DOPACARD® 50mg/5ml Concentrate for Solution for Infusion

Dopexamine hydrochloride

Doctor information

Trade Name of the Medicinal Product

DOPACARD® 50mg/5ml Concentrate for Solution for Infusion.

Qualitative and Quantitative Composition

Dopexamine hydrochloride as a 1% solution (w/v). Each 5ml ampoule contains 50mg of dopexamine hydrochloride.

Pharmaceutical Form

Concentrate for solution for infusion.

Clinical Particulars

Therapeutic indications

DOPACARD is indicated for short-term intravenous administration to patients in whom afterload reduction, (through peripheral vasodilatation, and/or renal and mesenteric vasodilatation), combined with a mild positive inotropic effect is required for the treatment of exacerbations of chronic heart failure, or heart failure associated with cardiac surgery.

Posology and method of administration

For intravenous use only.
DOPACARD must be diluted before use.

Dosage

Adults and the elderly:

Infusion should begin at a dose of 0.5 microgram/kg/min and may be increased to 1 microgram/kg/min and then in increments (0.5-1 microgram/kg/min) up to 6 micrograms/kg/min at not less than 15 minute intervals according to the patient's haemodynamic and clinical response. Smaller increments (0.5 microgram/kg/min) may be justified in certain patients according to haemodynamic and clinical response.

Children:

The safety and efficacy of DOPACARD for use in children have not been established.

Administration

DOPACARD should only be administered intravenously by infusion through a cannula or catheter in a central or large peripheral vein. Contact with metal parts in infusion apparatus should be minimised. A device which provides accurate control of the rate of flow is essential.

Central administration: DOPACARD can be administered via a cannula or catheter sited in a central vein. The concentration of the infusion solution for administration via this route must not exceed 4mg/ml.

Peripheral administration: DOPACARD can be administered via a cannula in a large peripheral vein. The concentration of the infusion solution for administration via this route must not exceed 1mg/ml. Thrombophlebitis has been reported with peripheral administration using concentrations of DOPACARD exceeding 1mg/ml.

During the administration of DOPACARD, as with any parenteral catecholamine, the rate of administration and duration of therapy should be adjusted according to the patient's response as determined by heart rate and rhythm (ECG), blood pressure, urine flow and, whenever possible, measurement of cardiac output.

It is recommended that the infusion of DOPACARD is reduced gradually rather than withdrawn abruptly.

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The duration of therapy is dependent upon the patient's overall response to treatment. Extended therapy beyond 48 hours has not been fully evaluated.

Contra-indications

Known hypersensitivity to dopexamine hydrochloride or excipients (disodium edetate).

Patients who are receiving monoamine oxidase inhibitors (MAOIs).
Phaeochromocytoma.
Thrombocytopenia.

Patients with left ventricular outlet obstruction such as hypertrophic obstructive cardiomyopathy or aortic stenosis. In such patients, positive inotropic activity may increase left ventricular outflow obstruction and sudden vasodilatation may cause hypotension.

Special warnings and precautions for use

Correction of hypovolaemia must be achieved prior to administration of DOPACARD. Hypovolaemia should also be corrected during therapy as vasodilatation occurs due to treatment.

Care should be exercised so as to restrict the sodium and fluid load during administration of DOPACARD.

DOPACARD should not be administered to patients with severe hypotension or a markedly reduced systemic vascular resistance until specific resuscitative measures have been taken to restore blood pressure to a clinically acceptable level.

In patients with a marked reduction in systemic vascular resistance, DOPACARD should not be used as a direct substitute for pressor agents or other inotropes.

As with other catecholamines, DOPACARD should be administered with caution to patients with a clinical history of ischaemic heart disease especially following acute myocardial infarction or recent episodes of angina pectoris as a tachycardia may increase myocardial oxygen demand and further exacerbate myocardial ischaemia.

As has been observed with other β_2-adrenergic agonists, a small reversible fall in circulating platelet numbers has been observed in some patients. No adverse effects attributable to alterations in platelet count have been seen in clinical studies.

