Package leaflet: Information for the user

Clindamycin 150 mg/ml Solution for injection/infusion

Clindamycin

Read all of this leaflet carefully before you are given 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, nurse or healthcare personnel.
- If you get any side effects, talk to your doctor, pharmacist, nurse or healthcare personnel. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Clindamycin is and what it is used for

Clindamycin contains the active substance Clindamycin. Clindamycin is an antibiotic. It is used to treat infections in adults, adolescents and children aged over 1 month.

Clindamycin is used for the treatment of severe infections especially when other antibiotics have been unable to clear the infection and when the infection is caused by bacteria that are sensitive to clindamycin.

Clindamycin is used for the treatment of:
- bone and joint infections
- chronic infections of paranasal sinuses
- infections of the lower respiratory tract
- abdominal infections (peritonitis)
- infections of the female reproductive organs
- skin and soft tissue infections
- dental infection
- treatment of bacteraemia that occurs in association with, or is suspected to be associated with any of the infections listed above

and
- infections caused by *Toxoplasma gondii* and *Pneumocystis jirovecii* in adult patients with low immune defenses

2. What you need to know before you are given Clindamycin

You must not be given Clindamycin in the following cases:
- if you are allergic to clindamycin or lincomycin or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions

Talk to your doctor, pharmacist, or nurse before you are given Clindamycin

- if you suffer from impaired liver or kidney function,
- if you have problems with your muscle functions caused by e.g. Myasthenia gravis (pathological muscular weakness) or Parkinson disease (so called shaking palsy),
- if you have diarrhoea or usually get diarrhoea when you take antibiotics or have ever suffered from gastro-intestinal diseases (e.g. previous inflammation of the colon),
- if you suffer from any kind of allergies, e.g. hypersensitivity to penicillin because in individual cases allergic reactions to clindamycin have been reported for people with a known penicillin hypersensitivity.
- if you suffer from asthma, eczema or hayfever.

You should consult your doctor if one of the precautions and warnings mentioned above are or were applicable to you in the past.

Some patients treated with clindamycin have experienced severe hypersensitivity reactions, including severe skin reactions such as drug reactions with increased number of eosinophiles (a certain type of blood cells) and symptoms affecting the entire body (DRESS syndrome), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis (AGEP). If you experience any sign of hypersensitivity or severe skin reactions during treatment with Clindamycin, talk to your doctor immediately.

Severe allergic reactions can occur even after the first application. In this event your doctor will discontinue the treatment with Clindamycin immediately and will implement the standard emergency measures.

Rapid intravenous injection causes undiserable effects and must be avoided.Your doctor will dilute the medicine prior to administration into a vein and will ensure that it will be infused over atleast 10-60 minutes.

If you are given Clindamycin for a long time (more than 10 days), your doctor should monitor your blood count and liver and renal function regularly.

Acute kidney disorders may occur. Please inform your doctor about any medication you currently take and if you have any existing problems with your kidneys. If you experience decreased urine output, fluid retention causing swelling in your legs, ankles or feet, shortness of breath, or nausea you should contact your doctor immediately.

Long-term and repeated use of Clindamycin may cause an infection of skin and soft mucosa with pathogens not sensitive to clindamycin. It may also lead to the development of a fungal infection.

During treatment with clindamycin a severe infection of the colon (colitis) may occur. Therefore, you should immediately inform your doctor if you suffer from severe and persisiting diarrhoea during or up to two months after treatment, especially when mucus or blood is in the stool.

Children and adolescents
This medicine should not be given to children below the age of 1 month because its safety has not been established.

Other medicines and Clindamycin

Tell your doctor, pharmacist, or nurse if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor if you are using:

- Warfarin or similar medicines – used to thin the blood. You may be more likely to have a bleed. Your doctor may need to take regular blood tests to check how well your blood can clot.
- Erythromycin. Clindamycin should not be given in combination with medicinal products containing erythromycin because a mutual reduction of efficacy cannot be excluded.
- Lincomycin. Clindamycin should not be given after treatment with lincomycin, due to cross resistance.
- Muscle relaxants. Clindamycin may increase the efficacy of muscle relaxants which may lead to unexpected, life-threatening incidences during surgery measures.
- CYP3A4 inducers like rifampicin (an antibiotic to treat tuberculosis), their use may impact the effectiveness of Clindamycin.

