

PACKAGE LEAFLET: INFORMATION FOR THE USER

Lanoxin 500 micrograms/2ml Solution for Injection (Digoxin)

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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Lanoxin Solution for Injection is and what it is used for
2. What you need to know before you use Lanoxin Solution for Injection
3. How to use Lanoxin Solution for Injection
4. Possible side effects
5. How to store Lanoxin Solution for Injection
6. Contents of the pack and other information

1. What Lanoxin Solution for Injection is and what it is used for

Lanoxin contains the active substance digoxin, which belongs to a group of medicines called cardiac glycosides. It is used to treat arrhythmias and heart failure. An arrhythmia is an irregularity in the heart-beat, which causes the heart to skip a beat, beat irregularly or beat at the wrong speed. This medicine works by correcting irregular heartbeats to a normal rhythm and strengthens the force of the heart-beat, which is why it is useful in heart failure.

2. What you need to know before you use Lanoxin Solution for Injection

Do not use Lanoxin Solution for Injection if you:

- Are allergic to digoxin, other cardiac glycosides or any of the other ingredients of this medicine (listed in section 6).
- Have serious heart problems, such as those with the conduction of the electrical impulses in the heart, especially if you have a history of Stokes-Adams attacks (abrupt, short-lived loss of consciousness caused by a sudden change in heart rate or rhythm).
- Have an irregular heart-beat caused by cardiac glycoside intoxication or conditions such as Wolff-Parkinson-White syndrome.
- Have obstructive cardiomyopathy (enlargement of the heart muscle).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using this medicine:

- If you are taking this medicine, your doctor may ask you to have regular blood tests to determine the amount of Lanoxin in the blood. This may be useful in the case of patients with kidney disorders.
- If you develop digoxin toxicity, this can lead to various forms of heart rhythm disturbances, some of which resemble the rhythm disturbances for which the product was prescribed.

- If you have abnormal heart rhythm (heart block) and you are taking this medicine, contact your doctor immediately if you feel one or more of the following symptoms: fainting, short-lasting loss of consciousness, dizziness or light-headedness, fatigue (tiredness), shortness of breath, chest pain, irregular heart-beat or confusion.
- If you have a sinoatrial disorder (a disorder in the conduction of electrical impulses in the heart such as Sick Sinus Syndrome), in some patients with a sinoatrial disorder this medicine can cause a slow and/or irregular heart-beat. Sometimes this will cause tiredness, weakness and dizziness and when your heartbeat is very slow you may faint.
- If you have recently suffered a heart attack.
- When heart failure occurs along with the collection of an abnormal protein in the heart tissue (cardiac amyloidosis), an alternative therapy may be prescribed by the doctor.
- If you have myocarditis (inflammation of the heart muscle) this may cause vasoconstriction (narrowing of the blood vessels) on rare occasions. Your doctor may prescribe you a different medicine.
- If you have Beri-beri disease (caused by a vitamin B1 deficiency).
- If you have constrictive pericarditis (inflammation of the sac which contains the heart).
- If you are taking diuretics (drugs which promote urine production and help reduce the amount of water in your body) with or without an ACE inhibitor (mainly used to treat high blood pressure), your doctor will prescribe a lower dose of Lanoxin. Do not stop taking Lanoxin without talking to your doctor.
- If you have a heart test called an ECG (electrocardiogram), tell the person doing the test that you are taking Lanoxin as it can affect the meaning of the results.
- If you have severe respiratory (lung) disease (as you may have an increased sensitivity to Lanoxin).
- If you have low levels of oxygen reaching certain parts of your body, low levels of potassium, abnormally low levels of magnesium or increased levels of calcium in your blood.
- If you have thyroid disease (such as an under-active or over-active thyroid) as you might require changes in the dose of this medicine.
- If you have malabsorption syndrome (you cannot absorb minerals from your food properly) or if you have ever had gastro-intestinal reconstruction surgery.
- If you will receive electric shock treatment to correct an abnormal heart-beat.

Other medicines and Lanoxin Solution for Injection

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Taking several medicines can sometimes have harmful consequences or lead to unwanted interactions.