Care must be exercised when administering DOPACARD in the presence of hypokalaemia or hyperglycaemia. In common with other β_2-agonists, DOPACARD depresses plasma potassium and raises plasma glucose. These effects are minor and reversible. Monitoring of potassium and glucose is advisable in patients likely to be at risk from such changes, e.g. diabetics, patients with myocardial infarction or patients being treated with diuretics or cardiac glycosides.

Benign arrhythmias such as ventricular premature beats and, more rarely, serious arrhythmias have been reported in some patients. If excessive tachycardia occurs during DOPACARD administration, then a reduction or temporary discontinuation of the infusion should be considered.

As with other parenteral catecholamines, there have been occasional reports of partial tolerance, with some attenuation of the haemodynamic response developing during long-term infusions of DOPACARD.

The risk of thrombophlebitis and local necrosis may be increased if the concentration of DOPACARD administered via a peripheral vein exceeds 1mg/ml. Thrombophlebitis is rare when the concentration of drug used for peripheral administration is less than 1mg/ml.

Interaction with other medicaments and other forms of interaction

As DOPACARD inhibits the Uptake-1 mechanism, it may potentiate the effects of exogenous catecholamines such as noradrenaline. Caution is recommended when these agents are administered concomitantly with DOPACARD or soon after its discontinuation.

There is no evidence of an interaction with dopamine, other than possible attenuation of the indirect sympathomimetic inotropic effects of higher doses of dopamine due to Uptake-1 blockade by DOPACARD.

Concomitant use with β_2-adrenergic and dopamine receptor antagonists requires caution since possible attenuation of the pharmacological effects of DOPACARD may occur.

Pregnancy and lactation

There is no experience of the use of DOPACARD in pregnant or lactating women and therefore its safety in these situations has not been established.
There is insufficient evidence from animal studies to indicate it is free from hazard.
DOPACARD is not therefore currently recommended for use in pregnant or lactating women.

Effects on ability to drive and use machines

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DOPACARD® 50 mg/5 ml Concentrate for Solution for Infusion

(Dopexamine hydrochloride as a 1% solution w/v)

PACKAGE LEAFLET: INFORMATION FOR THE USER

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT DOPACARD IS AND WHAT IT IS USED FOR

The name of this medicine is DOPACARD 50 mg/5 ml Concentrate for Solution for Infusion. The active ingredient in this medicine is dopexamine hydrochloride which belongs to a group of medicines called sympathomimetics.
DOPACARD is used to widen your blood vessels and allow your heart to pump blood easily to your vital organs, such as kidneys or liver.
It is also used as a supportive treatment during times when your heart is not pumping blood around your body properly.

2. BEFORE YOU ARE GIVEN DOPACARD

You should not be given DOPACARD if you:
- Are **allergic** (hypersensitive) to dopexamine hydrochloride or any of the other ingredients of DOPACARD.
- Are taking, or have recently taken, medicines for **depression** called monoamine oxidase inhibitors (MAOI).
- Have a disorder of the **adrenal glands** which causes you to have high blood pressure (phaeochromocytoma).
- Have a **blood disorder** that affects the number of platelets in your blood (thrombocytopenia).
- Have any **heart** problems (for example, a partially blocked artery).

DOPACARD is not suitable for use in children.

Take special care with DOPACARD if you:
- Have very **low blood pressure**.
- Have been told by your doctor you have poor blood circulation.
- Have recently had any **chest pains** or if you have a history of chest pain.
- Have ever had a **heart attack**.
- Have any condition which can affect your blood sugar level e.g. diabetes

If any of the above apply to you, you should speak to your doctor before taking this medicine.