Pregnancy, breast-feeding and 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 using this medicine.

Tell your doctor if:
- you are pregnant or think you might be pregnant. The doctor will decide how to use Clindamycin after comparing risk and benefit of your treatment with Clindamycin.
- you are breast-feeding. This medicine passes into breast milk, therefore, should not be used during breast-feeding.

Driving and using machines

You may feel dizzy, tired or suffer from headaches when taking this medicine. If you are affected, do not drive or use any tools or machines.

Clindamycin contains sodium

This medicine contains 7.72 mg sodium (main component of cooking/table salt) in each ml. This is equivalent to 0.39 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How Clindamycin is given

Clindamycin is administered by intramuscular injection (into a muscle) of the undiluted solution or by intravenous infusion (into a vein) of the diluted solution. It will usually be given by a doctor or a nurse.

Your doctor will decide on the correct dose of clindamycin therapy for you.

Adults and adolescents older than 12 years are given

- for the treatment of less complicated infections:
  1200 to 1800 mg clindamycin daily,

- for the treatment of severe infections:
  1800 to 2700 mg clindamycin daily,

in two to four equal doses.

Normally the maximum daily dosage for adults and adolescents older than 12 years is 2700 mg of Clindamycin in two to four equal doses. In life-threatening infections doses up to 4800 mg/day can be given.

Hepatic and renal impairment
In patients with liver and renal diseases, the metabolism of clindamycin is reduced. However, in most cases a dosage adaption is not necessary. Monitoring of the blood level of clindamycin is recommended.

Clindamycin is not haemodialysable (removal of waste products from the blood by means of artificial filtration, used to treat kidney failure). Therefore, no additional dose is necessary before or after haemodialysis.

Use in children
Depending on the severity and site of infection children aged older than 4 weeks up to 12 years obtain 15 – 40 mg clindamycin per kg body weight in three to four equal doses. Clindamycin should be dosed based on total body weight regardless of obesity.

The duration of treatment depends on the disease and its development.

If you have been given more Clindamycin than you should
This medicine will always be given to you under carefully controlled conditions. Please contact your doctor or nurse immediately if you think you have been given too much Clindamycin.

If you forget to take Clindamycin
Clindamycin will be given to you by a doctor or nurse. However, if you have the impression that an application has been forgotten, please contact your doctor or nurse.

If you stop taking Clindamycin
Do not stop taking Clindamycin until your doctor tells you to.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Tell your doctor immediately if you develop:
- signs of a severe allergic reaction such as sudden wheeziness, difficulty in breathing, dizziness, swelling of the eyelids or face or lips or throat or tongue, rash or itching (especially affecting the whole body).
- severe, persistent or bloody diarrhoea (which may be associated with abdominal pain or fever). This may occur with some antibiotics and can be a sign of a serious bowel inflammation.
- signs of serious and potentially life-threatening skin reactions such as blistering and peeling of large areas of skin, fever, cough, feeling unwell and swelling of the gums, tongue or lips.
- yellowing of the skin and whites of the eyes (jaundice).
- fluid retention causing swelling in your legs, ankles or feet, shortness of breath or nausea.
- drop in blood pressure (drowsiness, dizziness, fainting) if the injection is too rapid and, rarely, cardiac arrest.
- increased incidence of infections which manifest themselves as fever, severe chills, sore throat or mouth ulcers (infections can be a sign of low white blood cell count).

Other possible side effects may include:

Very common: may affect more than 1 in 10 people
- diarrhoea, abdominal pain, vomiting, nausea

Common: may affect up to 1 in 10 people
- Disorders of the blood vessels like thrombophlebitis (inflammation of the vein).
- Skin disorders like exanthema (widespread rash with small nodules), urticaria (nettle rash).
- Liver function tests may be affected.

