

מאי 2012

Fucidin LEO

צוות רפואי נכבד,
חברת דקסל פארמה מבקשת להודיעכם על עדכון בעלון לצרכן ובעלון לרופא של התכשיר
Fucidin LEO.
העלון לצרכן והעלון לרופא נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם
מודפסים ע"י פנייה לבעל הרישום:
דקסל בע"מ, רח' דקסל 1, אור- עקיבא 30600 ישראל, טל': 04-6364000.

הרכב:

פוסידין ליאו מכיל Sodium fusidate 250 mg

התוויות מאושרות:

For the treatment of infections caused by Staphylococcus.

העלון לצרכן עודכן באפריל 2012, העדכון הינו בסעיפים הבאים:

הרכב:

כל טבליה מכילה:

מרכיב פעיל:

Sodium Fusidate 250 mg.

מרכיבים בלתי פעילים:

Microcrystalline cellulose, Lactose monohydrate, Crospovidone, Talc, Hypromellose,
Magnesium stearate, Silica colloidal anhydrous, All-*rac*- α -Tocopherol, Titanium dioxide.

כל טבליה מכילה כ – 72 מ"ג לקטוז **מונוהידרט ו- 11 מ"ג סודיום.**

אין להשתמש בתרופה מבלי להיוועץ ברופא לפני התחלת הטיפול:

אם הינך בהריון או חושבת שהינך בהריון, אם הינך מיניקה, אם הינך סובלת או סבלת בעבר
מחסימה **או בעיה** בדרכי המרה (כגון: אבנים בדרכי המרה). מליקוי בתיפקוד הכבד או אם חלית
לאחרונה בצהבת, **אם השתמשת בתרופה לאורך זמן (משום שיעילותה עלולה להיפגם).**
יש לדווח לרופא אם נכנסת להריון במהלך הטיפול בתרופה.

אזהרות:

בתקופת הטיפול בתרופה זו יתכן ותידרש/י לערוך בדיקות דם, כאשר התרופה ניתנת לזמן
ממושך או במינונים גבוהים או אצל חולים עם בעיית כבד.
אם הינך רגיש/ה למזון כלשהו או לתרופה כלשהי, עליך להודיע על כך לרופא לפני נטילת התרופה.
תרופה זו מכילה לקטוז, אם נאמר לך בעבר על ידי רופא שיש לך אי סבילות לסוכרים מסוימים, יש
להיוועץ ברופא לפני התחלת הטיפול בתרופה זו.
תרופה זו מכילה סודיום. יש לקחת זאת בחשבון במידה והינך בדיאטה דלת מלח.

תגובות בין תרופתיות:

אם הינך נוטל/ת תרופה נוספת, או אם סיימת זה עתה הטיפול בתרופה אחרת, כולל תרופות הנמכרות ללא מרשם ותוספי תזונה, עליך לדווח לרופא המטפל כדי למנוע סיכונים או אי יעילות הנובעים מתגובות בין תרופתיות, במיוחד לגבי תרופות מהקבוצות הבאות:

אנטיביוטיקה-אחרות תרופות המפונות מהגוף דרך הכבד או המרה, כגון לינקומיצין או ריפאמפיצין;
 נוגדי קרישה (כגון: וארפרין); תרופות לטיפול בנגיף האידס (HIV) או בזיהומים ויראליים אחרים;
 ציקלוספורין (לדיכוי מערכת החיסון), תרופות הידועות כגורמות נזק לכבד.

איך תשפיע התרופה על חיי היום יום שלך?

תרופה זו אינה משפיעה בדרך-כלל על יכולת הנהיגה או הפעלת מכונות. עם זאת, פנה/י לרופא אם הינך חש בתופעות לוואי העשויות לפגום בכושר הנהיגה או בהפעלת מכונות מסוכנות (כגון: סחרחורת, עייפות וכדומה).

תופעות לוואי:

תופעות לוואי: בנוסף לפעילות הרצויה של התרופה, בזמן השימוש בה עלולות להופיע השפעות לוואי כגון:

תופעות לוואי שכיחות (פחות מ-1 ל-10 אנשים):

קלקול קיבה, תחושת חולי/בחילה או קשיי עיכול, כאב בטן, שלשול, תחושת נמנום או סחרחורת.

תופעות לוואי לא שכיחות (פחות מ-1 ל-100 אנשים): כאב ראש, עייפות, נמנום, או חולשה, חוסר תיאבון, פריחה גירוד או חרלת.

תופעות לוואי נדירות (פחות מ-1 ל-1,000 אנשים): עלייה ברמת אנזימי כבד בבדיקות דם. אם תופעות אלו מטרידות או ממשיכות במשך יותר מימים ספורים יש לפנות לרופא.

תופעות המחייבות התייחסות מיוחדת (יש לפנות לרופא מיידית, ייתכן ויהיה צורך בהפסקת הטיפול)

כאב, קושי, קשיחות, נפיחות או חולשה בשרירים; שתן כהה או מתן שתן באופן מופחת, הפרעות בקצב הלב.

תגובה אלרגית חמורה שסימניה: קושי בנשימה או בבליעה, פריחה חמורה, דופק מהיר, נפיחות בלשון, בגרון או בפנים.