Sensitivity to Lanoxin can be increased by medicines which lower the level of potassium in the blood.

These include:

- diuretics
- lithium salts (antidepressants),
- corticosteroid based products,
- carbenoxolone (a product which strengthens the gastric mucosa).

The following medicines increase the level of Lanoxin in the blood, which can increase the risk of toxicity:

- certain products which affect the heart: amiodarone, flecainide, prazosin, propafenone, quinidine,
- certain antibiotics: erythromycin, clarithromycin, tetracycline, gentamicin, trimethoprim,
- itraconazole (used to treat fungal infections),
- spironolactone (a drug which increases the amount of urine you produce),
- alprazolam (a sedative which may be used to treat anxiety),
- indomethacin (used to treat inflammation),
- quinine (may be used to prevent malaria infection),
- propantheline (used to prevent muscle spasms),

- nefazodone (an antidepressant),
- atorvastatin (lowers blood cholesterol),
- cyclosporine (an immunosuppressant often used to prevent transplant rejection),
- epoprostenol (used to treat pulmonary arterial hypertension),
- tolvaptan (used to treat low blood sodium levels)
- conivaptan (used to treat low blood sodium levels),
- carvedilol (used to treat mild to severe congestive heart failure and high blood pressure),
- ritonavir (used to treat HIV infection and AIDS),
- telaprevir (used to treat hepatitis C infection),
- dronedarone (used to treat irregular heart-beat),
- ranolazine (used to treat chest pain),
- telmisartan (used to treat high blood pressure),
- lapatinib (used to treat breast cancer),
- ticagrelor (used to prevent heart attack or stroke),
- verapamil (used to treat high blood pressure),
- felodipine (used to treat high blood pressure),
- tiapamil (used to treat chest pain),
- P-glycoprotein inhibitors.

The following medicines may increase or have no effect on the levels of Lanoxin in the blood:

- nifedipine, diltiazem, angiotensin receptor blockers (ARBs) and ACE inhibitors (used to treat high blood pressure and congestive heart failure),
- non-steroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 enzyme (COX-2) inhibitors (used to treat pain and inflammation).

If you have heart failure and are taking sennosides (increase the amount of stools you produce to help you have bowel movements) along with Lanoxin you may have a moderately increased risk of digoxin toxicity.

The following medicines reduce the level of Lanoxin in the blood:

- antacids (used to treat gastric acidity),
- some bulk-forming laxatives (increase the amount of stools you produce to help you have bowel movements),
- kaolin-pectin (used to treat diarrhoea),
- acarbose (used to treat some types of diabetes),
- certain antibiotics: neomycin, penicillamine, rifampicin,
- some cytostatic drugs (used as chemotherapy for cancer treatment),
- metoclopramide (a product for treating nausea and vomiting),
- sulfasalazine (a product to counteract inflammatory diseases of the intestine),
- adrenaline (used to treat severe allergic reactions),
- salbutamol (a product used to treat asthma),
- colestyramine (lowers blood cholesterol),
- phenytoin (used to treat epilepsy),
- St. John's wort (*Hypericum perforatum*) (used to treat depression),
- bupropion (used to treat depression),
- P-glycoprotein inducers,
- supplemental enteral nutrition (being fed by a feeding tube).

If you are taking Lanoxin along with the following medicines you may have an increased risk of irregular heart rhythm:

- intravenous calcium
- beta-blockers
- sympathomimetics (used to treat heart attack and low blood pressure),

If you are taking Lanoxin and suxamethonium (used to help muscle relaxation and treat short-term paralysis), you may have an increased risk of high potassium levels in the blood.

Pregnancy, breastfeeding and fertility

Pregnancy

Your doctor will prescribe this medicine with caution during pregnancy.

You may require a higher dose of this medicine if you are pregnant.

This medicine could be given to the mother to treat abnormally high heart rate and congestive heart failure in the unborn child.

Side effects of Lanoxin treatment affecting the mother may also affect the unborn child.

Breastfeeding

This medicine is excreted in breast milk, but in very small amounts. Therefore, this medicine can be used by women who are breast-feeding.

