PATIENT INFORMATION LEAFLET

LİNKOSOL 600 mg Ampoule Containing Injectable Solution
Sterile
Administered intramuscularly or intravenously

Each 2 mL ampoule contains;

- ***Active ingredient:***
  600 mg Lincomycin base (as Lincomycin hydrochloride).
- ***Excipients:***
  Benzyl alcohol and water for injection.

Before using this medicine, read all of this PATIENT INFORMATION LEAFLET carefully. Because, this leaflet includes important information for you.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow these instructions exactly as written. Do not use **higher or lower** dose other than your recommended dose.*

In this patient information leaflet:

Headings are included.

1. What LİNKOSOL is and what it is used for?

- LİNKOSOL contains lincomycin, a lincosamide antibiotic.
- LİNKOSOL is in colorless and clear solution in ampoules.
- If your doctor deems appropriate, LİNKOSOL is used in the treatment of the following infections caused by bacteria sensitive to lincomycin:
- Upper respiratory tract infections: Tonsillitis, pharyngitis (pharyngitis), middle ear inflammation, sinusitis.
- Lower respiratory tract infections: Diphtheria, acute bronchitis, infectious exacerbation periods of chronic bronchitis, pneumonia and other lower respiratory tract infections.

- Various skin infections: Cellulite, inflammation of the hair follicle (furuncle), abscess, infectious skin, erysipelas, an inflammatory skin disease characterized by superficial microbial infection (impetigo), infected wound, circumscribed redness and swelling (edema), lymph node inflammation (lymphadenitis), engorgement, mastitis and gangrene.
- Bone and joint infections: Bone and bone marrow inflammation (osteomyelitis), blood inflammation (septic arthritis).

LİNKOSOL can also be used in the treatment of more serious cases such as inflammation of the inner surface of the heart (endocarditis) and in cases where the infection spreads to the blood (septicemia).

2. Before you are given LİNKOSOL

DO NOT USE LİNKOSOL in the following cases:

If;

- You are hypersensitive (allergic) to Lincomycin or other substances contained in LİNKOSOL.
- Premature babies (born before 37 weeks of pregnancy) and newborns.

Take SPECIAL CARE with LİNKOSOL in the following cases:

If;

- Antibiotic-induced diarrhea (diarrhea) of varying severity can be seen in the use of almost all antibacterial drugs. If severe, persistent or bloody diarrhea (diarrhea) occurs during or after the use of your medicine; In this case, there may be bacterial diarrhea (Clostridium difficile-induced diarrhea). It may be an indication of intestinal inflammation (pseudomembranous colitis) that may occur while using the drug or after treatment and treatment may need to be discontinued. As with other antibiotics, resistant bacteria and fungal infections may develop in long-term use of LİNKOSOL (super infection). This occurs in the form of thrush in the mouth or vagina. For this possibility and emergency intervention, your treatment must be done under the control of a doctor. If you have a whitening in your mouth or tongue, pain or itching in your genitals, if you are using LİNKOSOL or immediately after using it, please inform your doctor immediately.
- You have kidney or liver problems (if you are going to use LİNKOSOL for a long time, your doctor may request kidney, liver and blood tests from you. Make sure that these checks are done regularly, without missing).
- It should be used with caution in people with gastrointestinal system diseases, especially colitis (inflammation of the large intestine).
- Since it increases the effect of muscle relaxant drugs, it should be used with caution in patients using these drugs.
- Care should be taken when using in allergic persons. If you experience allergic reactions such as swelling, redness, inflammation, rash, blistering, peeling on your skin, inform your doctor immediately.
- Not recommended in the treatment of meningitis (a disease caused by inflammation of the meninges).

- Inform your doctor if you are using anti-diarrhea drugs (diphenoxylates).
- LİNKOSOL may cause breathing difficulties (gasping syndrome) in babies and children up to 3 years of age because it contains benzyl alcohol. In such a case, contact your doctor immediately.
- You have asthma or obvious allergies, use it carefully.

If these warnings are valid for you, even at any time in the past, please consult your doctor.

