessels
- Infection
- Suppression of pituitary function
- Local necrosis due to extravasation (infusion escapes from the vein and damages surrounding tissue)

Reporting of side effects
If your child gets any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Neoatricon

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial and carton after 'EXP'. The expiry date refers to the last day of that month.

This medicinal product does not require any special temperature storage conditions. Keep the container in the outer carton in order to protect from light.

Neoatricon is a single use vial only. After first opening the medicine should be used immediately. Unused portions should be discarded.

Do not use this medicine if you notice an opaque, cloudy or discoloured solution.

6. Contents of the pack and other information

What Neoatricon contains

The active substance is dopamine hydrochloride.

Neoatricon 1.5 mg/mL solution for infusion
Each millilitre of solution contains 1.5 milligrams of dopamine hydrochloride. Each vial contains 45 mg of dopamine hydrochloride in 30 mL.

The other excipients are sodium metabisulfite (E223) (see section 2 "Neoatricon contains sodium metabisulfite"), water for injections, sodium hydroxide (for pH adjustment) and dilute hydrochloric acid (for pH adjustment).

What Neoatricon looks like and contents of the pack

Neoatricon solution for infusion is a clear, colourless or pale-yellow solution. It comes in clear glass vial with a rubber stopper and is sealed with an aluminium flip-off seal.

Pack size
Neoatricon 1.5 mg/mL is presented as one 30 mL vial, packed in an outer carton.

Marketing Authorisation Holder
BrePco Biopharma Limited,
Suite One, The Avenue, Beacon Court,
Sandyford,
Dublin D18 HX31,
Ireland

Manufacturer
Pharmadox Healthcare Ltd.,
KW20A Kordin Industrial, Park,
Paola PLA3000,
Malta

This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

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The following information is intended for healthcare professionals only:

Infusion of dopamine hydrochloride solution should begin at a rate of 5 µg/kg/min and increase gradually in 5 µg/kg/min increments. The recommended dose range is 5 – 10 µg/kg/min. Doses above 10 µg/kg/min up to a maximum of 20 µg/kg/min may be administered if considered justified.

Infusion rates may be calculated using the following formula:

[Dose (µg/kg/minute) x Weight (kg) x 60 (minutes/hour)]

$$\text{Infusion Rate (mL/hour)} = \frac{\text{Concentration (µg/mL)}}{\text{Concentration (µg/mL)}}$$

Instructions for use and handling
For intravenous use. Administer via a central line [Umbilical venous catheter (UVC), Longline, or Surgical central venous line (CVL)]. If no central access is available, use a cannula in large vein.
A suitable metering device is required in the infusion system to control the rate and flow.
For single use. Discard any unused contents.
Do not dilute.
Do not use if the solution is discoloured.
The maximum acceptable duration for one single vial administration is 24-hours.

Incompatibilities
Neoatricon solution for infusion should not be added to any alkaline intravenous solutions, i.e. sodium bicarbonate. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
It is suggested that admixtures containing gentamicin sulphate, cephalothin sodium, cephalothin sodium neutral or oxacillin sodium should be avoided unless all other viable alternatives have been exhausted.
Admixtures of ampicillin and dopamine in 5% glucose solution are alkaline and incompatible and result in decomposition of both drugs. They should not be admixed.
Admixtures of dopamine, amphotericin B in 5% glucose solution are incompatible as a precipitate forms immediately on mixing.

In use storage precautions
This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.

Package leaflet: Information for the user

Neoatricon 4.5 mg/mL solution for infusion
dopamine hydrochloride

Read all of this leaflet carefully before your child starts using this medicine because it contains important information for your child.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you are concerned about any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Neoatricon is and what it is used for

Neoatricon contains the active substance dopamine hydrochloride. Dopamine is a substance that occurs naturally in the body. It increases blood pressure by activating specific receptors (targets), which causes narrowing of the blood vessels.

Neoatricon is used to treat hypotension (low blood pressure) in newborn babies, infants and children less than 18 years of age.

2. What you need to know before your child uses Neoatricon

Your child should not be given Neoatricon
- If your child is allergic to dopamine hydrochloride or any of the other ingredients of this medicine (listed in section 6).
- If your child has phaeochromocytoma (a tumour of the adrenal gland).
- If your child has an uncorrected atrial or ventricular tachyarrhythmia (abnormal or irregular heartbeats in the upper or lower chambers of the heart) or ventricular fibrillation (dangerous, irregular and uncoordinated contractions of the lower chambers of the heart)
- If your child has an overactive thyroid gland.
- If your child is receiving cyclopropane or halogenated hydrocarbon anaesthetics.

Talk to your doctor if you are not sure if any of the above apply to your child.

