SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DOPASEL 200 mg/5 mL I.V. Ampoule Containing Concentrated Solution for Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Drug substance:
Each 1 mL solution contains 40 mg of dopamine hydrochloride.
5 mL ampoule contains 200 mg of dopamine hydrochloride.

Excipients:
Sodium metabisulfite(E 233)……. 10 mg/mL

Please see section 6.1 for excipients.

3. PHARMACEUTICAL FORM

Concentrated solution for infusion.
The ampoule contains a clear, colorless or light yellow solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Dopasel is indicated for the correction of hemodynamic disturbances in:

1. Acute hypotension or shock accompanied by myocardial infarction, endotoxic septicemia, trauma and renal failure.
2. As adjunctive therapy in case of persistent hypotension after correction of hypovolemia after open heart surgery.
3. In chronic cardiac decompensation as in congestive insufficiency.

4.2. Posology and method of administration

Posology /administrationfrequency and duration
Adults:
Where appropriate, the circulating blood volume should be replenished with whole blood or a plasma expander before dopamine hydrochloride is administered.

In patients likely to respond to the smallest increase in heart rate and renal perfusion, the initial dose of dopamine hydrochloride solution is 2.5 micrograms (mcg) / kg / minute.

In more severe cases, administration may be initiated at a rate of 5 micrograms / kg / minute and the dose may be increased in increments of 5-10 micrograms / kg / minute up to 20-50 micrograms / kg / minute as needed. If a dose of more than 50 micrograms / kg / minute is required, frequent checking of urine output is recommended.

If urine output decreases without hypotension, a reduction in dopamine dose should be considered. It has been shown that adequate results were obtained in 50% of patients with doses below 20 mcg/kg/minute.

In patients who do not respond to these doses, additional increases in Dopasel dose may be made to ensure adequate blood pressure, urine flow, and perfusion.

Blood volume, cardiac contractility, peripheral perfusion distribution and urine flow should be continuously evaluated during the treatment of all patients.

Dopasel dose should be adjusted according to the patient's response. Particular attention should be paid to the decrease in urine flow rate, increase in tachycardia and the formation of new rhythm disorders, which indicate a reduction in dose or temporary decapitation of dose.

Method of administration:
Infusion is administered intravenously only after dilution with appropriate diluents.

Additional information for special populations:
Renal/Hepatic Failure:
Because the effect of dopamine on renal and hepatic failure is unknown, close monitoring of patients is recommended.

Pediatric population:
The safety and efficacy of dopamine in children is unknown.

Geriatric population:
Dose adjustment is not recommended in elderly patients. However, close monitoring of the patient is recommended in terms of blood pressure, urine flow and peripheral tissue perfusion.

4.3. Contraindications
It should not be used in patients allergic to dopamine or sulfides; in patients with pheochromacytoma and hyperthyroidism, non-corrected atrial or ventricular tachyarrhythmia, or ventricular fibrillation.
It should not be used in patients with cyclopropane and halogenated hydrocarbon anesthetic due to **arterial arrhythmogenic potential.**

4.4. Special warnings and special precautions for use
Patients treated with MAO inhibitors before dopamine treatment should be given a reduced dose; the initial dose should be one tenth (1/10) of the normal dose.

Excessive administration of potassium-free solutions can cause hypokalemia.
Intravenous administration of these solutions can lead to excessive fluid and/or solute loading, resulting in dilution of serum electrolyte concentrations, excessive hydration,

congestion, and pulmonary edema.

Precautions
Before infusion of dopamine, the patient's hypovolemia and electrolytes should be corrected with blood or plasma supplementation, if necessary. Low doses should be used in shocks due to acute myocardial infarction.

If a sudden change in diastolic pressure (a significant decrease in heart rate) is observed, the infusion rate should be reduced or temporarily interrupted and the patient followed closely. If such an effect on vasoconstrictor efficacy is not desired in patients, the patient should be monitored carefully considering the possibility of vasoconstriction.

Patients with a history of peripheral vascular disease should be closely monitored in terms of color and temperature change in the skin of the arms and legs. If a change occurs in the color or temperature of the skin, it must be considered as a result of poor circulation. The benefit of continuing the dopamine infusion is weighed against the possible risk of necrosis. These changes can be reversed by reducing the infusion rate or by interrupting the infusion. IV administration of 5-10 mg phentolamine mesylate may correct ischemia.

Dopamine hydrochloride in 5% Dextrose should be infused into a large vein whenever possible to avoid possible infiltration into perivascular tissue adjacent to the infusion site. Extravasation can cause necrosis or peeling of the surrounding tissue. Infiltration of 10-15 mL of saline containing 5-10 mg of phentolamine mesylate may correct ischemia in this area. As soon as extravasation is detected, a syringe with a thin hypodermic needle should be used for infiltration into the ischemic area.

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

Close monitoring of patients is recommended as the effect of dopamine on impaired renal and hepatic function is unknown.

Dopamine infusion should be discontinued gradually to avoid hypotension.

