Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

What is in this leaflet:

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

1. What Kemicetine Succinate Injection is and what it is used for

This medicine contains chloramphenicol sodium succinate, which is an antibiotic used to treat severe infections such as typhoid and meningitis, and should only be used when other antibiotics do not help or are unsuitable. It is also used when oral chloramphenicol cannot be used or when higher amounts of the medicine is needed in the blood.

Chloramphenicol prevents bacteria making an essential nutrient required for growth and multiplication. In time, the number of bacteria are reduced and the infection is controlled, so that treatment can be continued using a more gentle antibiotic.

You must talk to a doctor if you do not feel better or if you feel worse.

2. What you need to know before you are given Kemicetine Succinate Injection

Do not use Kemicetine Succinate Injection:

- If you have had an allergic reaction (e.g. rash, wheezing) to chloramphenicol before.
- If you are pregnant, or are breast-feeding.
Warnings and precautions:

Talk to your doctor or pharmacist:
- If you have a history of kidney or liver disease.
- If you are already taking any other medicines which may also cause bone marrow depression.
- If you have a cold, viral influenza, throat infection and before using this medicine to prevent bacterial infections.
- If you have recently been or are about to be vaccinated.

This medicine is associated with various forms of anaemia (a decrease in red blood cells, white blood cells and platelets), which in turn leads to a loss of immunity and can progress into leukaemia. It should only be prescribed if less toxic antibiotics are not available.

New born babies should be treated with care to avoid Grey Syndrome, which is a serious condition arising from excessive toxic chloramphenicol metabolites. Treatment should be terminated as soon as symptoms are identified.

There is a risk of over-growth of non-susceptible organisms, which can lead to severe diarrhoea up to a few months after this medicine is given to the patient.

Other medicines and Kemicetine Succinate Injection:
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

The following medicines interact with Kemicetine Succinate Injection, which affects the way that one or the other medicine works:
- anticoagulants of the coumarin-type (to thin your blood or stop it clotting), antidiabetic agents (e.g. tolbutamide), anti-epileptic agents (e.g. phenytoin and phenobarbital) or rifampicin (an antibiotic).

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

Driving and using machines
No effect on the ability to drive or use machinery is expected with Kemicetine Succinate Injection.

3. How Kemicetine Succinate Injection is given to you

Kemicetine Succinate will be made into a solution and be given to you by injection into a vein, or into a muscle under the direction of a medical practitioner. Your doctor will prescribe the required amount (the dose). The dose is decided by taking into account the severity of your condition.

Adults:
The usual dosage for adults is; 1g of chloramphenicol every 6-8 hours.
Use in children and adolescents:
The usual dose for children is; 50 mg/kg of chloramphenicol daily in divided doses every 6 hours (no more than this should be given); and 25 mg/kg daily in divided equal doses every 6 hours in new-born and premature infants.

The doctor may give you more in certain cases e.g. if you have septicaemia or meningitis (100 mg/kg/day), but should then be decreased as soon as appropriate. Your doctor will decide how long you need to be treated for.

During treatment your doctor will carry out blood tests to check that:

- Your blood is functioning properly as Kemicetine Succinate Injection can damage your blood cells.
- Your liver and kidneys are functioning properly as Kemicetine Succinate Injection may affect these organs.

If you are given more Kemicetine Succinate Injection than you should
In the case of serious overdosage, charcoal haemoperfusion may be effective in removing chloramphenicol from your blood.

4. Possible side effects

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

Tell your doctor immediately if any of the following side effects occur:

- Severe allergic reaction e.g. red raised areas on your skin which may look like spots or be several inches across, which cause itchiness.
- Grey Syndrome – usually in new-born or premature infants, where the skin appears grey, and the infant is listless and weak.
- White blood cell counts (which fight infection) can also drop, increasing the chance of infections, bruising and fever. Anaemia (a low red blood cell count) that can leave you feeling tired and lethargic.

Other side effects may occur, but, the frequency cannot be estimated from the available data:

- Dry mouth.
- Nausea (feeling sick), vomiting (being sick) and diarrhoea.
- Headache.
- Depression.
- Inflammation or damage to the nerves causing numbness, tingling, pain or muscle weakness.
- Blurring, inflammation or temporary loss of vision.
- Chloramphenicol may slow down development of immunity, and you may develop infections more frequently, which are difficult to fight off.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any 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. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Kemicetine Succinate Injection

Your medicine should not be used after the expiry date given on the vial after EXP. The expiry date refers to the last day of that month

Keep container in the outer carton. Keep this medicine out of the sight and reach of children.

6. Contents of the pack and other information

What Kemicetine Succinate Injection contains:

The active substance is Chloramphenicol Sodium Succinate. There are no other ingredients found in Kemicetine Succinate Injection.