Use of LİNKOSOL with food and drink
It can be administered on an empty or full stomach as it does not interact with food and drinks.

Pregnancy
Consult your doctor or pharmacist before using the medicine.
It is not known whether LİNKOSOL is safe to use during pregnancy. For this reason, do not use LİNKOSOL during pregnancy unless your doctor recommends it.
If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breast-feeding
Consult your doctor or pharmacist before using the medicine.
It is known that LİNKOSOL passes into breast milk. For this reason, you should not use LİNKOSOL during breastfeeding unless your doctor recommends it.

Driving and using machines
Special studies have not been carried out on the effect of LİNKOSOL on the use of cars and dangerous machines.
Although LİNKOSOL treatment is not thought to have an effect on driving ability, if you have any questions, consult your doctor.

Important information about some of the excipients contained in LİNKOSOL content
LİNKOSOL ampoule contains 18.9 mg benzyl alcohol in each 2 mL ampoule.
It should not be administered to premature babies and newborns. It may cause toxic reactions and allergic reactions in infants and children up to the age of 3, and should be used with caution. Benzyl alcohol can cause multiple organ dysfunction, respiratory system disorder, severe metabolic acid poisoning (Gasping syndrome) in infants, and has been associated with serious side effects, including death. These situations are more likely to occur in babies born prematurely and at low weight.

Using other medicines
If you are currently using or have recently used any prescribed or non-prescribed medicine, please inform your doctor or pharmacist.
- Erythromycin (an antibiotic); The two drugs counteract each other.
- Tubocurarine and pancuronium (muscle relaxants) (LİNKOSOL may increase the effect

of these drugs).

- Kaolin (used to control diarrhea) can reduce the effect of LİNKOSOL.
- It should not be used with drugs that cause intestinal obstruction, such as diphenoxylate (anti-diarrhea drugs).

If you are currently using or have recently used any prescribed or non-prescribed medicine, please inform your doctor or pharmacist.

3. How to use LİNKOSOL

Instructions for use and dose/frequency of administration:

Your doctor will decide in what dose and how often you should take LİNKOSOL.
In adults, in severe infections, one ampoule (600 mg) of LİNKOSOL every 24 hours is administered intramuscularly or 600 mg - 1000 mg intravenously 2-3 times a day.
In more severe infections this dose may be increased.
The most important point to be considered during the administration is that 1 gram of LİNKOSOL should be diluted in at least 100 mL of a suitable solution and administered at an infusion rate of at least one hour.
Follow your doctor's instructions exactly and never change the dose yourself.

Route of administration and method:

Administered intramuscularly or intravenously.

Different age groups:

Use in children:

There is no data on its use in children younger than 1 month.
Your doctor will decide in what dosage and how often you should take LİNKOSOL.

Use in elderly:

Examining the experience to date reveals that the subgroup of elderly patients suffering from associated severe disease may be less tolerant of diarrhea. In this case, your doctor will watch for changes in your defecation frequency.
Your doctor will decide in what dosage and how often you should take LİNKOSOL.

Conditions of special use:

Renal impairment

Your doctor will decide in what dosage and how often you should take LİNKOSOL.
If your kidney function is severely impaired, when you need LİNKOSOL treatment, your doctor may reduce the dose of LİNKOSOL to 25-30% of the dose used by healthy individuals. If you have kidney dysfunction due to the long half-life of the drug, the frequency of LİNKOSOL administration can be reduced by your doctor. Your doctor may monitor your serum lincomycin level if you have kidney dysfunction and are taking a large amount of LİNKOSOL.

Hepatic impairment:

Your doctor will decide in what dosage and how often you should take LİNKOSOL.
If you have liver dysfunction due to the long half-life of the drug, the frequency of LİNKOSOL

administration can be reduced by your doctor. Your doctor may monitor your serum lincomycin level if you have liver dysfunction and if you are taking a large amount of LİNKOSOL.

If you have the impression that the effect of LİNKOSOL is too strong or too weak, talk to your doctor or pharmacist.