Uncommon: may affect up to 1 in 100 people
- Disorders of the nervous system like a neuromuscular-blocking effect (blocking of the rendering of nerve impulses on a muscle) and distortion of the sense of taste (dysgeusia).
- General disorders and disorders at the administration site like pain and abscess (boil) at the injection site.

Rare: may affect up to 1 in 1,000 people
- Pruritus
- Vaginitis (inflammation of the vaginal mucosa)

Very rare: may affect up to 1 in 10,000 people
- Inflammation of joints (polyarthritis)

Not known: frequency cannot be estimated from the available data
- Vaginal infection
- Sleepiness
- Dizziness
- Headaches
- Jaundice
- Irritation at the site of the injection

Reporting of side effects
If you get any side effects, talk to you doctor, pharmacist, nurse or healthcare personnel. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Clindamycin

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 carton and ampoule label after EXP. The expiry date refers to the last day of the month.

Store below 25 °C.

Shelf life after dilution
Chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C and 2-8 °C with sodium chloride 9 mg/ml (0.9 %) and glucose 50 mg/ml (5 %) solutions, at a concentration of clindamycin 6 and 18 mg/ml in polypropelene infusion bags.

From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

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 Clindamycin contains
- The active substance is clindamycin.
  Each ml of solution for injection/infusion contains 150 mg clindamycin (as phosphate).
  Each ampoule of 2 ml contains 300 mg clindamycin (as phosphate).

Each ampoule of 4 ml contains 600 mg clindamycin (as phosphate).
Each ampoule of 6 ml contains 900 mg clindamycin (as phosphate).

- The other ingredients are disodium edetate, sodium hydroxide 5N (for pH adjustment), hydrochloric acid 5N (for pH adjustment) and water for injections.

What Clindamycin looks like and contents of the pack

Clindamycin is a clear, colourless to almost colourless solution for injection/infusion, free from visible particles in glass ampoules containing 2 ml, 4 ml or 6 ml of solution. Clindamycin is available in packs containing 1, 5, 10 or 25 ampoules. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Noridem Enterprises Ltd.
Evagorou & Makariou,
Mitsi Building 3, Office 115,
Nicosia 1065, Cyprus

Manufacturer
DEMO S.A. PHARMACEUTICAL INDUSTRY
21st Km National Road Athens–Lamia,
14568 Krioneri, Attiki, Greece
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This medicine is authorised in the Member States of the European Economic Area under the following names:

Germany	Clindamycin Noridem 150 mg/ml Injektions-/Infusionslösung
Greece	Clindamycin/DEMO
Sweden	Clindamycin Noridem 150 mg/ml Injektions-/infusionsvätska, lösning
Norway	Clindamycin Noridem
Finland	Clindamycin Noridem 150 mg/ml Injektio-/infuusioneste, liuos
Czech Republic	Clindamycin Noridem
Slovakia	Clindamycin Noridem 150 mg/ml Injekčný/infúzny roztok
Hungary	Klindamicin Noridem 150 mg/ml, Oldatos injekció/infúzió
Romania	Clindamicină Noridem 150 mg/ml Soluţie injectabilă/perfuzabilă
Poland	Clindamycin Noridem
Ireland	Clindamycin 150 mg/ml Solution for injection/infusion

This leaflet was last revised in

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The following information is intended for medical or healthcare professionals only:

Incompatibilities

The following active substances are physically incompatible with clindamycin: ampicillin, aminophylline, barbiturates, calcium gluconate, ceftriaxone sodium, ciprofloxacin, diphenylhydantoin, idarubicin hydrochloride, magnesium sulphate, phenytoin sodium, and ranitidine hydrochloride. Solutions of clindamycin salts have a low pH and incompatibility may reasonably be expected with alkaline preparations or with medicinal products unstable at low pH.

Posology

Adults and adolescents older than 12 years

- for the treatment of severe infections: 1800 to 2700 mg clindamycin daily in two to four equal doses, generally in combination with an antibiotic with good activity against aerobic Gram-negative bacteria.