This medicinal product contains sodium metabisulfite, an antioxidant. Therefore, it may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicinal product contains less than 1 mmol (23 mg) of sodium in each ampule, meaning it is essentially “sodium-free”.

4.5. Interaction with other medicinal products and other forms of interaction
i) Anesthetics:
The myocardium is sensitive to the effects of dopamine, cyclopropane and halogenated hydrocarbon anesthetics and their concomitant use should be avoided. This interaction

occurs due to both pressor activity and cardiac beta adrenergic stimulation.

ii) Alpha and Beta Blockers:
The cardiac effects of dopamine are antagonized by beta-adrenergic blocking agents such as propanol and metoprolol, and peripheral vasoconstriction caused by high-dose dopamine is antagonized by alpha-adrenergic blocking drugs. Dopamine-induced renal and mesenteric vasodilation is not antagonized by alpha or beta adrenergic blocking agents.

iii) Monoamine Oxidase (MAO) inhibitors:
MAO inhibitors potentiate the effect of dopamine and may increase its duration.
Dose reduction is recommended in patients on MAO inhibitor therapy prior to dopamine therapy. Therefore, significantly reduced doses should be applied (Initial dose should be reduced to at least 1/10 of the normal dose).

iv) Phenytoin:
Hypotension and bradycardia have been observed when IV phenytoin is administered in patients receiving dopamine; if phenytoin will be given to some patients on dopamine administration, extreme caution should be exercised.

Dopamine can increase the effect of diuretic drugs.

Ergo alkaloids should be avoided as there may be excessive vasoconstriction. Tricyclic antidepressants and guanetidine dopamine may increase presor response.

Important information on special populations

Pediatric population:
The reliability and benefit of dopamine in pediatric patients has not been proven.

Geriatric population:
In geriatric patients, dose adjustment is not required, but blood pressure, urine output and peripheral tissue perfusion should be closely monitored.

4.6. Pregnancy and lactation
General advice
Pregnancy category:C

Women with child-bearing potential / Contraception
There is insufficient data on the use of dopamine in women with childbearing potential.

Pregnancy

Animal studies are insufficient in terms of effects on pregnancy/and-or/embryonal/fetal development/and - or/birth/and—or/postpartum development. The potential risk to humans is unknown.
Dopamine should not be used during pregnancy unless necessary.

Lactation

Whether dopamine passes into breast milk and its effects on the newborn is unknown. Therefore, it should not be used in nursing mothers.

Fertility
Not valid.

4.7. Effects on ability to drive and use machines
There is no data on the impact on the ability to drive vehicles and machines.

4.8. Undesirable effects

Side effects of dopamine are associated with its pharmacological effect.

Side effects are usually dose dependent and are observed in about 10% of patients.

Very common (≥ 1/10), common (≥ 1/100 and < 1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10.000 and <1/1000), very rare (<1/10.000) and unknown (estimation based on the existing data is impossible).

Nervous system diseases
Very common: Headache
Not common: Piloerection

Eye diseases
Very common: Mydriasis

Cardiac diseases
Very common: Ectopic heartbeat, tachycardia, angina pain, palpitation, hypotension, vasoconstriction.
Uncommon: Aberrant conduction, bradycardia, QRS complex, hypertension, gangrene, fatal ventricular arrhythmia.

Vascular diseases
Uncommon: Foot gangrene has been seen in a few patients with pre-existing vascular disease at doses of 10-14 micrograms / kg / min and above.

Respiratory, thoracic and mediastinal disorders
Very common: Dyspnoea

Gastrointestinal diseases
Common: Nausea, vomiting

Research (laboratory findings)
Not common: Azotemia

Reporting of suspected adverse reactions
If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

4.9. Overdose
Especially in patients with a history of occlusive vascular disease, excessive increase in blood pressure and vasoconstriction may occur due to the alpha adrenergic effect of dopamine. This can be corrected by reducing the dose or discontinuing the infusion because dopamine has a half-life of less than 2 minutes in the body.

If these measures are not sufficient, an infusion of an alpha adrenergic blocker (e.g. phentolamine mesylate) may be considered.

Dopamine can cause local vasoconstriction at the infusion site. For this reason, a large vein should be selected for infusion. Infiltration with 10-15 mL of saline containing 5-10 mg of phentolamine mesylate can correct ischemia in this area. As soon as extravasation is observed, the ischemic area should be infiltrated using an injector with a thin hypodermic needle.

If an accidental overdose is noticed with excessive blood pressure, the dose deceleration or infusion should be interrupted, because the duration of dopamine action is very short.

If these measures are not sufficient, an infusion of phentolamine fesylate should be considered.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pharmacotherapeutic group : Cardiac stimulants (except Cardiac glycosides) - Adrenergic and dopaminergic agents
ATC code : C01CA04

Dopamine stimulates the adrenergic receptors of the sympathetic nervous system. The drug has a direct effect on beta1-adrenergic receptors and also acts indirectly by releasing norepinephrine. Dopamine also provides vasodilation by affecting specific dopaminergic receptors in renal, mesenteric, coronary and intracerebral vascular beds. The effect of the drug on beta2-adrenergic receptors is negligible.