Warnings and precautions
Talk to your doctor or nurse before using Neoatricon if:

- your child has any heart-related problems
- your child uses or has recently used monoamine oxidase inhibitors (MAOIs), which are for example used to treat depression; (see section 'Other medicines and Neoatricon').
- your child is suffering or has suffered from peripheral vascular disease (problems related to blood circulation in their hands and feet)

- your child has any kidney or liver diseases
- your child has low blood volume. Your child's doctor will take steps to get their blood volume up to normal before giving them dopamine hydrochloride
- your child has sepsis (a serious bacterial infection)
- your child has diseases associated with an increased pressure in the arteries of the lungs.
- your child suffers from a certain form of glaucoma (narrow-angle glaucoma)

Your doctor will monitor your child for any side-effects affecting the heart or kidneys while your child is receiving dopamine hydrochloride.

Your doctor will monitor your child's blood pressure and blood flow to reduce the risk of bleeding in the brain.

Neoatricon may increase the risk of infection, so your doctor will closely monitor your child and infection prevention measures will be put in place.

Your doctor will reduce the use of Neoatricon gradually to avoid low blood pressure.

Dopamine hydrochloride may lead to changes in your child's blood test. Your doctor may take blood samples to monitor for these.

Other medicines and Neoatricon
Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines, including those obtained without prescription.

Special care is needed if your child is using other medicines as some could interact with Neoatricon, for example:
- anaesthetics.
- certain medicines used to treat diabetes (e.g. repaglinide, sulfonylureas etc.) Dopamine hydrochloride may increase blood glucose levels may interfere with antidiabetic medicines.
- certain medicines used to treat depression (tricyclic antidepressants), such as amitriptyline , desipramine, doxepin, imipramine, nortriptyline.
- Monoamine-oxidase inhibitors (MAOI), a type of medicine used to treat depression, such as selegiline, isocarboxazid, phenelzine, tranylcypromine, rasagiline, linezolid.
- phenytoin, a medicine used to treat epilepsy.
- alpha- and beta-blockers (medicines which are often used for treating blood pressure and heart disorders), such as doxazosin, prazosin, terazosin, acebutolol, atenolol, bisoprolol, metoprolol, nadolol, nebivolol, propranolol.
- ergotamine, a medicine used to treat headaches.
- metoclopramide a medicine used to treat feeling sick (nausea) and being sick (vomiting)
- guanethidine, a medicine used to treat high blood pressure.
- diuretics (medicines that increase urine production), such as bumetanide, torsemide, and furosemide.

If your child is taking any of the medicines listed above, please ask your doctor for further information about the possible consequences of these interactions.

Pregnancy and breast-feeding
Neoatricon is intended for use in children. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

If you are a woman of child-bearing age, you should practise effective contraception during treatment with Neoatricon. Neoatricon is not recommended during pregnancy.
However, your doctor will only use this medicine if the expected benefits outweigh any potential risk to your baby.

It is not known whether Neoatricon is excreted into human-milk. However, since Neoatricon is quickly eliminated from your body, you can use Neoatricon during breast-feeding.

Driving and using machines
Do not drive or operate machinery if taking this product.

Neoatricon contains sodium metabisulfite
This excipient may rarely cause severe hypersensitivity (severe allergy) reactions and bronchospasm (excessive and prolonged contraction of the airway muscles causing breathing difficulty).

This medicinal product contains less than 23 mg of sodium in each dose and therefore is essentially 'sodium-free'.

3. How to use Neoatricon

Dose and method of administration
Your doctor will decide on the most suitable dose for your child. The dose will depend on your child's medical condition and body weight. The rate of administration will be carefully controlled and adjusted according to your child's response.

This medicine will be given by infusion (drip) in a large vein under the supervision of a doctor. In newborns, the medicine may also be given into the umbilical cord.

Your child's breathing, blood pressure, oxygen levels, kidney function and other vital signs will be watched closely while they are receiving Neoatricon.

If your child's blood volume is low, your child may be given a transfusion of blood or a plasma expander (fluids that increase the volume of circulating blood) before this medicine is given.

Tell your doctor or nurse if your child feels any burning, pain or swelling around the intravenous needle when dopamine hydrochloride is given. If the medicine infusion escapes from the vein into the surrounding tissues, it may damage (e.g. blister; tissue death) the surrounding tissues. Tell your doctor if you or your child notice any pain or swelling at the injection site so that the appropriate treatment may be given.

If you are given too much or too little dopamine hydrochloride
This medicine will be given to your child in a hospital, under the supervision of a doctor. It is unlikely that your child will be given too much or too little. However, tell your doctor or nurse if you have any concerns.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious adverse reactions
If you notice any changes in the way your child feels during or after the treatment, tell your doctor immediately:

- severe allergic reaction – your child may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and your child may feel they are going to faint (frequency unknown)
- gangrene (decay and death of tissue; you may notice a change in skin colour even to black) (frequency uncommon).
- severe palpitations (frequency unknown); ventricular tachycardia up to ventricular fibrillation (uncommon).

These are serious side effects. Your child may need urgent medical attention.

