Dalacin® C Phosphate Sterile Solution
clindamycin phosphate

PHYSICIAN LEAFLET
For further information consult the Summary of Product Characteristics (SPC).

Qualitative and quantitative composition
Each ml of solution contains clindamycin phosphate equivalent to 150 mg clindamycin, benzyl alcohol 9.45 mg/ml, disodium edetate and sterilised water for injections.

Directions for use
Parenteral (I.M. or IV. administration). Dalacin C Phosphate must be diluted prior to IV. administration and should be infused over at least 10-60 minutes.
Parenteral (I.M. or IV. administration)

Adults including the elderly:
Serious infections: 600-1200 mg/day in 2, 3 or 4 equal doses.
More severe infections: 1200-2700 mg/day in 2, 3 or 4 equal doses.
Single I.M. injections of greater than 600 mg are not recommended nor is administration of more than 1.2 g in a single one-hour infusion.

Children (over 1 month of age):
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.

The concentration of clindamycin in diluent for infusion should not exceed 18 mg per ml and INFUSION RATES SHOULD NOT EXCEED 30 mg PER MINUTE. The usual infusion rates are as follows:

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<thead>
<tr>
<th>Dose</th>
<th>Diluent</th>
<th>Time</th>
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<tbody>
<tr>
<td>300 mg</td>
<td>50 ml</td>
<td>10 min</td>
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<tr>
<td>600 mg</td>
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<td>900 mg</td>
<td>50-100 ml</td>
<td>30 min</td>
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<tr>
<td>1200 mg</td>
<td>100 ml</td>
<td>40 min</td>
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</table>

Indications
The management of serious infections due to organisms susceptible to this anti-infective.

Contra-indication etc.

Contra-indications:
Dalacin C Phosphate is contra-indicated in patients previously found to be sensitive to clindamycin, lincomycin, any component of the formulation, or to any excipients listed in section 6.1 of the SPC.

Clindamycin phosphate solution for injection must not be given to premature babies or neonates because of the benzyl alcohol content (see Warnings).
Warnings:
The clindamycin phosphate injectable formulation contains benzyl alcohol (9.45 mg/ml). Intravenous administration of the preservative benzyl alcohol has been associated with serious adverse events, and death in paediatric patients including neonates characterized by central nervous system depression, metabolic acidosis, gasping respirations, cardio-vascular failure and haematological anomalies (“gassing syndrome”). Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the “gassing syndrome”, the minimum amount of benzyl alcohol at which toxicity may occur is not known. Use only if it is necessary and if there are no alternatives possible. If given in high volumes, should be used with caution and preferably for short term treatment in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis) due to benzoic acid (a metabolite of benzyl alcohol). Premature and low-birth weight infants may be more likely to develop toxicity. Benzyl alcohol containing products should not be used in pre-term or full-term neonates unless strictly necessary.
Benzyl alcohol can cross the placenta and clindamycin should only be used during pregnancy if clearly needed.

Dalacin C Phosphate should only be used in the treatment of serious infections. In considering the use of the product, the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea which may develop, since cases of colitis have been reported during, or even two or three weeks following, the administration of clindamycin.

Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of Clostridium difficile. This has been reported with use of nearly all antibacterial agents, including clindamycin. Clostridium difficile produces toxins A and B which contribute to the development of Clostridium difficile associated diarrhoea (CDAD) and is a primary cause of ‘antibiotic-associated colitis’.

The disease is likely to follow a more severe course in older patients, or patients who are debilitated. Diagnosis is usually made by the recognition of the clinical symptoms, but can be substantiated by endoscopic demonstration of pseudomembranous colitis. Colitis is a disease, which has a clinical spectrum from mild, watery diarrhoea to severe, persistent diarrhoea, leucocytosis, fever, severe abdominal cramps, which may be associated with the passage of blood and mucus. If allowed to progress, it may produce peritonitis, shock and toxic megacolon. This may be fatal. The presence of the disease may be further confirmed by culture of the stool for C. difficile on selective media and assay of the stool specimen for the toxin(s) of C. difficile.

It is important to consider the diagnosis of CDAD in patients who present with diarrhoea subsequent to the administration of antibacterial agents. This may progress to colitis, including pseudomembranous colitis, which may range from mild to fatal colitis. If antibiotic-associated diarrhoea or antibiotic-associated colitis is suspected or confirmed, ongoing treatment with antibacterial agents, including clindamycin, should be discontinued and adequate therapeutic measures should be initiated immediately. When 125 mg to 500 mg of vancomycin are administered orally four times a day for 7-10 days, there is a rapid observed disappearance of the toxin from faecal samples and a coincident clinical recovery from the diarrhoea. Drugs inhibiting peristalsis are contraindicated in this situation.

