

PATIENT INFORMATION LEAFLET

COLIDUR 200 mg Film Tablet

Taken orally.

Active Ingredient: Contains 200 mg rifaximin

Inactive ingredients: sodium starch glycolate, microcrystal cellulose 200, colloidal silicon dioxide, magnesium stearate, glyceryl palmitostearate, talc, opadry OY-S 34907 pink (compound; hypromellose, Titanium Dioxide, Propylene glycol, Red iron oxide, Disodium EDTA)

Read this leaflet carefully before you start taking this medicine, as it contains important information for you.

- *Keep this leaflet. You may need to read it again.*
- *If you have any further questions or need advice, ask your doctor or your pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *If you should visit a doctor / hospital during usage of this medicine, tell your doctor that you are using this medicine.*
- *Follow the instructions exactly. Do not use **higher or lower** dosages other than prescribed to you.*

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

COLIDUR, is present in blister packages containing 12 pink colored, convex, circular film coated tablets.

Each film tablet contains 200 mg rifaximin.

COLIDUR is a group of drugs called antibiotics and contains rifaximin which is used as an effective antimicrobial agent in the intestine. It is used in severe gastrointestinal infections, in the case of

traveller's diarrhoea in adults when the diarrhoea is not accompanied by fever or blood in the stools, or 8 or more unformed (soft or liquid) stools in the last 24 hours, in order to increase the effect of the drug used when the amount of ammonia and its compounds increases in blood, and in diarrhea-dominant irritable bowel syndrome,

The use of children under the age of 18 is not recommended.

2. Points to consider before you take COLIDUR

DO NOT USE COLIDUR

If;

- You are hypersensitive to Rifaximin, other rifamisin (For example: rifampicin or rifabutin) or any other excipients in the medicines composition indicated above (If you think you are allergic),
- You have a fever,
- You passed 8 or more unformed stools in the last 24 hours
- You have constipation, bloody stools, abdominal pain and vomiting due to intestinal obstruction,
- You have a blockage of the bowel

USE COLIDUR WITH CAUTION under the below circumstances.

If;

- Your symptoms get worse during treatment, stop taking COLIDUR and consult a doctor.
- After 3 days of treatment, your symptoms continue or re-appear shortly afterwards do not take a second course of COLIDUR and consult your doctor

If you are using activated charcoal (eg for gas or diarrhea treatment), please take COLIDUR 200 mg film tablets at least 2 hours after taking the charcoal.

Rifaximin can be absorbed from intestines in small quantities. Therefore, the urine color may turn red.

It should be used with caution when it is necessary to use drugs that slow or stop the functioning of the P-glycoprotein enzyme, such as cyclosporine (a drug that suppresses the immune system).

Combination of warfarin (anti-coagulant drug) and rifaximin may reduce the efficacy of warfarin or increase its efficacy and cause bleeding. If you are using warfarin, your doctor may need to check your blood values. Please inform your doctor if you are taking warfarin or any blood anticoagulant medication.

Clinical data have shown that rifaximin is not effective in the treatment of travellers' diarrhoea caused by invasive enteric pathogens such as *Campylobacter jejuni*, *Salmonella* spp. and *Shigella*, which typically produce dysentery-like diarrhoea characterised by fever, blood in the stool and high stool frequency.

Treatment of *Clostridium difficile* with rifaximine may result in diarrhea and pseudomembranous colitis (inflammation of the large intestine) associated with *Clostridium difficile*.

Please consult your doctor even if these warnings are valid for any period in the past.

Taking COLIDUR with food and drink:

Does not change the effect of taking food with or without separate. It should be taken by mouth with a glass of water.

Taking this medicine may cause a reddish discolouration of your urine

Pregnancy

Consult your doctor or pharmacist before using this medication.

If you are pregnant or are considering getting pregnant, it is not recommended to use COLIDUR.

Animal studies showed transient effects on ossification and skeletal variations in the foetus (see section 5.3). The clinical relevance of these findings in humans is unknown.

Women with childbearing potential should use contraceptive methods that are considered to be medically effective during treatment.

Animal studies do not indicate direct or indirect harmful effects with respect to male and female fertility.

If;

- If you are pregnant, you think that you might be pregnant and you are considering getting pregnant, consult your doctor or pharmacist.

Consult your doctor or physician if you become pregnant during treatment.

Breast - feeding

Consult your doctor or pharmacist before using this medication.

- If you are breastfeeding or if you are considering breastfeeding, consult your doctor or pharmacist before starting to use.

It is unknown whether rifaximin/metabolites are excreted in human milk.

A risk to the breast-fed child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from rifaximin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Inform your doctor before using COLIDUR during breast-feeding.

