

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Neotricon 4.5 mg/mL solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Neotricon 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 sodium metabisulfite (E223).

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.

Neotricon 4.5 mg/ mL solution for infusion: Osmolarity is 50 mOsmol/kg

This medicinal product is hypotonic.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Neotricon 4.5mg/ml is a paediatric strength dopamine formulation, most suitable for infants and children weighing 10 kg or above, and adolescents, when use of this inotrope is indicated to provide cardiovascular support.

The decision to use dopamine should be based on an assessment of individual benefit-risk, taking into account the patient's clinical condition, haemodynamic status and in accordance with local guidelines.

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.

The rate of dopamine hydrochloride infusion 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 temporary discontinuation of the infusion (see section 4.4).

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

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, are generally not indicated in hypovolaemic 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 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 ($\geq 10 \mu\text{g}/\text{kg}/\text{min}$).

Because of variable, age-dependent clearance, titrate dosage 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 also involves 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.

Interference with laboratory tests

Infusion of dopamine hydrochloride suppresses pituitary secretion of thyroid stimulating hormone (TSH), and prolactin (see also 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 blocker

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 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 hyperglycemia is more common in this group. Metabolic parameters should be monitored during dopamine hydrochloride (or any other vasopressor) infusion.

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). Neotricon is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

It is unknown whether dopamine is excreted in breast milk. A risk to the suckling child cannot be excluded.

See section 4.4 for information on prolactin.

Fertility

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 ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1\ 000$ to $< 1/100$), rare ($\geq 1/10\ 000$ 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
	Not known	Ventricular tachycardia up to ventricular fibrillation
		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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store.

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, e.g., phentolamine mesylate 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 β 1-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 β 2-adrenergic receptors.

At higher doses (10 to 20 $\mu\text{g}/\text{kg}/\text{min}$) 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 $\mu\text{g}/\text{kg}/\text{min}$, dopamine hydrochloride acts predominantly on dopaminergic receptors; in IV doses of 2-10 $\mu\text{g}/\text{kg}/\text{min}$, dopamine also stimulates β 1-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 (PVR) 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 a duration of action of less than 10 minutes.

Distribution

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

Diluted 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 (see section 6.6).

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:

Neotricon 4.5 mg/mL solution for infusion: single vial carton containing 1 × 50 mL vial.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Inspect this medicinal product before use.

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.

Maintaining aseptic technique during the transfer of medication from a vial to a suitable metering device is essential to prevent contamination and ensure patient safety. This involves proper hand hygiene, using sterile equipment, and following meticulous procedures to avoid introducing microorganisms.

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.

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

7 MARKETING AUTHORISATION HOLDER

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Dublin D18HX31.
Ireland.

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 43267/0004

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

21/02/2025

10 DATE OF REVISION OF THE TEXT

25/07/2025