Package leaflet: Information for the user

Neupedix 500 micrograms/ml concentrate for solution for infusion

alprostadil

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- This medicine has been prescribed for your baby. Do not pass it on to others. It may harm them, even if their signs of illness are the same as in your baby.
- If your baby gets any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Neupedix is and what it is used for

Neupedix contains the active substance alprostadil. Alprostadil is a synthetic copy of a prostaglandin chemical that occurs naturally in your body. Prostaglandins are a complex set of chemicals made by the body tissues. Some of them can cause muscles, which occur in the walls of certain blood vessels, to relax.

Neupedix is a medicine given to new born babies through an injection into the vein or a catheter (fine tube) into an artery.

While a baby is in the womb, before it is born, it does not breathe. For this reason, in a baby's heart there is a special, small blood vessel called the ductus arteriosus that allows blood to pass through the heart without going through the lungs. Once the baby is born and breathing normally, this is no longer needed, and the ductus arteriosus would close off.

If the baby has certain conditions affecting the heart it may still be beneficial to keep this channel (the ductus arteriosus) open until the heart condition can be corrected by surgery. This is what Neupedix can do i.e. it relaxes the muscles in the wall of the ductus arteriosus while the baby still requires this. Once the baby has had an operation to correct the heart problem, then the ductus arteriosus will no longer be needed and can be allowed to close.

Your baby may have one of several problems in which it is necessary to keep the ductus arteriosus open until an operation can take place. Your baby's doctor will explain which problem affects your baby.

2. What you need to know before your baby is given Neupedix

Do not use Neupedix
- if your baby is allergic to alprostadil (or any other prostaglandin) or any of the other ingredients of this medicine (listed in section 6).
- The symptoms of an allergic reaction can be the following: wheezing, breathlessness, swelling of the face, hands, itchy rash or redness of the skin.

Warnings and precautions
There are some circumstances where special precautions may need to be taken. These include:

• if your baby has a tendency to bleed easily. The doctor will be cautious when using this medicine as it may prevent blood from clotting properly.
• if your baby suffers from an obstruction of the blood flow into the lungs, blood will be flowing through the ductus arteriosus from the main artery of the lungs. In this case, Neupedix can be given through a catheter (fine tube) placed at or just above the junction between the main artery and the ductus arteriosus or can be given intravenously (by a drip into a vein).
• if your baby develops interrupted breathing (apnoea) or a slow heartbeat, this medicine should be stopped and appropriate medical treatment should be given. This most often occurs in babies weighing less than 2 kg at birth. It usually happens within the first hour of the medicine being given. Doctors and nurses will watch your baby carefully in case they need to ventilate him or her (give oxygen) until normal breathing starts again. This medicine will only be used where there are facilities to do this. If the baby develops a high temperature or low blood pressure, the drug should be given at a slower rate until these symptoms subside.
• if your baby suffers from feeding problems. This medicine may cause thickening of the stomach wall, such that emptying of the stomach contents may be difficult. This effect has been linked with the total amount of medicine given and the length of time it is given for. If your baby is given this medicine for more than 120 hours, the doctor will watch carefully for this problem which will cause the baby to vomit after feeds.
• if this medicine is given for a very long time period the walls of the ductus arteriosus and of the artery that connects the heart to the lungs (pulmonary artery) may weaken.
• this medicine may cause abnormalities of long bones. Your doctor will monitor your baby's symptoms and may decide if this medicine needs to be withdrawn.
• if your baby has respiratory distress syndrome (hyaline membrane disease). This medicine must not be used in babies with this condition therefore your baby's doctor will ensure correct diagnosis.

Children

Neupedix contains alcohol (ethanol) and is likely to affect children (see Neupedix contains alcohol (ethanol)). All babies can have Neupedix if they really need it. The doctor will carry out tests before deciding whether to give this medicine to your baby.

Other medicines and Neupedix
Tell your doctor if your baby is using, has recently used or might use any other medicines.

