Approved professional information for Dopamine HCl 200 mg/5 ml Fresenius

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

DOPAMINE HCl 200 mg/5 ml FRESENIUS solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml ampoule contains 200 mg dopamine hydrochloride.

Sugar free.

Excipient with known effect:

Potassium metabisulphite.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

Clear colourless to slightly yellow solution in clear 5 ml ampoules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DOPAMINE HCl 200 mg/5 ml FRESENIUS is used in the treatment of:

1. Shock unresponsive to replacement of fluid loss and especially where renal function is impaired.
2. To correct haemodynamic imbalances associated with myocardial infarction, trauma, septic shock, and cardiac surgery.
3. It is also used in the management of chronic refractory congestive heart failure.

4.2 Posology and method of administration

Posology:

Hypovolaemia should be fully corrected, if possible, before DOPAMINE HCl 200 mg/5 ml FRESENIUS is used.

The initial rate is 2 to 5 µg per kg body mass per minute, gradually increased by 5 to 10 µg per kg per minute according to the patient's blood pressure, cardiac output and urine output.

Up to 20 to 50 µg per kg per minute may be required in seriously ill patients.

A reduction in urine flow, without hypotension, may indicate a need to reduce the dose. To avoid tissue necrosis DOPAMINE HCl 200 mg/5 ml FRESENIUS is best administered into a large lumen vein. Large veins of the antecubital fossa are preferred to veins in the dorsum of the hand or ankle. Less suitable infusion sites should be used only if the patient's condition requires immediate attention. More suitable sites should be used as rapidly as possible.

Method of administration:

For intravenous infusion only.

DOPAMINE HCl 200 mg/5 ml FRESENIUS should be given via an infusion pump or another suitable metering device to control the rate of flow in drops per minute.

DOPAMINE HCl 200 mg/5 ml FRESENIUS MUST be diluted before administration to the patient. Dilution should be made just prior to administration.

For instructions on reconstitution of DOPAMINE HCl 200 mg/5 ml FRESENIUS before administration, see section 6.6.

4.3 Contraindications

- Patients with known hypersensitivity to dopamine hydrochloride or to any of the excipients listed in section 6.1.
- The safety of DOPAMINE HCl 200 mg/5 ml FRESENIUS in pregnancy and lactation has not been established.
- The safety and efficacy of DOPAMINE HCl 200 mg/5 ml FRESENIUS in children have not been established.
- DOPAMINE HCl 200 mg/5 ml FRESENIUS should not be given to patients receiving monoamine oxidase (MAO) inhibitors or within 14 days of discontinuing such treatment.
- DOPAMINE HCl 200 mg/5 ml FRESENIUS should not be used in patients suffering from phaeochromocytoma or in the presence of uncorrected tachydysrhythmias or ventricular fibrillation.

4.4 Special warnings and precautions for use

DOPAMINE HCl 200 mg/5 ml FRESENIUS should not be used in patients with hyperthyroidism.

At high concentrations DOPAMINE HCl 200 mg/5 ml FRESENIUS activates vascular alfa 1 adrenergic receptors, leading to vasoconstriction. Therefore, when DOPAMINE HCl 200 mg/5 ml FRESENIUS is used in life-threatening states of shock, blood pressure and renal function must be monitored.

Abrupt discontinuation of the infusion can lead to vascular collapse.

DOPAMINE HCl 200 mg/5 ml FRESENIUS should be avoided or extreme caution must be exercised when using DOPAMINE HCl 200 mg/5 ml FRESENIUS together with anaesthetics like cyclopropane, halothane and other halogenated anaesthetics (see section 4.5 below).

DOPAMINE HCl 200 mg/5 ml FRESENIUS should be infused into a large vein whenever possible to prevent the possibility of infiltration of perivascular tissue adjacent to the infusion site. Extravasation of dopamine hydrochloride may result in tissue necrosis and sloughing.

Angina may be precipitated in patients with angina pectoris.

Administer with care to patients with diabetes mellitus or closed angle glaucoma.

Great care is also needed in patients with cardiovascular disease such as ischaemic heart disease, dysrhythmia or tachycardia, occlusive vascular disorders including arteriosclerosis, hypertension, or aneurysms.

Regular clinical and biochemical assessment is necessary to monitor changes in fluid, electrolyte or acid-base status during prolonged treatment and whenever the patient condition demands it. The infusion site should be continuously monitored for free flow.

Close monitoring of the following parameters – urine flow, cardiac output and blood pressure – during dopamine hydrochloride infusion is necessary.

It is recommended that on gradual discontinuation of dopamine hydrochloride, care should be taken to avoid undue hypotension associated with very low dosage levels where vasodilatation could predominate.

DOPAMINE HCl 200 mg/5 ml FRESENIUS should be used with caution in patients with benign prostatic hyperplasia with urinary retention.