If you use more LİNKOSOL than you should:
If you have used LİNKOSOL more than you should use, immediately apply to a doctor or the nearest hospital emergency.

If you forget to use LİNKOSOL:
If you completely miss a dose of LİNKOSOL, inform your doctor.
Do not take double doses to make up for forgotten doses.

If LİNKOSOL treatment ends, effects may occur:
Use LİNKOSOL regularly and exactly as your doctor advises. Do not stop treatment even if you feel well; Because if the treatment is terminated early, the medicine may not have killed all the germs and the infection may recur.

4. Possible side effects
Like all other medicines, LİNKOSOL may cause side effects in patients with hypersensitivity to any component of the drug.
The frequency of adverse events is reported using the following categories;

Very common : can be seen at least 1 out of 10 patients.
Common : can be seen less than one in 10 patients, but more than one in 100 patients.
Uncommon : can be seen less than one in 100 patients, but more than one in 1,000 patients.
Rare : can be seen less than one in 1.000 patients, but can be seen more than 10,000 patients in one.
Very rare : can be seen less than one in 10,000 patients.
Unknown : cannot be estimated from available data.

If any of the following occur, stop using LİNKOSOL and IMMEDIATELY inform your doctor or go to the nearest emergency department:

- Sudden sneezing, difficulty in breathing, swollen face, eyelid and lips, skin flushing in the form of rash, itching (especially if it affects the whole body), cardiac and respiratory arrest

These are all very serious side effects. If you have one of these, it means you have a serious allergy to LİNKOSOL. You may need urgent medical assistance or hospitalization.
All of these very serious side effects are very rare.

If you notice any of the following, inform your doctor immediately or contact the emergency department of your nearest hospital:

- Uncommon severe, prolonged or bloody diarrhea (with severe cramping abdominal pain or fever). This is a side effect that can occur during or after treatment with antibiotics and indicates a serious intestinal infection.
- Thrush in the mouth or vagina (infection caused by a fungus)
- Jaundice (seen as yellowing of the skin or whites in the eyes)
- Decrease in blood cells; It may cause bruising, bleeding or weakening of the immune system.
- Large scale peeling and blistering of the skin

All these are serious side effects. Emergency medical attention may be required. Serious side effects are very rare.

Other side effects:

Common

- Diarrhea, nausea, vomiting

Uncommon

- Vaginal inflammation
- Rash

Rare

- Inflammation in the mouth, tongue inflammation
- Itching

Unknown

- Intestinal inflammation with bloody, watery diarrhea due to long-term antibiotic use, intestinal inflammation caused by a type of microorganism (Clostridium difficile)
- Decrease in the number of all cells in the blood (pancytopenia)
- White blood cell (leukocyte) disorders (decrease in the number of white blood cells, decrease in the number of fragmented cells in the blood)
- Disease with fever, pinhead redness, confusion, headache and a decrease in the number of platelets (thrombocytopenic purpura)
- Severe decrease in the number of blood cells (aplastic anemia)
- Sudden hypersensitivity reaction, swelling of the face and throat as a result of allergies, serum sickness
- Dizziness (vertigo) caused by balance disorder, tinnitus
- Heart and respiratory arrest
- Low blood pressure, blood clot formation due to inflammation of the veins (thrombophlebitis)
- Abdominal pain, abdominal discomfort, itching in the anus

- Jaundice, deterioration in liver function tests, increase in the number of transaminases, a liver enzyme
- Inflammation with blood, swelling and redness on the skin and around the eyes (Stevens-Johnson syndrome); Hypersensitivity (erythema multiforme), which usually resolves spontaneously, with lace-like rash on the hands, face and feet; your skin
- skin disease that causes blistering or peeling, a type of skin disease (vesiculobullous dermatitis) consisting of blisters filled with a serum-like fluid; red, swollen areas (acute diffuse exanthematous pustulosis) with many small purulent skin blisters; skin rash, blisters, peeling (toxic epidermal necrolysis)
- Kidney failure, decrease in the amount of urine, protein detection in the urine, nitrogen detection in the blood
- Headache, dizziness, drowsiness
- Hardening, irritation at the injection site, pink to red colored pus-filled swelling (abscess) and pain occurring on the surface and / or under the skin

If you experience any side effects that are not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of the side effects:

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store LİNKOSOL

Keep LİNKOSOL in places out of sight and reach of children and within the packaging.