Fertility

There is no information available on the effect of Lanoxin on fertility.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Since dizziness and blurred or yellow vision have been reported, you should exercise caution before driving a vehicle, using machinery or participating in dangerous activities.

Lanoxin Solution for Injection contains ethanol and sodium

Ethanol:

- This medicine contains less than 0.2 ml of ethanol (alcohol) in each 2 ml (0.5 mg digoxin) ampoule, i.e. up to 176 mg of ethanol per ampoule, equivalent to approximately 5 ml (one teaspoon) of beer, or less than 2 ml of wine. Depending on the dose the amount of ethanol will vary. Harmful to those suffering from alcoholism. Ask your doctor to explain this further if your child is taking this medicine. To be taken into account in pregnant or breast-feeding woman, children and high-risk groups such as patients with liver disease, or epilepsy.

Sodium:

- This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially sodium free.

3. How to use Lanoxin Solution for Injection

This medicine is available as an injectable solution for intravenous administration.

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Your doctor will have decided how much of this medicine is right for you:

- It depends on what heart problem you have and how serious it is
- It also depends on your age, weight and how well your kidneys work
- While you are taking this medicine, your doctor will take regular blood tests. This is to determine how you are responding to treatment.

- Your doctor will adjust your dose based on your blood test results and on how you are responding to treatment. This is why you must strictly adhere to the treatment course prescribed your doctor.
- If you have taken another cardiac glycoside in the past 2 weeks, your doctor may prescribe a lower dose.
- If you feel that the effect of this medicine is too strong or too weak, talk to your doctor or pharmacist.

Taking this medicine

You usually take this medicine in two stages:

- **Stage 1 - loading dose**

The loading dose gets your Lanoxin levels up to the correct level quickly. You will either:

- take one large single dose and then begin your maintenance dose or
- take a smaller dose each day for a week and then begin your maintenance dose

- **Stage 2 - maintenance dose**

After your loading dose you will take a much smaller dose every day, until your doctor tells you to stop.

Intravenous Administration

Each dose of Lanoxin Solution for Injection should be given as a slow infusion into a vein over a period of 10 to 20 minutes. Your doctor will discuss the best method of treatment for you.

Adults and children over 10 years

- loading dose
 - Usually between 0.5 mg and 1.0 mg
 - This should be given in divided doses. Around half of the total loading dose will be given to you in the first injection and the rest of the loading dose may be split into several injections which will be given to you between 4 and 8 hours apart
- maintenance dose
 - Your doctor will decide this, depending on your response to Lanoxin
 - Usually between 0.125 and 0.25 mg daily

Children under 10 years

- loading dose
 - This is worked out using your child's weight
 - Usually between 0.020 mg and 0.035 mg per kg of bodyweight
 - This should be given in divided doses. Around half of the total loading dose will be given to your child in the first injection and the rest of the loading dose may be split into several injections which will be given to them between 4 and 8 hours apart
- maintenance dose
 - The doctor will decide this, depending on your child's response to Lanoxin
 - Usually a 1/5 (fifth) or a 1/4 (quarter) of the loading dose daily

Elderly

Elderly people may be given a lower dose than the usual adult dose. This is because older people may have reduced kidney function. Your doctor will check the levels of Lanoxin in your blood and may change your dose if necessary.

If you use more Lanoxin Solution for Injection than you should

As Lanoxin Solution for Injection is administered under the supervision of a doctor, it is unlikely that you will be given more or less than is necessary. However, if you have any concerns about the dose of your medicine discuss them with your doctor.

The main symptoms of Lanoxin toxicity are heart rhythm disturbances and gastrointestinal symptoms which may happen before heart rhythm disturbances. Gastrointestinal symptoms include loss of appetite, nausea and vomiting. Other symptoms of Lanoxin toxicity include dizziness, fatigue, a general feeling of being unwell and various neurological disturbances including visual disturbances (more yellow-green than usual). The neurological and visual symptoms may persist even after other signs of toxicity have been resolved. In chronic toxicity, non-heart related symptoms, such as weakness and a general feeling of being unwell, may be the main symptoms.