What Kemicetine Succinate Injection looks like and contents of the pack

Kemicetine Succinate Injection is available as single glass vials. Each vial contains a freeze-dried powder containing the equivalent of 1 g chloramphenicol.

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

Manufacturer: Actavis Italy S.p.A,
10 Via Pasteur,
Nerviano, Milan,
Italy.

For further information on your medicine, contact Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS. Tel: 01304 616161.

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After parenteral administration chloramphenicol is rapidly released from chloramphenicol sodium succinate. Kemicetine (chloramphenicol) is a broad spectrum antibiotic and is active against many gram-positive organisms and gram-negative organisms, spirillae and rickettsia. It acts by interfering with bacterial protein synthesis. Chloramphenicol is widely distributed in body tissues and fluids and enters the cerebrospinal fluid. Chloramphenicol sodium succinate, free chloramphenicol and metabolites are excreted in the urine.

After intravenous administration of chloramphenicol succinate every 6 hours elimination half lives were 4.03 hours for chloramphenicol and 2.65 hours for chloramphenicol succinate. After intravenous chloramphenicol sodium succinate, steady state peak concentrations were reached on average 18.0 minutes after cessation of the infusion. In infants and children aged 3 days to 16 years the apparent half-life was extremely variable ranging from 1.7 to 12.0 hours.

Indications
Kemicetine Succinate should not be used for trivial infections due to the possibility of severe blood dyscrasias which may prove fatal. Kemicetine succinate is indicated for typhoid, meningitis caused by *H. influenzae* and other serious infections caused by bacteria susceptible to chloramphenicol. It is also indicated wherever chloramphenicol is deemed the antibiotic of choice and oral administration is not possible, or where higher than usual blood concentrations are required.

Dosage and administration
Posology
The dose administered and the concentration used is dependent on the severity of the infection.
The recommended standard dosage is as follows:

*Adults:* The equivalent of 1 g of chloramphenicol every 6-8 hours.

*Elderly:* The usual adult dosage should be given subject to normal hepatic and renal function.

*Children:* The equivalent of 50 mg/kg chloramphenicol, according to body weight, daily in divided doses every 6 hours (this dose should not be exceeded). The patient should be carefully observed for signs of toxicity.

*Premature Infants and Neonates:* 25 mg/kg in divided doses.

In exceptional cases, such as patients with septicemia or meningitis, dosage schedule up to 100 mg/kg/day may be prescribed. However, these high doses should be decreased as soon as clinically indicated. To prevent relapses, treatment should be continued after the temperature has returned to normal for 4 days in rickettsial diseases and for 8-10 days in typhoid fever.
The 10% solution should be given by intravenous injection over a period of about a minute, or in a large volume of fluid, by slow intravenous infusion. The concurrent administration of intravenous Kemicetine succinate with topical treatment has been found to be very effective in the treatment of osteomyelitic foci, abscesses, empyema and skin and urinary infections.

Method of administration
To be given by intravenous or intramuscular injection.

In order to ensure rapid attainment of high blood levels, Kemicetine Succinate Injection is best administered by intravenous injection. Where this is not possible, however, intramuscular administration may be used, although it should be borne in mind that absorption may be slow and unpredictable.

The injection should be reconstituted with water for injections, sodium chloride injection, or dextrose injection 5%.

The following dilution table may be useful for the administration of a proportion of the contents of a vial:

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Solution strength</th>
<th>Volume of diluent to be added</th>
<th>Total volume after dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>40%</td>
<td>400 mg/ml</td>
<td>1.7 ml</td>
<td>2.5 ml</td>
</tr>
<tr>
<td>25%</td>
<td>250 mg/ml</td>
<td>3.2 ml</td>
<td>4.0 ml</td>
</tr>
<tr>
<td>20%</td>
<td>200 mg/ml</td>
<td>4.2 ml</td>
<td>5.0 ml</td>
</tr>
</tbody>
</table>

Contraindications and warnings
Kemicetine Succinate is contraindicated in patients with a previous history of sensitivity and/or toxic reactions to chloramphenicol. It is also contraindicated in pregnancy and whilst breast feeding. Kemicetine Succinate is to be administered only under the direction of a medical practitioner. It should be reserved for serious infections caused by organisms susceptible to its antimicrobial effects when less toxic antibiotics are ineffective or contraindicated. However, chloramphenicol may be chosen to initiate antibiotic therapy based on the clinical impression. In vitro sensitivity tests should be performed concurrently so that the drug may be discontinued as soon as possible if a less toxic antibiotic is indicated by the results of such tests. The decision to continue use of chloramphenicol, rather than another antibiotic when both are suggested by in vitro studies to be effective against a specific pathogen, should be based upon severity of the infection, susceptibility of the pathogen to the various antimicrobial drugs, and the efficacy of the various drugs in the infection.