Store at room temperature below 30 ° C, do not freeze.

Use in accordance with the expiry date.

Do not use LİNKOSOL after the expiration date which is stated on the package.

Do not throw away expired or unused medicines! Give to the collection system determined by the Ministry of Environment and Urbanization.

Marketing Authorization Holder and
Osel İlaç San. ve Tic. A.Ş.
Akbaba Mah. Maraş Caddesi No: 52
Beykoz / İSTANBUL

Manufacturing Site:
Osel İlaç San. ve Tic. A.Ş.
Akbaba Mah. Maraş Caddesi No: 52
Beykoz / İSTANBUL

This leaflet was approved on 22/07/2020

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

LİNKOSOL 600 mg Ampoule Containing Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2 mL ampoule contains;

Active Substance:

600 mg Lincomycin base (as Lincomycin hydrochloride).

Excipients:

Benzyl alcohol ..... 18,9 mg

Water for injection (q.s.)..... 2.0 mL

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Ampoule containing sterile solution.

Colorless, clear liquid.

4. CLINICAL PARTICULARS

4.1. Therapeutical indications

LİNKOSOL is indicated for the treatment of serious infections caused by Gram-positive aerobic or anaerobic bacteria, such as streptococci, pneumococci and staphylococci susceptible to lincomycin. It is effective against infections caused by Staphylococcus aureus and Streptococcus pneumonia. It is also effective in vitro against microorganisms such as Streptococcus pyogenes, Streptococcus viridans, Corynebacterium diphtheriae, Propionibacterium acnes, Clostridium tetani, Clostridium perfringens.

1. Tonsillitis, pharyngitis, otitis media, sinusitis and other upper respiratory tract infections (also used as additional treatment in diphtheria.)
2. Acute bronchitis, infectious exacerbation periods of chronic bronchitis, pneumonia and other lower respiratory tract infections
3. Cellulitis, furuncle, abscess, impetigo, infected wound and other skin and soft tissue infections, erysipelas, lymphadenitis, paronychia, mastitis and gangrene caused by bacteria sensitive to LİNKOSOL
4. Osteomyelitis, septic arthritis and other bone and joint infections
5. Septicemia and / or endocarditis

4.2. Posology and method of administration

Posology / frequency and duration of administration:

In adults:

A. Intramuscular administration:
1. 600 mg every 24 hours.
2. For more severe infections, 600 mg every 12 hours (or more often).

B. Intravenous administration: (See infusion and dilution rates)
1. 600-1000 mg every 8-12 hours.
2. In more severe infections, these doses may need to be increased.
3. In infections that threaten the life of the patient, up to 8 g per day can be increased intravenously. The maximum daily dose is 8 g.

In children older than 1 month:
A. Intramuscular administration:
1. 10 mg / kg / day as intramuscular injection.
2. In more severe infections, 10 mg / kg every 12 hours or more frequently.

B. Intravenous administration: (See infusion and dilution rates)

Depending on the severity of the infection, 10-20 mg / kg of LİNKOSOL per day is administered as described in the infusion and dilution rates section.

Matters needing attention while using:
In beta-hemolytic streptococcal infections, LİNKOSOL treatment should be continued for at least 10 days.

Method of Administration:
Dilution Rate and Infusion Rate for Intravenous Administration:
In intravenous administration, the most important point to be considered is that 1 gram of LİNKOSOL should be diluted in at least 100 mL of an appropriate solution (See Section 6.2) and should be administered at an infusion rate of at least one hour.

Dose	**Used Diluent amount**	**Infusion rate**
600 mg	100 mL	1 hr
1 g	100 mL	1 hr
2 g	200 mL	2 hr
3 g	300 mL	3 hr
4 g	400 mL	4 hr

These doses can be repeated as necessary, provided that they do not exceed 8 g, the highest

recommended daily dose of LİNKOSOL.
Serious heart-lung reactions may occur if LİNKOSOL is administered intravenously at a higher concentration and infusion rate than recommended.

