PATIENT INFORMATION LEAFLET

Kolistate 150 mg I.M./I.V. Vial Containing lyophilized powder for Injection and Inhalation

Sterile- Apyrogenic

IV or IM injection

- ***Active substance :*** Each vial contains kolistimetate sodium equivalent to 150 mg colistin base.
- ***Excipients :*** Water for injection

Read all of this leaflet carefully before you start using this medicine because it contains important information for you
Keep this leaflet. You may need to read it again.
If you have any further questions, ask your doctor or pharmacist.
This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs or illness are the same as yours.
If you get any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

The active ingredient of KOLISTATE is colistimethate sodium. It belongs to the antibiotic group called polymyxin.

KOLISTATE, is used to cut off some infections in the human body caused by some types of bacteria. Like all antibiotics, KOLISTATE can cut off only some types of bacteria. Therefore, it is only suitable for the treatment of some types of infections.

KOLISTATE, is packed in 10 mL clear glass vial and 2 mL ampoule containing water for injection and presented in cardboard boxes.

KOLISTATE is used in the treatment of bacterial infections in different parts of the body.

KOLISTATE is used by intravenous route as a solution to treat serious infections caused by existing bacterial types. These infections include some pneumonias and some renal and bladder infections. KOLISTATE is not used usually to treat such infections. But if the other antibiotics are not suitable for a reason, KOLISTATE can be used.

In addition, KOLISTATE, in patients with cystic fibrosis - including in childhood -should be used with Nebulizer in the treatment of lung infections caused by *Pseudomonas aeruginosa* with inhalation and indicated in the following conditions :

- As a long-term inhalation with systemic antibiotic treatment if there is Pseudomonas aeruginosa growth for the first time in respiratory tract isolates, whether or not patient's has symptoms
- As a long-term inhalation in patients under 6 years old with Pseudomonas aeruginosa colonization, if the symptoms develop
- As a long - term inhalation where the breeding Pseudomonas aeruginosa strain is tobramycin resistant

2. What you need to know before you use KOLISTATE

Do not use KOLISTATE

- If you have hypersensitivity to colistimetate sodium or any compound present in the formulation

Warnings and precautions

- If you have renal insufficiency

If you have ever had any of these conditions, tell your doctor before you use KOLISTATE

KOLISTATE with food and drink

There is no interaction with food and drink due to the way of use.

Pregnancy

Consult your doctor or pharmacist before using the medicine

If you are pregnant, think you may be pregnant or planning to have a baby, inform your doctor before taking this medicine. Your doctor will assess whether you can use KOLISTATE while you are pregnant or planning to get pregnant and explain potential risks.

Consult your doctor or pharmacist if you notice that you are pregnant during treatment.

Lactation

Consult your doctor or pharmacist before using the medicine

It is not known whether colistimethate sodium is excreted in human milk. It should be considered that breastfeeding is beneficial for the child and benefit from KOLISTATE treatment for breastfeeding mothers when deciding whether or not to stop breastfeeding or to avoid treatment should be carefully evaluated.

Effects on ability to drive and use machines

Patients should not drive and use machines during the use of KOLISTATE. Because temporary neurological disorders can be seen. These include dizziness and speech impairment.

Important information about some of the excipients present in KOLISTATE

KOLISTATE contains sodium less than 1 mmol (23 mg) in each dose, it is basically sodium free.

KOLISTATE with other medicinal products
Please tell your doctor if you are taking or have recently taken any other medicines, given below.

KOLISTATE can increase the effects and side effects of aminoglycosides, polymyxins, muscle relaxants (eg tubocurarin) and ether, succinylcholine, galamine, decamethonium and other drugs, including sodium citrate.

Sodium cefalotin can increase the nephrotoxicity of KOLISTATE. Co-administration of KOLISTATE and sodium cefalotin should be avoided.

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

3.How to use KOLISTATE ?
Instructions for proper use and dose / application frequency:
Your doctor will determine how many doses of your medication will be given, how long your treatment will last according to your disease, body weight and renal function and will apply to you.

KOLISTATE is given according to the severity of infection, patients with normal renal function total daily dose is 5 mg / kg / day and given divided by 2 or 3.

Use of administration and method:
KOLISTATE is injected intramuscularly or via the intravenous infusion route (dropwise application.

KOLISTATE (150 mg / vial) is dissolved in 2.0 ml of water for injection. Solution prepared by dilution contains colistimetate sodium at a concentration equivalent to 75 mg / ml of colistin base activity.

It is slowly rotated during reconstitution to prevent foam formation.

Application by inhalation:
Local treatment of lower respiratory tract infections 50-75 mg is administered 2-3 times daily with 3-4 mL of saline with nebuliser.

Different age groups
Pediatric population :
The dose prescribed for adults is administered.

Geriatric population :
Care must be taken when selecting doses for the elderly population, like starting at the smallest dose interval and indicating poor kidney functions. Precautions should be taken in selecting the dose and renal function should be monitored.