Other adverse reactions
If any of the following happens, tell your doctor as soon as possible:

Common side effects (may affect up to 1 in 10 people)
- sinus tachycardia (rapid heartbeat)
- palpitation (a forceful heartbeat that may be rapid or irregular)
- anginal pain (a type of chest pain caused by reduced blood flow to the heart)
- ectopic heartbeat (change in a heartbeat that is otherwise normal)
- dyspnoea (shortness of breath)
- hypotension (low blood pressure)
- vasoconstriction (narrowing of blood vessels)
- nausea (feeling sick)
- vomiting
- headache

Uncommon side effects (may affect up to 1 in 100 people)
- hypertension (high blood pressure)
- abnormalities in the electrocardiogram (a tracing of electrical currents in the heart – aberrant conduction)
- mydriasis (dilation of the pupil of the eye)
- bradycardia (slow heart rate)
- azotaemia (abnormally high levels of nitrogen-containing compounds, such as urea, in the blood)
- episodes of abnormally fast heart rate (supraventricular tachycardia and ventricular tachycardia)
- very fast contractions of the lower heart chambers, rendering the heart unable to pump blood effectively (ventricular fibrillation)
- piloerection (goose bumps)
- gangrene *(decay and death of tissue; you may notice a change in skin colour even to black)*
- skin necrosis (death of tissue)

Not known (cannot be estimated from the available data)
- increased risk of bleeding after operations in the abdominal (belly) region or in patients with a tendency to bleed in the gastrointestinal tract (stomach and gut)
- an increase in hypoxemia (a low level of oxygen in the blood) in ventilator-dependent patients
- decrease in renal (kidney) blood flow at higher doses, due to narrowing of blood vessels
- Infection
- Suppression of pituitary function
- Local necrosis due to extravasation (infusion escapes from the vein and damages surrounding tissue)

Reporting of side effects
If your child gets any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Neoatricon

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial and carton after 'EXP'. The expiry date refers to the last day of that month.

This medicinal product does not require any special temperature storage conditions. Keep the container in the outer carton in order to protect from light.

Neoatricon is a single use vial only. After first opening the medicine should be used immediately. Unused portions should be discarded.

Do not use this medicine if you notice an opaque, cloudy or discoloured solution.

6. Contents of the pack and other information

What Neoatricon contains

The active substance is dopamine hydrochloride.

Neoatricon 4.5 mg/mL solution for infusion
Each millilitre of solution contains 4.5 milligrams of dopamine hydrochloride. Each vial contains 225 mg of dopamine hydrochloride in 50 mL.

The other excipients are sodium metabisulfite (E223) (see section 2 "Neoatricon contains sodium metabisulfite"), water for injections, sodium hydroxide (for pH adjustment) and dilute hydrochloric acid (for pH adjustment).

What Neoatricon looks like and contents of the pack

Neoatricon solution for infusion is a clear, colourless or pale-yellow solution. It comes in clear glass vial with a rubber stopper and is sealed with an aluminium flip-off seal.

Pack size
Neoatricon 4.5 mg/mL is presented as one 50 mL vial, packed in an outer carton.

Marketing Authorisation Holder
BrePco Biopharma Limited,
Suite One, The Avenue, Beacon Court,
Sandyford,
Dublin D18 HX31,
Ireland

Manufacturer
Pharmadox Healthcare Ltd.,
KW20A Kordin Industrial, Park,
Paola PLA3000,
Malta

This leaflet was last revised in.

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

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The following information is intended for healthcare professionals only:

Infusion of dopamine hydrochloride solution should begin at a rate of 5 µg/kg/min and increase gradually in 5 µg/kg/min increments. The recommended dose range is 5 – 10 µg/kg/min. Doses above 10 µg/kg/min up to a maximum of 20 µg/kg/min may be administered if considered justified.

Infusion rates may be calculated using the following formula:

$$\text{Infusion Rate (mL/hour)} = \frac{\text{[Dose (µg/kg/minute) x Weight (kg) x 60 (minutes/hour)]}}{\text{Concentration (µg/mL)}}$$

Instructions for use and handling
For intravenous use. Administer via a central line [Umbilical venous catheter (UVC), Longline, or Surgical central venous line (CVL)]. If no central access is available, use a cannula in large vein.
A suitable metering device is required in the infusion system to control the rate and flow.
For single use. Discard any unused contents.
Do not dilute.
Do not use if the solution is discoloured.
The maximum acceptable duration for one single vial administration is 24-hours.

Incompatibilities
Neoatricon solution for infusion should not be added to any alkaline intravenous solutions, i.e. sodium bicarbonate. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
It is suggested that admixtures containing gentamicin sulphate, cephalothin sodium, cephalothin sodium neutral or oxacillin sodium should be avoided unless all other viable alternatives have been exhausted.
Admixtures of ampicillin and dopamine in 5% glucose solution are alkaline and incompatible and result in decomposition of both drugs. They should not be admixed.
Admixtures of dopamine, amphotericin B in 5% glucose solution are incompatible as a precipitate forms immediately on mixing.

In use storage precautions
This medicinal product does not require any special temperature storage conditions.
Keep the container in the outer carton in order to protect from light.