SUMMARY OF PRODUCT CHARACTERISTICS

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1. Name of the Medicinal Product:

1.1 Product Name:
VASOCON
Epinephrine Injection B.P.

1.2 Strength (Composition):
1 mg/ml

1.3 Pharmaceutical dosage form:
Liquid Injection

2. Qualitative and Quantitative composition:

Sr. No.	Particulars	Grade	Qty./ ml	O.A. %	Function
1.	Epinephrine Acid Tartrate equivalent to Epinephrine (Adrenaline Bitartrate)	B.P.	1 mg	7%	Active
2.	Sodium Metabisulphite	B.P.	1 mg	----	Antioxidant
3.	Sodium Chloride	B.P.	8 mg	----	Isotonisity
4.	Tartaric Acid	B.P.	0.08 mg	----	For pH adjustment
5.	Water for Injections	B.P.	q.s.	----	Vehicle

3. Pharmaceutical form:
A clear, colourless solution.

4. Clinical Particulars:

4.1 Therapeutic indications:
Epinephrine is a direct-acting sympathomimetic agent. Epinephrine may be used to provide rapid relief of severe hypersensitivity reaction to drugs and other allergens, and in the emergency treatment of anaphylactic shock.

4.2 Posology and method of administration:
Epinephrine Injection BP. 1/1000 (1 mg/ml) may be administered undiluted by S.C. or I.M injection. The intramuscular route is recommended as absorption from the intramuscular site is more rapid and reliable than from the subcutaneous site.

I.M Injection:
Adults: The usual dose is 500 micrograms (0.5ml of Epinephrine 1/1000).
If necessary, this dose may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.
Half doses of Epinephrine may be safer for patients who are taking amitriptyline, imipramine or a beta blocker.

Children: The following doses of Epinephrine 1/1,000 are recommended:

Age	Dose
Over 12 years	500 micrograms (0.5 mL)
	250 micrograms (0.25 mL) if child is small or prepubertal
6 - 12 years	250 micrograms (0.25 mL)
6 months - 6 years	120 micrograms (0.12 mL)
Under 6 months	50 micrograms (0.05 mL)

If necessary, these doses may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

4.3 Contra-indications:

Epinephrine Injection B.P. is contraindicated as below :

1) Use during labour
2) Use with local anaesthesia of peripheral structures including digits, ear lobe.
3) Use in the presence of ventricular fibrillation, cardiac dilatation, coronary insufficiency, organic brain disease or atherosclerosis, except in emergencies where the potential benefit clearly outweighs the risk.
4) Use if solution is discoloured.

4.4 Special warning and precautions for use:

Epinephrine should be used with caution in patients with hyperthyroidism, diabetes mellitus, phaeochromocytoma,narrow angle glaucoma,hypokalaemia, hypercalcaemia, severe renal impairment, prostatic adenoma leading to residual urine, cerebrovascular disease, organic brain damage orarteriosclerosis, in elderly patients, in patients with shock (other than anaphylactic shock) and in organic heart disease or cardiac dilatation (severe angina pectoris, obstructive cardiomyopathy, hypertension) as well as most patients with arrhythmias. Anginal pain may be induced when coronary insufficiency is present.

Repeat administration may produce local necrosis at the sites of injection.Prolonged administration may produce metabolic acidosis, renal necrosis and Epinephrine fastness or tachyphylaxis. Epinephrine should be avoided or used with extreme caution in patients undergoing anaesthesia with halothane or other halogenated anaesthetics, in view of the risk of inducing ventricular fibrillation.
Do not mix with other agents unless compatibility is known.

Epinephrine should not be used during the second stage of labour. Accidental intravascular injection may result in cerebral haemorrhage due to the sudden rise in blood pressure. Epinephrine 1 in 1000 should not be diluted to 1 in 10,000 for use in cardiac resuscitation - when the 1 in 10,000 strength of Epinephrine is required for this indication a “ready touse” preparation should be selected.

Monitor the patient as soon as possible (pulse, blood pressure, ECG, pulse oximetry) in order to assess the response to Epinephrine. The best site for IM injection is the anterolateral aspect of the middle third of the thigh. The needle used for injection needs to be sufficiently long to ensure that the Epinephrine is injected into muscle. Intramuscular injections of Epinephrine into the buttocks should be avoided because of the risk of tissue necrosis. Epinephrine Injection contains sodium metabisulphite, which can cause allergic-type reactions, including anaphylaxis and life-threatening or less severe asthmatic episodes, in certain susceptible individuals. The presence of sodium metabisulphite in parenteral Epinephrine and the possibility of allergic-type reactions should not deter use of the drug when indicated for the treatment of serious allergic reactions or for other emergency situations.