Precautions:
History of gastro-intestinal disease; use in atopic individuals; super-infection with resistant organisms. Since clindamycin does not diffuse adequately into cerebrospinal fluid, the drug should not be used in the treatment of meningitis.

If therapy is prolonged, liver and kidney function tests should be performed. Such monitoring is also recommended in neonates and infants. Safety and appropriate dosage in infants less than one month old have not been established. The use of clindamycin phosphate may result in overgrowth of non-susceptible organisms, particularly yeasts.

The dosage of Dalacin C Phosphate may require reduction in patients with renal or hepatic impairment due to prolongation of the serum half-life.

Clindamycin phosphate should not be injected intravenously undiluted as a bolus, but should be infused over at least 10-60 minutes as directed in section “directions for use”.

Interactions:
Use with caution in patients receiving neuromuscular blocking agents.

Vitamin K antagonists
Increased coagulation tests (PT/INR) and/or bleeding, have been reported in patients treated with clindamycin in combination with a vitamin K antagonist (e.g. warfarin, acenocoumarol and fluindione). Coagulation tests, therefore, should be frequently monitored in patients treated with vitamin K antagonists.

Fertility, pregnancy and lactation:
Oral and subcutaneous reproductive toxicity studies in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus due to clindamycin, except at doses that caused maternal toxicity. Animal reproduction studies are not always predictive of human response. Orally and parenterally administered clindamycin has been reported to appear in human breast milk in ranges from 0.7 to 3.8 μg/ml. Because of the potential for serious reactions in nursing infants, clindamycin should not be taken by nursing mothers.

Clindamycin crosses the placenta in humans. After multiple doses, amniotic fluid concentrations were approximately 30% of maternal blood concentrations.

Benzyl alcohol can cross the placenta (see Warnings).

Undesirable effects:
Adverse reactions identified from post-marketing experience are included in italics.

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very Rare</th>
<th>Not Known</th>
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<tbody>
<tr>
<td></td>
<td>≥ 1/100 to &lt; 1/10</td>
<td>≥ 1/1000 to &lt;1/100</td>
<td>≥ 1/10000 to &lt;1/1000</td>
<td>&lt; 1/10000</td>
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<td>Vaginal infection</td>
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<td>Blood and Lymphatic System Disorders</td>
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<td>Agranulocytosis, Leukopenia, Neutropenia,</td>
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<td>System Organ Class</td>
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<td>Uncommon [≥ 1/1000 to &lt;1/100]</td>
<td>Rare [≥ 1/10000 to &lt;1/1000]</td>
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<td>Thrombocytopenia, Eosinophilia</td>
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<td>Anaphylactoid reactions, Drug reactions with eosinophilia and systemic symptoms (DRESS)</td>
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<td>Dysgeusia</td>
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<td>Cardi-respiratory arrest Hypotension</td>
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<td>Vascular Disorders</td>
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<td>Abdominal pain, Vomiting</td>
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<td>Gastrointestinal Disorders</td>
<td>\textit{Pseudomembranous colitis}</td>
<td>Diarrhoea, Nausea,</td>
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<td></td>
<td>Jaundice</td>
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<tr>
<td>Hepatobiliary Disorders</td>
<td>Liver function test abnormal</td>
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<td>Skin and Subcutaneous Tissue Disorders</td>
<td>Rash maculopapular</td>
<td>Erythema multiforme, Pruritus, Urticaria</td>
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<td></td>
<td>Toxic epidermal necrolysis, Stevens Johnson Syndrome, Acute generalised exanthematous pustulosis (AGEP), Dermatitis exfoliative, Dermatitis bullous, Rash morbilliform</td>
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<tr>
<td>General Disorders and Administrative Conditions</td>
<td>Pain, Abscess</td>
<td></td>
<td></td>
<td></td>
<td>Injection site irritation</td>
</tr>
</tbody>
</table>

**Reporting of side-effects**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.
Overdose
In cases of overdosage no specific treatment is indicated.

The serum biological half-life of lincomycin is 2.4 hours. Haemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

Handling and Storage requirements
Do not store this product above 25°C.
Do not refrigerate or freeze.
This product is for single dose only.
Any unused solution should be discarded.