Driving and using machines:

COLIDUR has no influence on the ability to drive and use machines.

If you feel dizzy or drowsy you should not drive or operate machinery

Important information about some of the ingredients of COLIDUR:

If you do not have an extreme sensitivity to the ingredients in the content of COLIDUR, no adverse effect due to these substances is expected.

Taking other medicines:

To date, no interaction has been identified.

- There is no experience of administering rifaxime to those who use another rifamycin antibacterial drug to treat a bacterial infection spread to different organs.
- Please tell your doctor if you are taking cyclosporine (immunosuppressive, a medicine to suppress the body's immune system), warfarin (medicine to prevent blood clotting) or oral contraceptives (medicines to prevent pregnancy).
- There are no drug interaction studies investigating the simultaneous uptake of rifaxime and other drugs (eg loperamide, activated charcoal) that can be used during tourist diarrhea.
- If you are using activated charcoal (eg to treat wind or diarrhoea), please take COLIDUR at least 2 hours after taking the charcoal.
- If you have liver failure disease, the efficacy of these drugs may be reduced when using drugs such as warfarin, antiepileptic (anti-epileptic drugs), antiarrhythmics (drugs used in the

treatment of cardiac arrhythmia), contraceptive drugs, which are affected by a liver enzyme called CYP3A4, together with COLIDUR.

- Since the combination of warfarin (anti-coagulant drug) and rifaximine reduces or increases the efficacy of warfarin, the INR values (international normalized rate) should be monitored by your doctor. Adjustments to the dose of oral anticoagulants may be required. Tell your doctor if you are using warfarin.

In healthy subjects, co-administration of a single dose of cyclosporine (600 mg), a potent P-glycoprotein inhibitor, with a single dose of rifaximin (550mg) resulted in 83-fold and 124-fold increases in rifaximin mean C_{max} and AUC_∞ respectively.

The clinical significance of this increase in terms of the amount expected to pass into the bloodstream (systemic exposure) is unknown.

Inform your doctor / physician about any prescribed or over-the-counter medication you are using or have been using lately.

3. How to take COLIDUR?

Instructions for proper use and dose / frequency of administration:

Doctors may recommend altering doses and frequency of the drug use.

The duration of treatment should not exceed 3 days unless advised otherwise by the doctor. The duration of treatment should be determined by the doctor according to the clinical response of the patient.

In cases of necessary repeated treatment, each treatment period should be splited up with non-drug period for 20-40 days.

Total time of periodic treatment should be determined by your doctor.

Recommended dose:

In treatment of acute gastrointestinal infection, travelers' diarrhea:

Adults: 1 tablet every 8 hours (600 mg rifaximin)

Adjuvant treatment for increased level of ammonium in blood

Adults: 2 tablets every 8 hours (1200 mg rifaximin)

Treatment of diarrhea-dominant irritable bowel syndrome (Diarrhea predominantly sensitive intestinal disease)

Adults: 2 tablets every 8 hours (1200 mg rifaximin)

Route and method of administration

- Remove the film tablet from the blister and swallow the tablet whole with a glass of water.
- COLIDUR can be taken with food or on an empty stomach.

Different age groups:

Paediatric Population:

Taking COLIDUR is not suggested for children under 18 since safety and efficacy of the drug in children under 18 is not established.

Geriatric Population:

Experience in rifaximin treatment with geriatric population is limited. However, it has been determined that drug tolerance is high at the recommended doses.

Special cases:

Renal / Hepatic failure:

No clinical data are available on the use of rifaximin in patients with impaired renal function.

Dose adjustment is not recommended in patients with hepatic impairment due to limited systemic absorption of rifaximine (drug absorption from the intestines)

If you think that the effect of COLIDUR is too strong or too weak, talk to your doctor or pharmacist.

If you take more COLIDUR than you should:

Clinical studies with patients complaining about tourist diarrhea did not show any serious clinical findings at doses up to 1800 mg per day.

In healthy subjects, doses of rifaxime administered up to 2400 mg per day for 7 days did not cause high dose-related clinical symptoms.

In patients in whom overdose is recognized, it is advisable to determine the appropriate and supportive treatment.

If you have used COLIDUR more than you need to use, talk to a doctor or pharmacist.

If you forget to take COLIDUR

Take the missed dose as soon as you remember and take the next scheduled dose at its regular time.

Do not take extra medicine to make up the missed dose.

The effects that may occur when treatment with COLIDUR is terminated:

If you do not continue treatment for three days, your symptoms may get worse. If you have any further questions about the use of this product, consult your doctor or pharmacist.