4.5 Interaction with other drugs, other forms of interactions:

Sympathomimetic agents/Oxytocin :
Epinephrine should not be administered concomitantly with oxytocin or other sympathomimetic agents because of the possibility of additive effects and increased toxicity.

Alpha-adrenergic blocking agents :
Alpha-blockers such as phentolamine antagonise the vasoconstriction and hypertension effects of Epinephrine. This effect may be beneficial in Epinephrine overdose.

Beta-adrenergic blocking agents :
Severe hypertension and reflex bradycardia may occur with non-selective beta-blocking drugs such as propranolol, due to alpha-mediated vasoconstriction. Beta-blockers, especially non-cardioselective agents, also antagonise the cardiac and bronchodilator effects of Epinephrine. Patients with severe anaphylaxis who are taking non-cardioselective beta-blockers may not respond to Epinephrine treatment.

General Anaesthetics :
Administration of Epinephrine in patients receiving halogenated hydrocarbon general anaesthetics that increase cardiac irritability and seem to sensitise the myocardium to Epinephrine may result in arrhythmias including ventricular premature contractions, tachycardia or fibrillation.

Antihypertensive agents :
Epinephrine specifically reverses the antihypertensive effects of adrenergic neurone blockers such as guanethidine, with the risk of severe hypertension. Epinephrine increases blood pressure and may antagonise the effects of antihypertensive drugs.

Antidepressant agents :
Tricyclic antidepressants such as imipramine inhibit reuptake of directly acting sympathomimetic agents, and may potentiate the effect of Epinephrine, increasing the risk of development of hypertension and cardiac arrhythmias. Although monoamine oxidase (MAO) is one of the enzymes responsible for Epinephrine metabolism, MAO inhibitors do not markedly potentiate the effects of Epinephrine.

Phenothiazines :
Phenothiazines block alpha-adrenergic receptors. Epinephrine should not be used to counteract circulatory collapse or hypotension caused by phenothiazines; a reversal of the pressor effects of Epinephrine may result in further lowering of blood pressure.

Other drugs :
Epinephrine should not be used in patients receiving high dosage of other drugs (e.g. cardiac glycosides) that can sensitise the heart to arrhythmias. Some antihistamines (e.g. diphenhydramine) and thyroid hormones may potentiate the effects of Epinephrine, especially on heart rhythm and rate.

Hypokalaemia :
The hypokalaemic effect of Epinephrine may be potentiated by other drugs that cause potassium loss, including corticosteroids, potassium-depleting diuretics, aminophylline and theophylline.

Hyperglycaemia :
Epinephrine-induced hyperglycaemia may lead to loss of blood-sugar control in diabetic patients treated with insulin or oral hypoglycaemic agents.

4.6 Pregnancy and lactation:

Pregnancy:
Epinephrine crosses the placenta. There is some evidence of a slightly increased incidence of congenital abnormalities. Injection of Epinephrine may cause anoxia, foetal tachycardia, cardiac irregularities, extra systoles and louder heart sounds. Epinephrine usually inhibits spontaneous or oxytocin induced contractions of the pregnant human uterus and may delay the second stage of labour. In dosage sufficient to reduce uterine contractions, the drug may cause a prolonged period of uterine atony with haemorrhage. Parenteral Epinephrine should not be used during the second stage of labour.

Use in Lactation:
Epinephrine is distributed into breast milk. Breast-feeding should be avoided in mothers receiving Epinephrine injection. Epinephrine should not be used in pregnancy unless clearly necessary.

4.7 Effects on ability to drive and operate machine:
The patients' ability to drive and use machines may be affected by the anaphylactic reaction, as well as by possible adverse reactions to Epinephrine.

4.8 Adverse effects:
The adverse events of Epinephrine mainly relate to the stimulation of both alpha- and beta-adrenergic receptors. The occurrence of undesirable effects depends on the sensitivity of the individual patient and the dose involved.

Immune system disorders:
Anaphylaxis, possibly with severe bronchospasm.

Metabolism and nutrition disorders:
Hypokalaemia, metabolic acidosis.
Inhibition of insulin secretion and hyperglycaemia even with low doses, gluconeogenesis, glycolysis, lipolysis and ketogenesis.

Psychiatric disorders :
Psychotic states, Anxiety, fear, confusion, irritability, insomnia.

Nervous system disorders :
Headache, dizziness, tremors, restlessness. In patients with Parkinsonian Syndrome, Epinephrine increases rigidity and tremor. Subarachnoid haemorrhage and hemiplegia have resulted from hypertension, even following subcutaneous administration of usual doses of Epinephrine.