Dilution and Compatibility:
*In-vitro* compatibility studies monitored for 24 hours at room temperature using a concentration no greater than 6 mg/ml have demonstrated no inactivation or physical incompatibility with the use of Dalacin C Phosphate in IV solutions containing sodium chloride, glucose or potassium usually used clinically.
Dalacin C Phosphate has been shown to be physically and chemically compatible for at least 24 hours in dextrose 5% water and sodium chloride injection solutions containing the following antibiotics in usually administered concentrations: amikacin sulphate, aztreonam, cefamondole nafate, cephalzin sodium, cefotaxime sodium, cefoxitin sodium, ceftazidime sodium, ceftriaxone sodium, gentamicin sulphate, netilmicin sulphate, piperacillin, tobramycin and ciprofloxacin.
The compatibility and duration of stability of drug admixtures will vary depending upon concentration and other conditions.

Incompatibilities:
Solutions of clindamycin salts have a low pH and incompatibilities may reasonably be expected with alkaline preparations or drugs unstable at low pH. Incompatibility has been reported with: ampicillin sodium, aminophylline, barbiturates, calcium gluconate, ceftriaxone sodium, diphenhydantoin, idarubicin hydrochloride, magnesium sulphate, phenytoin sodium and ranitidine hydrochloride.

Marketing Authorisation Holder
Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ, UK.

Manufacturer
Pharmacia NV/SA, Rijksweg 12, B-2870 Puurs, Belgium.
Date of preparation: 04/2018
Ref: DA 19_0
Read all of this leaflet carefully before you start using this medicine
• Keep this leaflet. You may need to read it again.
• If you have any further questions, ask your doctor or your pharmacist.
• 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 your pharmacist.

In this leaflet:
1. What Dalacin C Solution is and what it is used for
2. Before you are given Dalacin C Solution
3. How Dalacin C Solution is given to you
4. Possible side effects
5. How to store Dalacin C Solution
6. Further Information

1. What Dalacin C Solution is and what it is used for

Dalacin C Solution is a sterile solution for injection into a vein (intravenously) or into a muscle (intramuscularly). The solution contains clindamycin phosphate which is an antibiotic used in the treatment of serious bacterial infections.

2. Before you are given Dalacin C Solution

Do not use
- If you are allergic (hypersensitive) to clindamycin, lincomycin or to any of the other ingredients in this medicine (listed in section 6).
- In premature babies or neonates.

Take special care with Dalacin C Solution
Before you are given this medicine make sure that your doctor knows if you:
• have diarrhoea or usually get diarrhoea when you take antibiotics or have ever suffered from problems with your stomach or intestines (bowel disease). If you develop severe or prolonged or bloody diarrhoea during or after using Dalacin C Solution tell your doctor immediately since it may be necessary to interrupt the treatment. This may be a sign of bowel inflammation (pseudomembranous colitis) which can occur following treatment with antibiotics.
• you suffer from problems with your kidneys or liver.
• you suffer from asthma, eczema or hayfever.
Dalacin C does not get into the brain and is therefore not suitable for treating serious infections in and around the brain. Your doctor may need to give you another antibiotic if you have these infections.

Taking other medicines
Some medicines can affect the way Dalacin C Solution works, or Dalacin C itself can reduce the effectiveness of other medicines taken at the same time. These include:
• muscle relaxants used during operations.
• oral contraceptive pills. You should use extra contraception such as condoms whilst receiving Dalacin C and for seven days after receiving Dalacin C.
• 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.
Please tell your doctor if you are taking or have recently taken any other medicines including medicines obtained without a prescription.

**Pregnancy**
If you are pregnant or think you might be pregnant you should contact your doctor before being given Dalacin C Solution.

**Breast-feeding**
Do not breastfeed while taking Dalacin C.

**Driving and using machines**
No effects on the ability to drive or use machines have been seen with Dalacin C Solution.

**Important information about some of the ingredients of Dalacin C Solution**
Dalacin C Solution contains benzyl alcohol (9.45 mg/ml as preservative) and must not be given to premature babies or babies less than one month old. It may cause allergy and toxic reactions and has caused serious side effects in the brain, heart, blood, and breathing rate in children, which have been fatal in some cases.

3. **How Dalacin C Solution is given to you**

Your doctor will give you your medicine as an injection into your vein (intravenous) or your muscle (intramuscular). If it is given into a vein, it is always mixed with a sugar or saline (salt) solution before use and given using a drip.