- or for the treatment of less complicated infections: 1200 to 1800 mg clindamycin daily administered in three or four equal doses.

Normally the maximum daily dose for adults and adolescents older than 12 years is 2700 mg clindamycin in two to four equal doses. In life-threatening infections doses up to 4800 mg/day have been given.

Paediatric Population

Children (over 1 month of age up to 12 years):
Serious infections: 15-25 mg/kg/day in three or four equal doses.

More severe infections: 25-40 mg/kg/day in three or four equal doses. In severe infections, it is recommended that children be given no less than 300 mg/day regardless of body weight.

Clindamycin should be dosed based on total body weight regardless of obesity.

The maximum daily dose should not exceed that of adults.

Elderly patients:

The half-life, volume of distribution and clearance, and extent of absorption after administration of clindamycin phosphate are not altered by increased age. Analysis of data from clinical studies has not revealed any age-related increase in toxicity. Therefore, no dose adjustment is required in elderly patients with normal hepatic function and normal (depending on age) renal function.

Patients with hepatic impairment

In patients with liver disease of moderate to severe degree, elimination half-life of clindamycin is prolonged. A reduction in dosage is generally not necessary if clindamycin is administered every 8 hours. However, the plasma concentration of clindamycin should be monitored in patients with severe hepatic insufficiency. Depending on the results, this measure can make a reduction in dosage or an increase in the dose intervals necessary.

Patients with renal impairment:

In the presence of kidney disease, elimination half-life is prolonged; however, a dosage reduction is not necessary in the event of mild to moderate impairment of renal function. Nevertheless, the plasma

concentration should be monitored in patients with severe renal insufficiency or anuria. Depending on the results, this measure can make a reduction in dosage or an increase in the dose interval of 8 or even 12 hours necessary.

Dosage in the event of haemodialysis

Clindamycin cannot be removed by haemodialysis. Therefore, no additional dose is necessary before or after haemodialysis.

Duration of treatment

In case of proven or even suspected infections with ß-haemolytic streptococci the treatment with clindamycin should be continued for at least 10 days to prevent the development of rheumatic fever or glomerulonephritis.

Method of administration

Clindamycin is administered by intramuscular injection or intravenous infusion.
Clindamycin must be diluted prior to intravenous administration and should be infused over at least 10-60 minutes. The concentration should not exceed 18 mg clindamycin per ml solution.
For intramuscular administration Clindamycin should be used undiluted.
For instructions on dilution of the medicinal product before administration, see section Instructions on handling.

Single intramuscular (IM) injections of greater than 600 mg are not recommended nor is administration of more than 1.2 g in a single one-hour infusion.

Alternatively, the medicinal product may be administered in the form of a single rapid infusion of the first dose followed by continuous intravenous (IV) infusion.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Overdose

No overdose symptoms have yet been observed. Haemodialysis and peritoneal dialysis are ineffective. There is no known specific antidote. Clindamycin is administered via i.m. or i.v. route therefore gastric lavage is not useful.

Instructions on handling

Clindamycin must be diluted prior to intravenous administration (not exceeding 18 mg clindamycin per ml) and should be infused over at least 10 - 60 minutes (not exceeding 30 mg/min). It can never be injected as an intravenous bolus.

Dose of clindamycin	Quantity of Diluent	Minimum infusion-time
300 mg	50 ml	10 minutes
600 mg	50 ml	20 minutes
900 mg	50 -100 ml	30 minutes
1200 mg	100 ml	60 minutes

Clindamycin may be diluted with sodium chloride solution 9 mg/ml (0.9 %) or 5 % glucose 50 mg/ml (5 %) solution.

After dilution:

Please refer to Section 5 of the package leaflet above for the storage conditions after dilution.

Intramuscular administration is indicated when intravenous infusion is not possible for any reasons.

For single use only.

The medicinal product is to be visually inspected prior to use and also after dilution.
Only clear solutions free of visible particles should be used.