Additional information on special populations:
Renal impairment:
In patients with severe renal impairment, when LİNKOSOL treatment is required, it is recommended to use 25-30% of the dose in healthy individuals.
In patients with impaired renal function, the reduction of the frequency of LİNKOSOL administration should be considered due to the long half-life.
It is recommended to monitor serum lincomycin levels in patients with severe renal impairment who are under high-dose LİNKOSOL therapy.

Hepatic impairment:
In patients with hepatic impairment, the reduction of the frequency of LİNKOSOL administration should be considered due to the long half-life. In patients with abnormal liver function, the serum half-life may be twice as long as in patients with normal liver function. Hemodialysis and peritoneal dialysis are not effective in clearing lincomycin from serum.
It is recommended that serum lincomycin levels are monitored in patients with hepatic impairment who are under high-dose LİNKOSOL therapy.

Pediatric population:
Its efficacy and safety in pediatric patients less than one month old are unknown. Premature and low-weight babies are at higher risk of developing benzyl alcohol-related toxicity.

Geriatric population:
Examining the experience to date reveals that the subgroup of elderly patients suffering from associated severe disease may be less tolerant of diarrhea. When lincomycin is given to these patients, the patient should be carefully monitored for changes in stool frequency.

4.3. Contraindications
LİNKOSOL should not be used in persons known to be hypersensitive to lincomycin and clindamycin or any ingredient in the formulation, premature infants and neonates.

4.4. Special warnings and precautions for use
Benzyl Alcohol Toxicity in Pediatric Patients (Gasping Syndrome)
Almost all antibacterial agents, including lincomycin, have been reported to cause pseudomembranous colitis of severity ranging from mild to life-threatening. Therefore, it is important to consider the diagnosis of pseudomembranous colitis in patients with diarrhea following antibacterial medication.
Severe cases of diarrhea and pseudomembranous colitis have been reported during the use of many

antibiotics, including lincomycin.

Diarrhea due to Clostridium difficile

Clostridium difficile-induced diarrhea (CDAD) has been reported with the use of almost all antibacterial agents, including lincomycin, and the severity of the disease can range from mild diarrhea to fatal colitis. Antibacterial drug therapy changes the normal flora of the large intestine, leading to overgrowth of C. difficile.

C. difficile produces A and B toxins that contribute to the development of CDAD. Hypertoxin-producing strains of C. difficile cause increased morbidity and mortality, as these infections can be resistant to antimicrobial therapy and may require colectomy. CDAD should be considered in all patients presenting with diarrhea after antibacterial use. Since CDAD has been reported to occur two months after taking antibacterial drugs, a careful medical history should be taken.

If CDAD is suspected or CDAD is confirmed, ongoing antibacterial use against C. difficile may need to be discontinued. As indicated clinically, appropriate fluid and electrolyte therapy, protein supplementation, antibacterial treatment of C. difficile and surgical evaluation should be performed.

Prescribing lincomycin in the absence of proven or strongly suspected bacterial infection or a prophylactic indication will not benefit the patient and increase the risk of developing drug-resistant bacteria.

Recurrences are treated with vancomycin. As another treatment option, 25,000 units of bacitracin can be given 4 times a day for 7-10 days.

Drugs that cause intestinal stasis, such as diphenoxylate, should be avoided.

LİNKOSOL should be used with caution in people with a gastrointestinal system disease, especially colitis.

It is not recommended in the treatment of meningitis, as it does not pass into the cerebrospinal fluid in sufficient amount.

LİNKOSOL sterile solution **must not be administered intravenously as a bolus**, should not be given undiluted into the vein, should be administered at least 60 minutes later as specified in the method of administration section. Liver and kidney functions should be closely monitored during long-term treatments.

Liver and kidney function tests and blood counts should be performed periodically during long-term treatment with LİNKOSOL.

During the treatment, microorganisms that are not sensitive to the preparation may grow, especially yeast fungi.