Babies born with heart problems usually have to be given several different medicines. These medicines may be to:
• improve the pumping action of the heart. These drugs act directly on the heart muscle and belong to a group of drugs called cardiac glycosides, e.g. digoxin.
• raise the blood pressure, e.g. dopamine or isoproterenol.
• reduce the volume of the blood and hence the workload on the heart. These drugs are called diuretics or water tablets, e.g. furosemide.
• fight infections (antibiotics), e.g. penicillin or gentamicin.

Neupedix can be given at the same time as these medicines as no interactions with these medicines have been reported.

Neupedix contains alcohol (ethanol)
This medicinal product contains ethanol. Your doctor will take this into account when deciding to give this medicine to your baby.

Neupedix contains 790 mg alcohol (ethanol) in each 1 ml ampoule which is equivalent to 790 mg/ml (79 % w/v). The amount of alcohol in each 1 ml ampoule is equivalent to less than 20 ml beer or 8 ml wine.

The amount of alcohol in this medicine is likely to affect children. These effects may include feeling

sleepy and changes in behaviour. Because this medication is administered slowly over 24 hours the effects of ethanol may be reduced.

Co-administration with medicines containing e.g. propylene glycol or ethanol may lead to accumulation of ethanol and induce adverse effects, particularly in young children with low or immature metabolic capacity.

If your baby has epilepsy or liver problems, talk to your doctor or pharmacist before taking this medicine.

The amount of alcohol in this medicine may alter the effects of other medicines.

3. How to use Neupedix

This medicine must only be given by a doctor in a hospital or in a place where intensive care facilities are immediately available if needed.

This medicine can be given by an intravenous drip or through an artery by way of a tube (catheter).

The small volume (1 ml) of medicine must be diluted with larger volumes of a special salt or sugar solution. The amount of solution used will depend on how the medicine is to be given.

Different babies need different amounts of Neupedix. Your doctor will give the smallest amount needed for the shortest length of time to give a good result. The doctor will have carefully worked out the risks of giving the medicine over a long period in a very ill baby, against the possible benefits that the baby will get from the treatment or the risks of reducing or stopping Neupedix treatment early.

As soon as tests show that the baby is responding, the rate will be reduced to the lowest possible dose that will maintain the response. (If your baby has an obstruction to the flow of blood to the lungs, the doctor will be looking for an increase in the amount of oxygen in the blood; if your baby has an obstruction in the flow of blood to the rest of the body, the doctor will be looking for an increase in the blood pressure and a fall in the acidity of the blood). As soon as the baby starts to have the medicine, the pressure of the blood in the arteries will be checked at regular intervals.

As Neupedix relaxes muscles in other blood vessels this may cause a lowering of the baby's blood pressure. In order to do this, the doctor may use the catheter through which the drug is being given, or a stethoscope or an ultrasound device. If pressure falls significantly, the rate at which Neupedix is being given will be reduced straight away.

If you have any further questions on the use of this medicine, as your baby's doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Starting with the most common and decreasing in frequency, the reactions that he or she may develop are:

Very common side effects (may affect more than 1 in 10 people)
• interrupted breathing (apnoea)
• a high temperature for a short time period (transient pyrexia).

Common side effects (may affect up to 1 in 10 people)
• fits (seizures)
• a heartbeat that is slower than normal (bradycardia)
• low blood pressure
• a heartbeat that is faster than normal (tachycardia)

• diarrhoea
• flushing of the skin. This happens more often when the medicine is given by catheter into an artery and is usually relieved by repositioning the tip of the catheter
• low potassium levels in the blood (potassium deficiency).

Uncommon side effects (may affect up to 1 in 100 people)
• narrowing of the stomach outlet (gastric obstruction)
• irregular thickening of the stomach lining (gastric mucosal hypertrophy)
• growth of new bone upon bone (exostosis)
• blood vessels prone to leaking (vascular fragility).