Taking other medicines
Please tell your doctor if you are taking or have recently taken other medicines, including medicines obtained without a prescription. This is especially important if you are taking any of the following:
- Water tablets (diuretics)
- Medicines for a heart condition e.g. digoxin
- Beta-blockers e.g. atenolol
- Medicines for nausea and sickness e.g. prochlorperazine
- Noradrenaline or dopamine

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Pregnancy and breast-feeding

DOPACARD is not recommended for use during pregnancy and breast-feeding. If you are pregnant, think you might be pregnant, or are breast-feeding tell your doctor or pharmacist before being given DOPACARD.

3. HOW DOPACARD WILL BE GIVEN

Your doctor will ensure you have sufficient fluid circulating in your body before giving DOPACARD.
The doctor or other health care professional will make up the correct dose of DOPACARD for you and it will be given as a solution by a slow injection or by a drip into a vein (infusion), for a maximum of 48 hours.
Your doctor will monitor your response to DOPACARD.

If you are given too much DOPACARD
It is unlikely you will be given too much DOPACARD, but if this happens your doctor will treat any symptoms that may occur.

4. POSSIBLE SIDE EFFECTS

Like all medicines, DOPACARD can cause sides effects, although not everybody gets them. The following side effects have been reported:

- Racing or irregular pulse.
- Slow pulse.
- High or low blood pressure.
- Worsening heart failure.
- Heart attack.
- Chest pain (angina).
- Nausea and vomiting.
- Shortness of breath.
- Sweating.
- Headaches.
- Shaking.

Rarely redness and soreness may occur at the site where the drip enters the vein.
More rarely, there have been reports of the following side effects being experienced by patients who have been given DOPACARD while undergoing heart surgery, although these may have been due to the condition of the patient:

- Kidney failure.
- Severe breathing difficulties.
- Fluid on the lungs.
- Blood poisoning.
- Bleeding.

If you experience any side effects while receiving DOPACARD tell your doctor or health care professional immediately.

5. HOW TO STORE DOPACARD

Keep all medicines out of the reach and sight of children.
Keep the ampoule in the outer carton.
DOPACARD must not be used after the expiry date printed on the ampoule.

6. FURTHER INFORMATION

What DOPACARD contains
DOPACARD contains 5 ml of 1% dopexamine hydrochloride as the active substance. It also contains disodium edetate, hydrochloric acid and water for injections as the inactive ingredients.

What DOPACARD looks like and contents of the pack
DOPACARD comes in boxes of 10 clear glass ampoules each containing 5 ml 1% w/w solution of dopexamine hydrochloride.

Marketing Authorisation Holder
Cephalon UK Limited, 1 Albany Place, Hyde Way, Welwyn Garden City, Hertfordshire, AL7 3BT, UK.

Manufacturer
Hospira S.p.A., Via Fosse Ardeatine 2, 20060 Liscate (MI), Italy.

This leaflet was last approved in March 2010

For more information please call free on 0800 783 4869 or e-mail:
UKMedInfo@cephalon.com

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Not applicable.

Undesirable effects

The most common undesirable effect reported with DOPACARD administration in studies of use in heart failure is tachycardia (11.8% in studies of exacerbations of chronic heart failure; 19.4% in studies of use in cardiac surgery). The increases in heart rate are dose-related and, in most cases, not clinically significant.

Hypertension and transient hypotension have been reported after cardiac surgery (at an incidence of 8.8% and 7.0% respectively). These events, however, are not uncommon as compensatory mechanisms following cardiac surgery. Transient hypotension was reported in studies of exacerbations of chronic heart failure at an incidence of 6.3%.

Other undesirable effects reported in clinical trials in both exacerbations of chronic heart failure and cardiac surgery at an incidence of 1% or more include:

Cardiovascular: A number of tachyarrhythmias such as premature ventricular contractions (PVCs) and atrial fibrillation, bradycardia, both sinus and nodal, worsening heart failure leading to asystole and cardiac arrest, angina, myocardial infarction, cardiac enzyme changes and non-specific ECG changes have occurred.

Non-cardiovascular: Nausea and vomiting, tremor, headache, diaphoresis and dyspnoea.

Careful titration of the dose may minimise the incidence of adverse events.