The use of LİNKOSOL may cause excessive growth of non-susceptible organisms, especially yeasts. In the event of superinfections, appropriate measures should be taken as the clinical situation dictates.

When LİNKOSOL treatment is required to patients with previous monilial infections, concomitant antimonial therapy should be given. Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis and severe cutaneous adverse reactions such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP), and erythema multiforme, have been reported with the use of LİNKOSOL. If an allergic reaction occurs against LİNKOSOL, the drug should not be continued

(See Section 4.8).
LİNKOSOL should be used with caution in patients with asthma or a significant history of allergies.
Certain infections may require incision and drainage or other surgical procedures in addition to antibacterial therapy.

Benzyl Alcohol Toxicity in Pediatric Patients (Gasping Syndrome)
LİNKOSOL solution for injection contains 18 mg benzyl alcohol in each 2 mL ampoule. Preservative benzyl alcohol has been associated with serious side effects in infants, including Gasping syndrome (may cause multiple organ dysfunction, respiratory system disorder, severe metabolic acidosis) and death. Although the normal therapeutic dose of this product is significantly less than the dose associated with benzyl alcohol gasping syndrome, the minimum amount of benzyl alcohol where toxicity occurs is unknown. The risk of benzyl alcohol toxicity depends on the amount administered and the capacity of the liver and kidneys to detoxify chemicals. Babies born prematurely and underweight are more prone to develop toxicity.

It should not be administered to premature babies and newborns.
It may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years of age..

4.5. Interactions with other medical products and other forms of interaction

In vitro antagonism has been reported between LİNKOSOL and erythromycin, the concomitant use of these two drugs is not recommended.
Combined use of LİNKOSOL with kaolin reduces the gastrointestinal absorption of lincomycin by 90%. This situation lowers the plasma concentration of lincomycin. In cases where it is necessary to use both drugs together, it is recommended that patients use kaolin 2 hours before lincomycin.
The neuromuscular blocking effect of LİNKOSOL has been demonstrated. Therefore, it may increase the effect of neuromuscular blocking drugs such as tubocurarine and pancuronium. Lincomycin should be used with caution in patients taking such drugs.
Drugs that cause intestinal stasis, such as diphenoxylate, should be avoided.

Additional information on special populations
No clinically significant pharmacokinetic drug-drug interaction was observed in studies with Lincomycin 600 mg Ampoule.

Pediatric population:
No interaction studies in the pediatric population have been identified.

4.6. Pregnancy and lactation

General advice
Pregnancy category: C

Women with childbearing potential/Contraception

There is no recommendation for the use of the drug in women with childbearing potential and those who use contraception.

Pregnancy

There are no adequate and controlled studies about the use of Lincomycin in pregnant women.

Animal studies are insufficient for effects on pregnancy and / or embryonal / fetal development and / or parturition and / or postnatal development.

The potential risk for humans is unknown.

LİNKOSOL contains benzyl alcohol as a preservative. Benzyl alcohol may cross the placenta (see 4.4 Special warnings and precautions for use).

LİNKOSOL should not be used during pregnancy unless absolutely necessary.

Lactation

Lincomycin has been shown to pass into breast milk. A decision should be made to discontinue breastfeeding or LİNKOSOL treatment, as it may cause serious side effects in breastfed babies.

The reproductive capability/Fertility

In fertility studies conducted in rats at doses up to 300 mg / kg per day (approximately 0.36 times the highest recommended dose for humans on a mg / m^2 basis), no effect on reproduction was observed.

4.7. Effects on ability to drive and use machines

There is no data that it affects the ability to drive and use machines.

4.8. Undesirable effects

The effects observed with lincomycin are generally dependent on dose or concentration.

Undesirable effects are ranked according to system-organ class and frequency grouping using the following principles:

Very common (≥ 1/10), common (≥ 1/100 and < 1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10.000 and <1/1000), very rare (<1/10.000) and unknown (estimation based on the existing data is impossible).