At IV doses of 0.5-2 micrograms / kg per minute, the drug acts on dopaminergic receptors; At doses of 2-10 micrograms / kg per minute, the drug also stimulates beta1-adrenergic receptors. In higher treatment doses, alpha-adrenergic receptors are also stimulated and the net effect of the drug is seen as a result of alpha-adrenergic, beta1-adrenergic and dopaminergic stimulation. The actual effect of dopamine depends on the dose

administered. At low doses, cardiac stimulation and renal vascular dilatation occur, and at higher doses, vasoconstriction occurs. It is believed that alpha-adrenergic effects occur as a result of inhibition of the production of cyclic adenosine 31, 51-monophosphate (cAMP) by inhibition of the adenylate cyclase enzyme, while beta-adrenergic effects are caused by stimulation of adenylate cyclase activity.

5.2 Pharmacokinetic properties

Absorption:

Dopamine administered orally is rapidly metabolized in the gastrointestinal tract. After IV administration, the effect of dopamine begins within 5 minutes, the duration of action of the drug is less than 10 minutes.

Distribution:

The drug is completely distributed throughout the body, but most of it cannot cross the blood brain barrier. It is not known whether dopamine passes into the placenta.

Biotransformation:

The plasma half-life of dopamine is about 2 minutes. Dopamine is metabolized in the liver, kidneys, and plasma by monoaminoxidase (MAO) and catechol-O-methyltransferase to inactive compounds homovanilic acid (HVA) and 3,4-dihydroxyphenylacetic acid. In patients taking MAO inhibitors, the duration of dopamine action can be extended up to 1 hour. Approximately 25% of the dopamine dose is metabolized to norepinephrine at adrenergic nerve terminals.

Elimination:

Dopamine is mainly excreted in the urine as HVA and its sulphate and glucuronide conjugates and 3,4-dihydrophenylacetic acid. A very small portion of the dose is excreted unchanged. Following the administration of radiolabeled dopamine, approximately 80% of the radioactivity is excreted in the urine within 24 hours.

Linearity/Nonlinearity:

There is no data.

5.3 Preclinical safety data

There is no preclinical data other than those mentioned in other sections of summary of product characterictics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulfite
Water for injection

6.2 Incompatibilities

DOPASEL should not be added to any alkaline intravenous solution such as sodium bicarbonate. Solutions that show physical or chemical incompatibility in the form of

discoloration or precipitation should not be administered.

It is recommended that mixtures containing gentamicin sulfate, cephalothin sodium, cephalothin sodium neutral or oxalicin sodium should be avoided, unless there is another alternative. The mixture of ampicillin and dopamine in a 5% glucose solution is alkaline and incompatible, and the situation causes deterioration in both drugs. Therefore, the two drugs should not be mixed. The mixture of dopamine and amphotericin B in a 5% glucose solution is incompatible, precipitating occurs immediately after mixing the drugs.

6.3 Shelf life
24 months when stored in its packaging.

When the recommended solvents are used (see 6.6), their chemical and physical stability during use is 48 hours at temperatures below 30 ° C.

However, microbiologically the drug should be used immediately. If not used immediately, the storage time and conditions during use are the responsibility of the user and the stability is not more than 24 hours at 2-8°C unless the normally prepared solution is controlled and validated under aseptic conditions.

6.4 Special precautions for storage
Store at room temperature below 30°C in its original package, protected from light.
For in-use storage conditions see 6.3.

6.5 Nature and contents of container
Transparent Type I glass ampoule. Package content; 5 ampoules of 5 mL or 10 ampoules of 5 mL.

6.6 Instructions for use and handling and disposal

For single use only. Do not use if the solution has changed color.

Unused products or waste materials must be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulation".

Preparation of the infusion solution

As shown in the table below, aseptically transfer DOPASEL ampoule into I.V. solution:

Content of Concentrate	Volume of Concentrate mL	Volume of IV Solution mL	Final Concentration microgram/mL
200mg/5 mL	5	500	400
200mg/5 mL	5	250	800
200mg/5 mL	10	250	1600
200mg/5 mL	20	500	1600
200mg/5 mL	5	500	1600
200mg/5 mL	5	250	3200

Dopamine hydrochloride can be diluted with the following solutions:
(0.9%) Sodium Chloride intravenous infusion
(5%) Dextrose, (0.45%) sodium chloride solution
Sodium Lactate Intravenous Infusion, Compound (Hartmann's Solution for Injection)

7. MARKETING AUTHORISATION HOLDER

HAVER FARMA İlaç A.Ş.
Akbaba Mah. Maraş Cad. No.:52/2/1
Beykoz / İstanbul
Phone: 0216 324 38 38
Fax: 0216 317 04 98
E-mail: info@haver.com.tr

8. MARKETING AUTHORISATION NUMBER

2016/99

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17.02.2016
Date of latest renewal: 16.03.2021

10. DATE OF REVISION OF THE TEXT