Additional information on special populations:
Hepatic failure:
In patients with hepatic insufficiency, there is no dose adjustment.

Renal failure:
In patients with renal insufficiency, daily dosing should be reduced.
The dosage changes recommended in patients with renal insufficiency are shown in the table below :

Creatinine clearance (ml/min)	**Total daily dose ***		**Frequency**
	Minimum	**Maximum**	
60	300 mg	420 mg	Every 12 hours
50	262.5 mg	367.5 mg	
40	225 mg	315 mg	
30	187.5 mg	262.5 mg	
20	150 mg	210 mg	
≤10	112.5 mg	157.5 mg	

* Total daily dose = Targeted blood concentration (mg / L) x [(1.5 x CrCln) + 30] (targeted blood concentrations is taken 2.5 mg / L at minimum doses and 3.5 mg / L at maximum doses).
The doses were calculated according to the individual with a body surface area (BSA) 1.73 m2 (average 70 kg). According to BSA for a complete calculation, corrected creatinine clearance should be used (CrCln = CrCl xBSA / 1.73m2).

Kolistate 150 mg I.M./I.V. Vial Containing lyophilized powder for Injection and Inhalation dose and dose range that should be used in patients undergoing hemodialysis are giving in the following table:

Hemodialysis	A total of 105 mg is administered every 12 hours daily (wo hemodialysis) On dialysis days, a total of 150 mg dose divided in two, the first half is given in the last hour of hemodialysis and the other half is 12 hours after.
CAPD	160 mg single dose per day
CRRT	The total dose is 672 mg for mean serum steady state concentration of 3.5 μg / mL. Dose is divided in two so that it is applied every 12 hours.

If you think that the effect of KOLISTATE is very strong or weak talk to your doctor or pharmacist.

If you use more KOLISTATE than you should :

If you use more KOLISTATE than you should, talk with your doctor or pharmacist.

If you forget to use KOLISTATE

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

If you stop using KOLISTATE

If you are considering to stop your KOLISTATE treatment, consult your doctor first.

If you have any other questions about the use of this product, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects if you have hypersensitivity to any compound present in the formulation

If any of the following happens to you, stop using KOLISTATE and talk to your doctor immediately:

- Fever**,** rash, swelling of your face, lips, your mouth (tongue and/or throat and/or difficulty swallowing)
- Allergic reactions like shortness of breath, swelling of your hands, feet and wrists

These are all very serious side effects.

If you have these, you have a serious allergic reaction to KOLISTATE. You may need to be admitted to an emergency medical intervention or hospital.

All of these very serious side effects are seen very rare.

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

- Fever and chills
- Trouble breathing
- Difficulty in urination
- Weakness in the muscles
- Cough
- Bronchospasm

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

If you notice any of the following, tell your doctor :
- Dizziness
- Speech impairment
- Stomach ache
- Numbness in the mouth or tongue
- Itching

These are the minor side effects of KOLISTATE.

If you experience any side effects not mentioned in this patient information leaflet, inform your doctor or pharmacist.

5. How to store KOLISTATE ?

Keep KOLISTATE out of the sight and reach of children, in its package.
Do not store above 25°C.
Reconstution solution stored in refrigerator (2-8°C) and used with in 7 days.

Use in accordance with expiration date

Do not use KOLISTATE after the expiry date which is stated on the carton

Do not use KOLISTATE if you notice that the pack is damaged or show signs of tampering.

Do not throw away this medicine via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Marketing Authorisation Holder : Biem İlaç San. ve Tic. A.Ş.
Anıttepe Mah. Turgut Reis Cad. No: 21
Tandoğan / Çankaya – Ankara

Manufacturer : Mefar İlaç Sanayii A.Ş.
Kurtköy/ Pendik/ İstanbul

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THE FOLLOWING INFORMATION IS FOR THE HEALTH PERSONNEL WHO WILL APPLY THIS MEDICINAL PRODUCT

INTRAVENOUS USE
Intermittent Direct Use: Half of the total daily dose is slowly injected IV in every 12 hours for 3-5 minutes.

Continuous Infusion: Half of the total dose is slowly injected IV for 3-5 minutes . The remaining half of the total daily dose of KOLISTATE is added in one of the following solutions:

• 0.9% NaCl
• 5% dextrose in 0.9% NaCl
• 5% dextrose in water
• 5% dextrose in 0.45% NaCl
• 5% dextrose in 0.225% NaCl
• Lactate ringer solution
• 10% invert sugar solution

There is no recommended information for the use of other medicines in combination with KOLISTATE or the above-mentioned infusion solutions.

The other half of the total daily dose is given 1-2 hours after the first half by slow intravenous infusion for 22-23 hours. In the case of renal dysfunction, the infusion rate is reduced depending on the degree of renal failure.

The choice of intravenous solution and volume is determined by requirement of fluid and electrolyte management.

The colistimetate sodium-containing infusion solution should be freshly prepared and used within 24 hours.