Infections and infestations:

Uncommon: Vaginal infection

Unknown: Pseudomembranous colitis, Clostridium difficile-associated colitis (See Section 4.4)

Blood and lymphatic system disorders:

Not known: pancytopenia, agranulocytosis, aplastic anemia, leukopenia, neutropenia and thrombocytopenic purpura.

Immune system disorders:
Unknown: Anaphylactic reaction (see section 4.4), angioedema and serum sickness.

Nervous system disorders:
Not known: headache, dizziness, somnolence

Ear and labyrinth disorders:
Not known: Vertigo, tinnitus

Cardiac diseases:
Unknown: cardiopulmonary arrest (see section 4.2)

Vascular diseases:
Unknown: Hypotension (see section 4.2), thrombophlebitis

Gastrointestinal disorders:
Common: Diarrhea, nausea, vomiting
Rare: Glossitis, stomatitis
Not known: Abdominal pain, abdominal discomfort, anal pruritus

Hepatobiliary diseases:
Not known: Jaundice and impaired liver function tests, increased transaminases

Skin and subcutaneous tissue disorders:
Uncommon: Rash, urticaria
Rare: Pruritus
Unknown: Toxic epidermal necrolysis, Stevens-Johnson syndrome, acute generalized exanthematous pustulosis, bullous dermatitis, exfoliative dermatitis, erythema multiforme (See Section 4.4)

Kidney and urinary tract diseases: *
Unknown: Renal failure, oliguria, proteinuria, azotemia

General disorders and administration site conditions:
Not known: sterile abscess formation at the injection site *, hardening *, pain * and local irritation

* A direct relation of LİNKOSOL with renal damage has not been determined.
* Event reported by intravenous administration.
* Reported by intramuscular injection.

Reporting of suspected adverse reactions

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

4.9. Overdose and treatment

Experience with overdose is limited.
Lincomycin cannot be adequately separated from blood by hemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Systemic antibacterial, lincosamide
ATC Code: J01FF02

Lincomycin is a lincosamide group antibiotic with bactericidal or bacteriostatic effects depending on the sensitivity and antibiotic concentration of the microorganism.

Mechanism of action:
Lincomycin, like macrolide antibiotics, inhibits the first stage of protein synthesis by binding to the 50S subunit of bacterial ribosomes.
The in vitro spectrum of lincomycin is shown below.
Microorganisms sensitive to lincomycin:

- Spore-free Gram-positive anaerobic bacteria such as *Actinomyces, Propionibacterium and Eubacterium,*
- Gram-positive anaerobic and microaerophilic cocci, such as *Peptococcus, Peptostreptococcus and microaerophilic streptococci*
- Gram-positive aero- bacteria such as *Staphylococcus, Streptococcus, Pneumococcus, (Not effective on Enterococcus faecalis.)*

Microorganisms moderately sensitive to lincomycin:

- Gram-negative anaerobic bacteria that do not spore, such as *Bacteroides and Fusobacterium,*
- Gram-positive anaerobes sporting such as *Clostridium.*

Microorganisms that are less sensitive or resistant to lincomycin:

- Most strains of *Streptococcus faecalis, Neisseria, Haemophilus influenzae, Pseudomonas* and other Gram-negative bacteria.

5.2. Pharmacokinetic properties

General Particulars

Absorption:
One hour after intramuscular administration of a single 600 mg dose of lincomycin, the highest antibiotic levels in serum (11.6 microgram / mL) are achieved. This therapeutic level is maintained for up to 17-20 hours in the most susceptible gram-positive organisms.

When 600 mg of lincomycin is given as an intravenous infusion within 2 hours, the highest antibiotic level in serum (15.9 micrograms / mL) is achieved in 30 minutes, and the therapeutic level is maintained for 14 hours for the most susceptible gram-positive organisms.

Distribution:
Lincomycin concentrations in fetal blood, peritoneum and pleural fluid can reach 25-50% of the antibiotic concentration in plasma, 50-100% in breast milk, 40% in bone tissue and 75% in soft tissues around the bone. The penetration of lincomycin into the cerebrospinal fluid is slow (1-18% of the blood level). Antibiotic concentration in the cerebrospinal fluid in cases of meningitis can be up to 40% of the plasma concentration.