If you forget to use Lanoxin

Do not take a double dose to make up for the forgotten dose.

If you stop using Lanoxin

Your doctor will tell you how long you should take Lanoxin. Do not stop your treatment early without consulting your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you get any of the following, talk to your specialist doctor straight away or seek urgent medical advice:

Very rare (may affect up to 1 in 10,000 people)

- palpitations, chest pain, shortness of breath or sweating. These can be symptoms of a serious heart problem caused by new irregular heartbeats.

Other side effects may include:

Common (may affect up to 1 in 10 people)

- allergic reactions of the skin may occur (rash, urticaria)
- abnormal heart-beat
- nausea, vomiting, diarrhoea
- central nervous system disturbances such as dizziness
- visual disturbances (blurred or yellow vision)

Uncommon (may affect up to 1 in 100 people)

- depression

Very rare (may affect up to 1 in 10,000 people)

- decrease in blood platelets (symptoms include bruises and nose bleeds)
- loss of appetite (anorexia)
- psychosis, apathy, confusion
- headache
- stomach pain caused by lack of blood supply or damage to your intestines (ischaemia and necrosis)
- enlarged breast tissue in men (gynaecomastia)
- lack of energy (fatigue), a general feeling of being unwell and weakness

Reporting of side effects

If you get 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 national reporting system:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of medicine.

5. How to store Lanoxin Solution for Injection

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

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

Do not store above 25°C. Keep the ampoules in the outer carton to protect from light. Once opened use immediately and discard any unused contents.

Do not use this medicine if you notice any visible signs of deterioration.

Do not throw away any medicines via wastewater or household waste. These measures will help protect the environment.

6. Contents of the pack and other information

What Lanoxin Solution for Injection contains

Lanoxin Solution for Injection contains the active substance digoxin. Each ampoule contains 0.5mg (500 micrograms) digoxin.

The other ingredients are ethanol, propylene glycol, citric acid monohydrate, sodium phosphate and water for injections.

What Lanoxin Solution for Injection looks like and contents of the pack

Lanoxin 500 micrograms/2ml Solution for Injection is a clear, colourless, sterile aqueous solution.

Lanoxin Solution for Injection is available in packs containing 5 glass ampoules. Each ampoule contains 2 ml of solution.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland
Tel: +353 1 6308400

Manufacturer

GlaxoSmithKline Manufacturing S.p.A, Strada Provinciale Asolana 90, 43056 San Polo di Torrile, Parma, Italy

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The following information is intended for healthcare professionals only.

Handling Instructions

Dilution of Lanoxin

Lanoxin Solution for Injection can be administered undiluted or diluted with a 4-fold or greater volume of 0.9% Sodium Chloride Injection, 0.18 % Sodium Chloride/4% Glucose Injection or 5% Glucose Injection. A 4-fold volume of diluent equates to adding one 2 ml ampoule of digoxin to 6 ml of injection solution. The use of less than a 4-fold volume of diluent could lead to precipitation of digoxin.

Lanoxin Solution for Injection, when diluted in the ratio of 1 to 250 is known to be compatible with the following infusion solutions;

- Sodium Chloride I.V. Infusion, B.P., 0.9 % w/v.
- Sodium Chloride (0.18 % w/v) and Glucose (4 % w/v) I.V. Infusion, B.P.
- Glucose I.V. Infusion, B.P., 5 % w/v.

A ratio of 1 to 250 can be obtained for example by diluting one 2 ml ampoule with 500 ml of infusion solution.

Dilution should be carried out either under full aseptic conditions immediately before use. Any unused solution should be discarded

Administration of Lanoxin injection:

Each dose should be given by I.V. infusion over 10 to 20 mins.

The total loading dose should be administered in divided doses with approximately half of the total dose given as the first dose and further fractions of the total dose given at intervals of four to eight hours. An assessment of clinical response should be performed before giving each additional dose.

The I.M. route is painful and is associated with muscle necrosis. This route cannot be recommended.

Rapid I.V. injection can cause vasoconstriction producing hypertension and/or reduced coronary flow. A slow injection rate is therefore important in hypertensive heart failure and acute myocardial infarction.