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

The intravenous administration of these solutions can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary oedema.

DOPAMINE HCl 200 mg/5 ml FRESENIUS should not be added to sodium bicarbonate or other alkaline solution as medicine inactivation will occur.

Conditions like hypoxia, hypercapnia and acidosis can reduce dopamine efficacy and/or increase the incidence of adverse events and should therefore be identified and corrected before or during administration of DOPAMINE HCl 200 mg/5 ml FRESENIUS.

If tachydysrhythmias or increase in ectopic beats are observed, DOPAMINE HCl 200 mg/5 ml FRESENIUS should be reduced, if possible.

Hypovolaemia should be corrected where necessary prior to DOPAMINE HCl 200 mg/5 ml FRESENIUS infusion. Low doses should be used in shock due to acute myocardial infarction.

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.

Patients with a history of peripheral vascular disease 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 HCl 200 mg/5 ml FRESENIUS infusion should be weighed against the risk of possible necrosis. These changes may be reversed by decreasing the rate or discontinuing the infusion.

Ischaemia can be reversed by infiltration of the affected area with 10 – 15 ml of saline containing 5 to 10 mg phentolamine mesylate. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischaemic area as soon as extravasation is noted.

Dextrose solutions should be used with caution in patients with known subclinical or overt diabetes mellitus.

As the effect of dopamine on impaired renal and hepatic function is not known, close monitoring is advised.

DOPAMINE HCl 200 mg/5 ml FRESENIUS contains potassium metabisulphite, an excipient that may rarely cause severe hypersensitivity reactions and bronchospasm.

4.5 Interaction with other medicines and other forms of interaction

Anaesthetics:

DOPAMINE HCl 200 mg/5 ml FRESENIUS should be used with extreme caution and reduced dosage in patients receiving hydrocarbon anaesthetics, as there is an increased risk of severe ventricular dysrhythmias.

The results of animal studies indicate that ventricular dysrhythmias induced by DOPAMINE HCl 200 mg/5 ml FRESENIUS during anaesthesia can be reversed by propranolol.

Tricyclic antidepressants and guanethidine:

Tricyclic antidepressant medicines and guanethidine may potentiate the cardiovascular effects of DOPAMINE HCl 200 mg/5 ml FRESENIUS.

Alpha and beta blockers:

Beta adrenergic blocking medicines (e.g. propranolol) antagonise the cardiac effects of dopamine hydrochloride. The peripheral vasoconstriction caused by high doses of dopamine is antagonised by alpha adrenergic blocking medicines.

Monoamine oxidase inhibitors (MAOIs):

MAOIs (or for 3 weeks after withdrawal) prolong and intensify the effects of DOPAMINE HCl 200 mg/5 ml FRESENIUS (see section 4.3).

Reserpine, glycoside, metoclopramide:

The risk of dysrhythmias is greater in patients taking medicines that impact to the conduction in the heart, thyroid hormones and antidysrhythmics.

If concurrent use of dopamine hydrochloride and digitalis glycosides is necessary, there may be an increased risk of cardiac dysrhythmias.

Ergotamine:

DOPAMINE HCl 200 mg/5 ml FRESENIUS and ergot derivatives used concurrently may result in severe hypertension. The use of ergotamine with dopamine hydrochloride may produce peripheral vascular ischaemia and potentiate the possibility of gangrene.

Phenytoin:

Administration of IV phenytoin to patients receiving dopamine hydrochloride may result in bradycardia and hypotension; administer with care.

DOPAMINE HCl 200 mg/5 ml FRESENIUS may increase the effect of diuretic medicines.

Dopaminergic medicines (entacapone) may enhance the effects of DOPAMINE HCl 200 mg/5 ml FRESENIUS when both medicines are given simultaneously.

Doxapram may cause hypertension in patients receiving DOPAMINE HCl 200 mg/5 ml FRESENIUS.

4.6 Fertility, pregnancy and lactation

The safety of DOPAMINE HCl 200 mg/5 ml FRESENIUS in pregnancy and lactation has not been established (see section 4.3).

No information on fertility is available.

4.7 Effects on ability to drive and use machines

Patients should be advised to use caution when driving a car or operating machinery until they are reasonably certain that their performance is not affected by DOPAMINE HCl 200 mg/5 ml FRESENIUS.

4.8 Undesirable effects

Infections and infestations:

Less frequent: Gangrene.

Nervous system disorders:

Frequent: Headache, anxiety, tremor.

Less frequent: Piloerection.

Eye disorders:

Less frequent: Mydriasis.

Cardiac disorders:

Frequent: Ectopic heartbeats, tachycardia, anginal pain, palpitations.

Less frequent: Aberrant conduction, bradycardia, widened QRS complex, hypertension, fatal ventricular dysrhythmias.