Biotransformation:
Lincomycin is metabolized in the liver.

Elimination:
The half-life of lincomycin metabolized in the liver is 5.4 ± 1 hours. Impairment of liver and / or kidney functions may lead to prolongation of this period.
Therefore, in patients with liver or kidney dysfunction, the reduction of the frequency of LİNKOSOL administration should be considered.
1.8-24.8% (average 17.3%) of 600 mg lincomycin administered intramuscularly is excreted in urine and 4-14% in faeces. When the same dose is given intravenously within 2 hours, the amount of microbiologically active compound detected in urine is 4.9-30.3% of the administered dose.
(average 13.8%). The remainder of the antibiotic is excreted from the body as inactive metabolites.
LİNKOSOL cannot be removed from plasma by hemodialysis or peritoneal dialysis.

Linearity / Nonlinear case:
Data are not available.

5.3. Preclinical safety data

The carcinogenic potential of lincomycin has not been evaluated.
Lincomycin was not found to be mutagenic at the HGPRT locus of the *Ames Salmonella* recycling assay or V79 Chinese hamster lung cells. V79 does not cause breaks in the Chinese hamster DNA sequence or chromosomal abnormalities in human lymphocyte cell culture as measured by its alkaline elution. In vivo; Lincomycin was negative in both rat and mouse macronucleus assays and did not induce sex-related recessive lethal mutations in male *Drosophila* offspring. However, lincomycin caused unprogrammed DNA synthesis in newly isolated rat hepatocytes.
No impairment of fertility was observed in male and female rats given oral lincomycin at a dose of 300 mg / kg (0.36 times the highest recommended human dose on mg / m^2).
Reproduction studies have been conducted using oral doses of lincomycin up to 1000 mg / kg (1.2 times the highest recommended human dose at mg / m^2) and did not show any adverse effects on pup survival from birth to weaning.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Benzyl alcohol
Water for injection

6.2. Incompatibilities

Lincomycin sterile solution does not show any incompatibility with the following solutions for at least 24 hours:

- 5% dextrose solution
- 10% dextrose solution
- 5% dextrose and 0.9% sodium chloride solution
- 10% dextrose and 0.9% sodium chloride solution
- 5% and 10% dextrose solution in isotonic NaCl
- Ringer's solution
- 1/6 M sodium lactate solution
- Dextran solution in 6% saline

LİNKOSOL sterile solution does not show any physical incompatibility for at least 24 hours in injection solutions containing the following vitamins and antibiotics in the concentrations generally used:

- Vitamin B complex or vitamin B complex containing ascorbic acid,
- Penicillin G sodium (for 4 hours)
- Cephalothin
- Tetracycline hydrochloride
- Cephaloridine
- Colistimethate (for 4 hours)
- Ampicillin
- Methicillin
- Chloramphenicol
- Polymyxin B sulfate

The incompatibility and stability time of the drug mixture may vary depending on densities and other conditions.
These incompatibility definitions are entirely physical. It is not chemical. Clinical evaluation for safety and efficacy has not been performed with these combinations.
It shows physical incompatibility with lincomycin, novobiocin, phenytoin and kanamycin.

6.3. Shelf life

36 months

6.4. Special precautions for storage

Keep in its package and out of the reach and sight of children.
It should be stored at room temperature below 30 ° C.

6.5. Nature and contents of container
LİNKOSOL ampoule: In ampoules of 2 mL and boxes containing 1 or 100 ampoules.

6.6. Special precautions for disposal and other handling
Unused products or waste materials should be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulations".

7. MARKETING AUTHORIZATION HOLDER
Osel İlaç San. ve Tic. A.Ş.
Akbaba Mah., Maraş Cad. No: 52
34820 Beykoz / İstanbul
Tel: (0216) 320 45 50 (Pbx)
Fax: (0216) 320 41 45

8. MARKETING AUTHORIZATION NUMBER
192/47

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
First Authorization Date: 30.06.1999

10. DATE OF REVISION OF THE TEXT