When giving you Dalacin C, your doctor will ensure that the concentration of clindamycin does not exceed 18 mg per ml and the rate it is given to you does not exceed 30 mg per minute. If Dalacin is given too fast it could rarely cause a heart attack.

**Adults/Elderly**
The recommended dose of Dalacin C Solution is 600 to 2700 mg clindamycin per day in two to four equal doses, depending on the severity of your infection. Higher doses than this (up to 4800 mg daily) may be given by your doctor for very severe infections.

**Children**
The recommended dosage for children (over 1 month of age) is 15 to 40 mg of clindamycin per kg bodyweight each day in three or four equal doses. Higher doses of up to 300 mg per day (regardless of body weight) may be given by your doctor for very severe infections until a full response to treatment is observed.

Normally Dalacin C is only given to patients in hospital. The medical staff will be keeping a close eye on you during your treatment. If you need to have more than one course of treatment with clindamycin, your doctor may want to check that the clindamycin is not having any effect on the way your kidneys and liver are working.

Long term use can also make you more likely to get other infections that do not respond to Dalacin C treatment.

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

4. **Possible side effects**
Tell your doctor immediately if you develop:

- severe, persistent or bloody diarrhoea (which may be associated with stomach pain or fever).
  This is an uncommon side effect which may occur during or after completing treatment with antibiotics and can be a sign of serious bowel inflammation
- signs of a severe allergic reaction such as sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body)
- potentially life threatening skin rashes:
  - blistering and peeling of large areas of skin, fever, cough, feeling unwell and swelling of the gums, tongue or lips
  - a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome), and a more severe form, causing extensive peeling of the skin (more than 30% of the body surface - toxic epidermal necrolysis)
  - widespread red skin rash with small pus-containing blisters (exfoliative dermatitis bullous)
  - fever, swollen lymph nodes or skin rash, these may be symptoms of a condition known as DRESS (Drug reaction with eosinophilia and systemic symptoms) can be severe and life-threatening. The symptoms of DRESS usually begins several weeks after exposure to Clindamycin
  - a rare skin eruption that is characterised by the rapid appearance of areas of red skin studded with small pustules (small blisters filled with white/yellow fluid) (Acute Generalised Exanthematous Pustulosis (AGEP))
- yellowing of the skin and whites of the eyes (jaundice).
- a marked decrease in the number of blood cells which may cause bruising or bleeding or weaken the immune system (agranulocytosis), a slight decrease in the number of white blood cells (leukopenia), reduced blood platelet (thrombocytopenia)

Common side effects, (may affect up to 1 in 10 people):
- blood clot (vein inflammation)
- abnormalities in liver function tests
- rash characterised by a flat, red area on the skin that is covered with small bumps

Uncommon (may affect up to 1 in 100 people):
- change of sense of taste
- low blood pressure (feeling light headed, dizzy or faint), heart and lungs stop functioning (when the heart suddenly stops pumping blood around the body)
- feeling sick, diarrhoea
- skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge – (erythema multiforme)
- itchy skin
- hives
- pain, abscess (boil)

Frequency not known (cannot be estimated from available data):
- an increase in the number of white blood cells (eosinophilia)
- stomach pain, being sick (throwing up)
- infection inside and around the vagina
- irritation at the site of the injection

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Dalacin C Solution

- Keep out of the reach and sight of children.
- Dalacin C Solution will not be used after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- This medicine will not be stored above 25°C.
- This medicine will not be refrigerated or frozen.

6. Further information

What Dalacin C Solution contains
The active substance is clindamycin phosphate. Each ml of solution contains clindamycin phosphate equivalent to 150 mg of clindamycin.
The other ingredients are benzyl alcohol, disodium edetate and sterilised water for injections

What Dalacin C Solution looks like and contents of the pack
Dalacin C Solution is a clear, colourless solution. It is supplied in glass ampoules containing either 2 ml or 4 ml of solution. Each ampoule is packed in a cardboard carton with a leaflet.

Marketing Authorisation Holder
Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK.

Manufacturer
Pharmacia NV/SA, Rijkswig 12, B -2870, Puurs, Belgium.

Company Contact address
If you have any comments on the way this leaflet is written, please contact Medical Information at Pfizer Limited in Walton Oaks, Tadworth, Surrey. Tel: 01304 616161.

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