Contact your doctor or physician if you think COLIDUR has a very strong or weak effect.

4. What are the possible side effects?

Like all medicines, COLIDUR may have side effects in people who are sensitive to the substances contained in its contents.

Side effects of the medicines are classified as indicated below.

Very common: it can be seen in at least 1 of 10 patients.

Common: less than one in 10 patients, but more than one in 100 patients.

Uncommon: less than one in 100 patients, but more than one in 1,000 patients.

Rare: less than one in 1,000 patients, but more than one in 10,000 patients.

Very rare: less than one in 10,000 patients.

Frequency not known: Can not be estimated from the available data

Stop taking COLIDUR and consult your doctor IMMEDIATELY if any of the below occurs:

Severe allergic reaction that manifests itself with rash, itch and swelling on the face, on the lips, on the tongue and/or in the throat, which can make it difficult to breathe.

All of these are very serious side effects. If any of them is present, it means you have severe allergy to COLIDUR. You may need emergency care or to be hospitalized.

Other side effects associated with COLIDUR are reported below:

Common

- Headache
- Dizziness
- Wind
- Abdominal bloating
- Constipation
- Abdominal pain
- Diarrhoea
- Defecation urgency
- Nausea
- Involuntary and painful or ineffective straining
- Vomiting
- Fever

Uncommon

- Fungal disease in various parts of the body, thrush (candidiasis) Thrush
- Flu
- Swelling of the throat
- Cold sore, liquid filled bubble
- Nasal and pharyngeal inflammation
- Increase in white blood cells in blood
- Abnormal increase in monocyte count in blood
- Decrease in the number of neutrophils in blood
- Reduced appetite
- Water loss
- Insomnia
- Abnormal dreams
- Depressed mood
- Irritability
- Severe headache (migraine)
- Loss of sense
- Numbness

- Drowsiness
- Sinus headache
- Double vision
- Severe dizziness, (vertigo, sensation of the room going round)
- Earache
- Palpitation
- Hot flush
- Increase in blood pressure
- Shortness of breath
- Nasal obstruction
- Cough
- Mouth and pharyngeal pain
- Dry throat
- Nasal congestion
- Indigestion
- Disorder in gastrointestinal motility
- Upper abdominal pain
- Secretory stool
- Solid stool
- Blood in stool
- Lip dryness
- Sensory loss in taste
- Blood test results: increased liver enzyme values: Increase in an enzyme called aspartate aminotransferase
- Rash
- Blotchy skin
- Sunburn
- Stained skin
- Virus-induced rash
- Back pain
- Muscle contraction
- Continuous muscle pain (myalgia)

- Muscle weakness
- Neck pain
- Loss of strength
- Sugar in the urine
- Too often but little urination
- Excess urination
- Blood in the urine
- Protein in the urine
- Frequent menstruation (less than 21 days between two periods)
- Weakness
- Pain and discomfort
- Environmental edema (swelling of the arms)
- Influenza-like illness
- Shivering
- Cold sweat
- Excessive sweating

The frequency not known

- Bacterial infections (Clostridial infections)
- Abnormal blood tests (decrease in platelets liver function tests outside the normal range, international normalized rate changes – INR)
- Severe acute reactions to medicine (anaphylactic reactions), hypersensitivity to the drug allergic reactions
- Feeling like you will faint
- Redness, itching, watering, barking on the skin etc. a non-communicable skin disease manifested by tissue disorders (eczema)
- Painful and bumpy swellings (angioedema), most commonly seen on the lips, tongue, around the eyes, around the face, neck, arms, legs, abdomen and the skin of the sexual region
- Itchy pink or red rash (dermatitis)
- Common redness and scaling on the skin due to the drugs used or unknown causes (dermatitis exfoliative)
- Skin inflammation (erythema) which causes mostly reddish and painful heels on the knees.
- Redness

- Itching
- A reddish purple colored, purpura skin rash (purpura)
- Hives

Treatment with any antibiotic may result in diarrhea (CDAD) associated with Clostridium difficile (a bacterium that has many enzymes and poisons with a devastating effect on the organ). During high-dose long term treatment or damage of the inner layer of intestine, small portion (less than 1%) of the drug may be absorbed and cause urine to become reddish.

Inform your doctor or pharmacist if you encounter any side effects other than remarked in this patient information leaflet.

5. How to store COLIDUR

Keep COLIDUR out of reach and sight of children in its original package.

Store in original package and below 25°C.

Use in accordance with expiration dates.

Do not use COLIDUR after the expiration date which is printed on its package.

Do not use COLIDUR, if you notice defects in the product and / or its packaging.

Marketing Authorization Holder:

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