More rarely a number of serious adverse events have been reported in patients undergoing cardiac surgery: renal failure, respiratory failure, acute respiratory distress syndrome (ARDS), pulmonary oedema, pulmonary hypertension, bleeding and septicaemia. However, such events may also be due to the condition of the patients in such populations.

Overdose
The half-life of DOPACARD in blood is short. Consequently, the effects of overdosage are likely to be short-lived provided that administration is discontinued. However, in some cases, it may be necessary to initiate prompt supportive measures.

Effects of overdosage are likely to be related to the pharmacological actions and include tachycardia, tremulousness and tremor, nausea and vomiting, and anginal pain. Treatment should be supportive and directed to these symptoms.

Pharmacological Properties

Pharmacodynamic properties

The primary actions of DOPACARD (dopexamine hydrochloride) are the stimulation of adrenergic $ß_2$-receptors and peripheral dopamine receptors of DA_1 and DA_2 subtypes. In addition, DOPACARD is an inhibitor of neuronal re-uptake of noradrenaline (Uptake-1). These pharmacological actions result in an increase in cardiac output mediated by afterload reduction ($ß_2$, DA_1) and mild positive inotropism ($ß_2$, Uptake-1 inhibition) together with an increase in blood flow to vascular beds (DA_1) such as the renal and mesenteric beds. DOPACARD therefore provides an increase in systemic and regional oxygen delivery. DOPACARD is not an α-adrenergic agonist and does not cause vasoconstriction and is not a pressor agent.

Pharmacokinetic properties

DOPACARD is rapidly eliminated from blood with a half-life of approximately 6-7 minutes in healthy volunteers and around 11 minutes in patients with cardiac failure. Subsequent elimination of the metabolites is by urinary and biliary excretion. The response to DOPACARD is rapid in onset and effects subside rapidly on discontinuation of the infusion.

Pre-clinical safety data

There is no information relevant to the prescriber, which has not been included in other sections of this Summary of Product Characteristics.

Pharmaceutical Particulars

List of excipients

Disodium edetate, Hydrochloric acid, Water for Injections.

Incompatibilities

DOPACARD should only be diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection, Hartmann's Solution (Compound Sodium Lactate Intravenous Infusion) or Dextrose 4%/Saline 0.18% Injection, and should not be added to sodium bicarbonate or any other strongly alkaline solutions as inactivation will occur.

DOPACARD should not be mixed with any other drugs before administration.
Contact with metal parts, in infusion apparatus for example, should be minimised.

Shelf-life

The shelf life of unopened ampoules is 3 years.

Prepared intravenous solutions in 0.9% Sodium Chloride Injection or 5% Dextrose Injection are stable for 24 hours at room temperature.

Special precautions for storage

Keep the ampoule in the outer carton.

Nature and contents of container

Box of 10 clear glass ampoules each containing 5ml of 1% (w/v) solution of dopexamine hydrochloride (50mg per ampoule).

Instructions for use/handling

The contents of four ampoules (20ml) should be injected aseptically into one of the following:

0.9%	Sodium Chloride Injection	500 or 250ml
5%	Dextrose Injection	500 or 250ml

These dilutions give a concentration for administration as follows:-

4 ampoules of DOPACARD diluted to 500ml = 400 micrograms/ml
4 ampoules of DOPACARD diluted to 250ml = 800 micrograms/ml

DOPACARD, in common with other catecholamines, may turn slightly pink in prepared solutions. There is no significant loss of potency associated with this change.

Marketing Authorisation Holder

Cephalon UK Limited
1 Albany Place,
Hyde Way,
Welwyn Garden City,
Hertfordshire,
AL7 3BT,
UK.

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Company contact:

Cephalon UK Limited
1 Albany Place,
Hyde Way,
Welwyn Garden City,
Hertfordshire,
AL7 3BT,
UK.

For more information please call free on 0800 783 4869 or e-mail:
UKMedInfo@cephalon.com

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