Cardiac disorders :
Disturbances of cardiac rhythm and rate may result in palpitation and tachycardia. Chest pain/angina may occur. Epinephrine can cause potentially fatal ventricular arrhythmias including fibrillation, especially in patients with organic heart disease or those receiving other drugs that sensitise the heart to arrhythmias. Epinephrine causes E.C.G. changes including a decrease in T-Wave amplitude in all leads in normal subjects

Vascular disorders :
Hypertension (with risk of cerebral haemorrhage). Coldness of extremities may occur even with small doses of Epinephrine.

Respiratory disorders :
Dyspnoea, Pulmonary oedema may occur after excessive doses or in extreme sensitivity.

Gastrointestinal disorders :
Dry mouth, Reduced appetite, nausea, vomiting, hypersalivation.

Renal and urinary disorders :
Difficulty in micturition, urinary retention.

General disorders and administrative site conditions :
Sweating & weakness.
Repeated injections of Epinephrine can cause local ischaemic necrosis as a result of vascular constriction at the injection site. Tissue necrosis may also occur in the extremities, kidneys and liver.

4.9 Overdoses:

Symptoms :
After overdosage or inadvertent intravenous administration of usual intramuscular subcutaneous doses of Epinephrine, systolic and diastolicblood pressure rise sharply; venous pressure also rises. Cerebrovascular or other haemorrhages and hemiplegia may result, especially in elderly patients. Pulmonary oedema may occur.

Epinephrine overdosage causes transient bradycardia followed by tachycardia and may cause other potentially fatal cardiac arrhythmias. Kidney failure, metabolic acidosis and cold white skin may also occur.

Treatment :

Because Epinephrine is rapidly inactivated in the body, treatment of acute toxicity is mainly supportive. The pressor effects of Epinephrine may be counteracted by an immediate intravenous injection of a quick-acting alpha adrenoreceptor blocking agent, such as 5-10mg of phentolamine mesylate, followed by a beta-adrenoreceptor blocking agent, such as 2.5 - 5mg of propranolol. Arrhythmias, if they occur, may be counteracted by propranolol injection.

5. Pharmacological properties:

5.1 Pharmacodynamic Properties:

Epinephrine is a naturally occurring catecholamine secreted by the adrenal medulla in response to exertion or stress. It is a sympathomimetic amine which is a potent stimulant of both alpha- and beta-adrenergic receptors and its effects on target organs are therefore complex. It is used to provide rapid relief of hypersensitivity reactions to allergies or to idiopathic or exercise-induced anaphylaxis. Epinephrine has a strong vasoconstrictor action through alpha- adrenergic stimulation. This activity counteracts the vasodilatation and increased vascular permeability leading to loss of intravascular fluid and subsequent hypotension, which are the major pharmacological features in anaphylactic shock. Epinephrine stimulates bronchial beta-adrenergic receptors and has a powerful bronchodilator action. Epinephrine also alleviates pruritus, urticarial and angioedema associated with anaphylaxis. The overall effect of Epinephrine depends on the dose used, and may be complicated by the homeostatic reflex responses. In resuscitation procedures it is used to increase the efficacy of basic life support. It is a positive cardiac inotrope.

5.2 Pharmacokinetic Properties:

Epinephrine has a rapid onset of action after intramuscular administration and in the shocked patient its absorption from the intramuscular site is faster and more reliable than from the subcutaneous site. Epinephrine is rapidly inactivated in the body, mostly in the liver by the enzymes catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO). Much of a dose of Epinephrine is excreted as metabolites in urine.

The plasma half-life is about 2-3 minutes. However, when given by subcutaneous or intramuscular injection, local vasoconstriction may delay absorption so that the effects may last longer than the half-life suggests.

5.3 Preclinical Safety Data:

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics

6. Pharmaceutical particulars:

6.1 List of excipients:

Sodium Metabisulphite	B.P.
Sodium Chloride	B.P.
Tartaric Acid	B.P.
Water for Injections	B.P.

6.2 Incompatibilities:

Do not admix with other agents unless compatibility is known.

6.3 Shelf – life:

12 Months.

6.4 Special precautions for storage:

Store below 25°C. Protect from light. Do not freeze.

6.5 Nature and contents of container:

1 ml amber, double band snap off ampoule (Green above & Blue on constriction).

6.6 Special Precautions for Handling and Disposal:

If only part used, discard the remaining solution. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder:

NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Indl. Estate,
Mahakali Caves Road, Andheri (East),
Mumbai - 400 093.

8. Marketing authorization number :

752

9. Date of first authorization / Renewal of authorization :

First Authorization: 05/04/2004

10. Date of revision of the text:

Dec 2018