The following have occurred in babies given Neupedix. It is possible that they are adverse reactions to the drug, but may not have been caused by it:
• infection
• stopping of the heart
• clotting and bleeding throughout the circulation (disseminated intravascular coagulation)
• low levels of potassium in the blood, which if not corrected can cause muscle weaknessand an abnormal heart rhythm
• swelling caused by too much fluid in the body.

Reporting of side effects
If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly 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.

5. How to store Neupedix

Keep this medicine out of the sight and reach of children.

Store in a refrigerator (2°C to 8°C).

Diluted solutions should be used within 24 hours.

Do not use this medicine after the expiry date which is stated on the label after EXP.
The expiry date refers to the last day of that month.

Do not use this medicine if you notice the solution is cloudy or the container is discoloured.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Neupedix contains
The active substance is alprostadil. Each ampoule contains 500 micrograms of alprostadil. The other ingredient is ethanol (see section 2 Neupedix contains alcohol (ethanol)).

What Neupedix looks like and contents of the pack
Neupedix is a clear, colourless, sterile concentrate for solution for infusion contained in 1 ml glass ampoules.

Neupedix is available in multipacks of 5 x 1 ml ampoules.

Marketing Authorisation Holder
Waymade PLC

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Manufacturer
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The following information is intended for healthcare professionals only:
For further information, refer to the Summary of Product Characteristics (SPC).

Posology and method of administration
For administration by intravenous drip or constant rate infusion pump.
In infants with lesions restricting pulmonary blood flow (blood is flowing through the ductus arteriosus from the aorta to the pulmonary artery), Neupedix may be administered by continuous infusion through an umbilical artery catheter placed at or just above the junction of the descending aorta and the ductus arteriosus, or intravenously. Adverse effects have occurred with both routes of administration, but the types of reactions are different. A higher incidence of flushing has been associated with intra-arterial than with intravenous administration.
The infusion is generally initiated at a rate of 0.05-0.1 micrograms/kg/min. The most experience has been with 0.1 micrograms/kg/min. After a therapeutic response (an increase in p02 in neonates with restricted pulmonary blood flow or an increase in systemic blood flow pressure and blood pH in neonates with restricted systemic blood flow) has been obtained, the infusion rate should be reduced to the lowest possible dosage that will maintain the desired response.

Paediatric population
Neupedix contains a quantity of ethanol that is likely to affect children (see section 4.4 of SPC).

Dilution instructions
To prepare infusion solutions, dilute 1 ml of Neupedix with sterile 0.9% sodium chloride intravenous infusion or sterile 5% dextrose intravenous infusion.
If undiluted Neupedix comes in direct contact with a plastic container, plasticisers are leached from the side walls. The solution may turn hazy and the appearance of the container may change. Should this occur, the solution should be discarded and the plastic container should be replaced. This appears to be a concentration-dependent phenomenon. To minimise the possibility of haze formulation, Neupedix should be added directly to the intravenous infusion solution, avoiding contact with the walls of plastic containers. Dilute to volumes appropriate for the delivery system available. Prepare fresh infusion solutions every 24 hours. Discard any solution more than 24 hours old.

Sample dilution and infusion rates to provide a dosage of 0.1 micrograms/kg body weight/minute:

Add 1 ml ampoule (500 micrograms alprostadil) to:	Concentration of resulting solution (micrograms/ml)	Infusion rate (ml/min/kg)
250 ml	2	0.05
100 ml	5	0.02
50 ml	10	0.01

25 ml	20	0.005

Example:
To provide 0.1 micrograms/kg/min to a 2.8 kg neonate, using a concentration of 5 micrograms/ml:
Infusion Rate = 0.02 ml/min/kg x 2.8 kg = 0.056 ml/min or 3.36 ml/hr

Change the dosage from 0.1 micrograms/kg/min to 0.05 micrograms/kg/min by reducing the pump rate to half of the original rate.

The diluted solution should contain no more than 20 micrograms/ml alprostadil.
PARTICULAR CARE SHOULD BE TAKEN IN CALCULATING AND PREPARING DILUTIONS OF NEUPEDIX.