Vascular disorders:

Frequent: Hypotension, vasoconstriction.

Respiratory, thoracic and mediastinal disorders:

Frequent: Dyspnoea.

Gastrointestinal disorders:

Frequent: Nausea, vomiting.

Renal and urinary disorders:

Frequent: Polyuria.

Less frequent: Azotaemia.

Investigations:

Frequent: Serum glucose level increased, blood urine nitrogen (BUN) level increased.

Description of selected adverse reactions:

Gangrene of the extremities has occurred following higher doses and in lower doses in patients with pre-existing vascular disease.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of DOPAMINE HCl 200 mg/5 ml FRESENIUS is important. It allows continued monitoring of the benefit/risk balance of DOPAMINE HCl 200 mg/5 ml FRESENIUS. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

Health care providers are asked to report any suspected adverse drug reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

4.9 Overdose

See section 4.8.

In case of accidental overdosage, as evidenced by excessive blood pressure elevation, reduce rate of administration or temporarily discontinue DOPAMINE HCl 200 mg/5 ml FRESENIUS until the patient's condition stabilises.

Further treatment is symptomatic and supportive.

Management of peripheral ischaemia: To prevent sloughing and necrosis in ischaemic areas, the area should be infiltrated as soon as possible with 10 to 15 ml of saline solution containing from 5 to 10 mg of phentolamine (alpha adrenoreceptor blocker).

A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischaemic areas.

Sympathetic blockade with phentolamine causes local hyperaemic changes if the area is infiltrated within 12 hours.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 6.1 - Cardiac stimulants

Pharmacotherapeutic group: 3.3 Sympathomimetic.

ATC code: C01CA04.

Dopamine hydrochloride exerts a positive inotropic effect on the myocardium, acting as an agonist at ß1 - adrenergic receptors.

In addition, it has the capacity to release norepinephrine (noradrenaline) from nerve terminals, and this also contributes to its effects on the heart. Dopamine hydrochloride appears to increase systolic and pulse pressure and has either no effect on or slightly increases diastolic blood pressure. Total peripheral resistance is usually unchanged when low or intermediate therapeutic doses are given. This is probably due to the ability of dopamine hydrochloride to reduce regional arterial resistance in the mesentery and the kidney, while producing minor increases in other vascular beds. The effect of dopamine hydrochloride on the renal vasculature appears to be mediated by a specific dopaminergic receptor. In relatively low doses, infusion of 2 µg/kg/minute dopamine hydrochloride is associated with an increase in glomerular filtration rate, renal blood flow, and sodium excretion (dopaminergic mechanism).

5.2 Pharmacokinetic properties

Absorption:

Following IV administration the maximum plasma concentration is reached within a few 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 is metabolised in the liver, kidneys, and plasma by monoamine oxidase (MAO) and catechol-*O*-methyltransferase (COMT) to the inactive compounds homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid. In patients receiving MAO inhibitors, the duration of action of dopamine may be as long as 1 hour. About 25 % of a dose of dopamine is metabolised to norepinephrine within the adrenergic nerve terminals.

Elimination:

Dopamine has a plasma half-life of about 2 minutes. Dopamine is excreted in urine principally as HVA and its sulphate 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, approximately 80 % of the radioactivity reportedly is excreted in urine within 24 hours.

5.3 Preclinical safety data

No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potassium metabisulphite (E224)

Hydrochloric acid (for pH-adjustment)

Water for injections.

6.2 Incompatibilities

Do not add DOPAMINE HCl 200 mg/5 ml FRESENIUS to 5 % sodium bicarbonate or any alkaline intravenous solution, since alkalinity inactivates DOPAMINE HCl 200 mg/5 ml FRESENIUS.

6.3 Shelf life

60 months.

In-use stability:

DOPAMINE HCl 200 mg/5 ml FRESENIUS is stable for at least 24 hours after dilution in saline or dextrose.

6.4 Special precautions for storage

Protect from light.

Store at or below 30 ºC.

6.5 Nature and contents of container

5 ml clear Type 1 glass OPC ampoule with blue dot, packed into a PVC blister tray and outer carton.

Pack size: 10 ampoules per outer carton.

6.6 Special precautions for disposal and other handling

Do not use the infusion if it is darker than slightly yellow or discoloured in any other way.

Suggested dilution:

To deliver a concentration of 200 µg/ml DOPAMINE HCl 200 mg/5 ml FRESENIUS:

Dissolve one ampoule of DOPAMINE HCl 200 mg/5 ml FRESENIUS in 1 litre of a suitable diluent.

Suitable diluents may contain sodium chloride and/or dextrose.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten 6020

Gqeberha

South Africa

8. REGISTRATION NUMBER

Y/6.1/415

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 March 1992

10. DATE OF REVISION OF THE TEXT

18 May 2022