Bone marrow depression and blood disorders
Serious and fatal blood dyscrasias (aplastic anaemia, hypoplastic anaemia, thrombocytopenia, granulocytopenia, and bone marrow depression) are known to occur after the administration of chloramphenicol. In addition, there have been reports of aplastic anaemia attributed to chloramphenicol, which later resulted in leukaemia. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. Chloramphenicol must not be used in the treatment of any infection for which a less toxic antibiotic is available.

Patient monitoring
Because of its toxic nature it is important to monitor serum levels of this antibiotic particularly in
new-born and premature infants, in the elderly, in patients with renal or hepatic disease and in
those receiving other drugs with which chloramphenicol may interact.

It is essential that adequate haematologic functions be closely monitored during treatment with
chloramphenicol. While haematologic determinations may detect early peripheral haematologic
changes, such as leucopenia, reticulocytopenia, or granulocytopenia, before they become
irreversible, such determinations cannot be relied on to detect bone marrow depression prior to
the development of aplastic anaemia.

It is desirable that patients be hospitalized during therapy, so that appropriate laboratory
determinations and clinical observations can be made.
Baseline haematologic determinations should be made and determinations repeated
approximately every two days during therapy. The drug should be discontinued upon appearance
of reticulocytopenia, leucopenia, thrombocytopenia, anaemia, or any other haematologic
findings attributable to chloramphenicol. However, such determinations do not exclude the
possible later appearance of the irreversible type of bone marrow depression.
Repeated courses of the drug should be avoided if at all possible. Treatment should not be
continued longer than required to produce a cure with little or no risk of relapse of the disease.
Concurrent therapy with other drugs that may cause bone marrow depression should be avoided.

The following may become apparent after chloramphenicol treatment: dryness of the mouth,
nausea and vomiting, diarrhoea, urticaria, optic neuritis with blurring or temporary loss of vision,
peripheral neuritis, headache and depression. Chloramphenicol has been shown to interact with,
and enhance the effects of coumarin anticoagulants, some hypoglycaemic agents (e.g.
tolbutamide) and phenytoin. When given concurrently, a dose reduction of these agents may,
therefore, be necessary. Plasma concentration of chloramphenicol may be reduced with
concomitant usage of phenobarbital and rifampicin. Chloramphenicol may impede the
development of immunity and should therefore not be given during active immunisation.

Hepatic or Renal Impairment
Excessive chloramphenicol serum levels may result from administration of the recommended
dose to patients with impaired liver or kidney function, including that due to immature metabolic
processes in the infant. Dosage should be adjusted accordingly or, preferably, the serum
concentration should be determined at appropriate intervals.

Grey syndrome in infants and neonates
Precaution should be used in therapy of premature and full-term neonates to avoid "Grey
Syndrome" toxicity. Serum drug levels should be carefully monitored during therapy of the
neonate (newborn infant).
Toxic reactions, including fatalities, have occurred in premature infants and neonates. The signs
and symptoms associated with these reactions have been referred to as the "Grey Syndrome".
Although "Grey Syndrome" has been reported in neonates born to mothers after having received
chloramphenicol during labour, in most cases therapy with chloramphenicol has been instituted
within the first 48 hours of life. The following summarizes the clinical and laboratory
determinations that have been made on these patients.
Symptoms first appeared after 3 to 4 days of continued treatment with high doses of
chloramphenicol. The symptoms appeared in the following order: abdominal distension with or
without emesis, progressive pallid cyanosis, vasomotor collapse, frequently accompanied by
irregular respiration, death within a few hours of onset of these symptoms.
The progression of symptoms from onset to death was accelerated with higher dose schedules. Serum drug levels revealed unusually high concentrations of chloramphenicol (over 90 mcg/mL after repeated doses). Termination of therapy upon early evidence of the associated symptomatology frequently reversed the process with complete recovery following.

**General**
Chloramphenicol must not be used in the treatment of trivial infections or where it is not indicated, as in colds, viral influenza, infections of the throat or as a prophylactic agent to prevent bacterial infections.

**Superinfections**
The use of chloramphenicol, as with other antibiotics, may result in an overgrowth of nonsusceptible organisms, including fungi. If infections caused by nonsusceptible organisms appear during therapy, appropriate measures should be taken.

*Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including chloramphenicol, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C difficile*.

*C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

**Pharmaceutical precautions**
Keep container in the outer carton.

**Package quantities**
Individual vials containing Kemicetine Succinate equivalent to 1 g chloramphenicol.

POM

PL 00057/1001

Keep all medicines out of the sight and reach of children.

Manufactured by:
Actavis Italy S.p.A ,
10 Via Pasteur,
Nerviano,
Milan,
Italy.

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

Further information is available to the medical and allied professions on request from:
Medical Information at Pfizer Limited, Walton Oaks, Tadworth, Surrey, KT20 7NS, UK.