תופעות לוואי מאד נדירות (פחות מ-1 ל-10,000 אנשים):

תגובה אלרגית חמורה שסימניה: קושי בנשימה או בבליעה, פריחה חמורה, דופק מהיר, נפיחות בלשון, בגרון או בפנים. צהבת (המתבטאת בהצהבת העור או הלבן של העיניים) העלולה לגרום לגירוד חמור, פעולות מעיים חלשות ושתן כהה, תיתכן גם פגיעה בכליות שתגרום לאי הטלת שתן (פגיעה בכליות).

זיהומים בתכיפות גבוהה יותר (כמו דלקות גרון), נטייה לחבורות ביתר קלות, קוצר נשימה, עייפות. פגיעה בכבד שתתבטא בעלייה ברמת אנזימי כבד בבדיקות דם.

בכל מקרה שבו הינך מרגיש/ה תופעות לוואי שלא צוינו בעלון זה, או אם חל שינוי בהרגשתך הכללית עליך להתייעץ עם הרופא מיד.

אחסנה:

במקום קריר. תכשיר זה אינו דורש תנאי אחסון מיוחדים.

גם לפי תנאי האריזה/אחסנה המומלצים, תרופות נשמרות לתקופה מוגבלת בלבד. נא לשים לב לתאריך התפוגה של התכשיר!
בכל מקרה של ספק, עליך להיוועץ ברוקח שסיפק לך את התרופה.
אין לאחסן תרופות שונות באותה אריזה.

העלון לרופא עודכן באפריל 2012, העדכון הינו בסעיפים הבאים:

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance: 250 mg of sodium fusidate (~~equivalent to 240 mg fucidic acid~~). Sodium fusidate is the sodium salt of fusidic acid.

List of Excipients: - contains lactose monohydrate 71.9 mg and sodium 11 mg (per tablet).

For a full list of excipients, see section 6.1.

~~Microcrystalline cellulose, Lactose monohydrate, Croscopovidone, Talc, Hypromellose, Magnesium stearate, Silica colloidal anhydrous, All rac- α -Tocopherol, Titanium dioxide.~~

3. PHARMACEUTICAL FORM

Film-coated tablet.

White to off-white greyish marbled film-coated oval biconvex tablets without embossing.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

~~Pharmacotherapeutic group: General anti-infective for systemic use.~~

~~ATC code: J01XC01~~

~~Fucidin® exerts powerful activity against a number of gram-positive organisms. Staphylococci including the strains resistant to penicillin and other antibiotics are particularly susceptible to Fucidin®. Concentrations of 0.03–0.12 micrograms/ml inhibit nearly all strains of *Staphylococcus aureus*. Fucidic acid is active against *Staphylococcus epidermidis* and methicillin resistant staphylococci.~~

~~In severe or deep-seated infections and when prolonged therapy may be required, Fucidin® should generally be given concurrently with other anti-staphylococcal antibiotic therapy.~~

Pharmacokinetic Properties

~~Fucidin® readily penetrates tissue. Bactericidal levels have been assayed in bone and necrotic tissue. Blood levels are cumulative, reaching concentrations of 20–35 micrograms/ml after oral administration of 250 mg twice daily for seven days and 50–100 micrograms/ml after oral administration of 500 mg three times daily for three to four days. Fucidin® is excreted mainly in the bile, little or none being excreted in the urine.~~

Preclinical Safety Data

~~Animal studies have indicated that Fucidin[®] is practically atoxic.~~

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of infections caused by Staphylococcus.

~~Fucidin[®] is indicated in the treatment of all staphylococcal infections due to susceptible organisms, such as: cutaneous infections, osteomyelitis, pneumonia, septicaemia, wound infections, endocarditis, superinfected cystic fibrosis.~~

4.2 Posology and method of administration

~~For staphylococcal cutaneous infections:~~

Adults only:

The usual total daily dose is 1500 mg in divided doses.

In severe infections doses may be doubled or appropriate combined therapy may be used.

Since fusidic acid is excreted in the bile, no dosage modifications are needed in renal impairment. The dosage in patients undergoing haemodialysis needs no adjustment as fusidic acid is not significantly dialysed.

~~standard dose: 250 mg (one tablet) sodium fusidate (equivalent to 240 mg fusidic acid) twice daily for 5–10 days.~~

~~For staphylococcal infections such as osteomyelitis, pneumonia, septicaemia, wound infections, endocarditis, superinfected cystic fibrosis:~~

~~Adults: standard dose: 500 mg (two tablets) sodium fusidate (equivalent to 480 mg fusidic acid) three times daily.~~

~~In severe cases of fulminating infections, the dosage may be doubled or appropriate combined therapy may be used.~~

~~Since Fucidin[®] is excreted in the bile, no dosage modifications are needed in renal impairment. The dosage in patients undergoing haemodialysis needs no adjustment as Fucidin[®] is not significantly dialysed.~~

~~Elderly: No dosage alterations are necessary in the elderly.~~

Children:

The usual total daily dose is 20 to 50 mg/kg in divided doses.

4.3 Contraindications

~~Use in patients with~~ known hypersensitivity to sodium fusidate/fusidic acid **and it's salts** or to any of the excipients.

Concomitant treatment with statins, see section 4.5.

4.4 Special warnings and **special** precautions for use

~~Fucidin[®] Fusidic acid administered systemically~~ is metabolised in the liver and excreted in the bile. Elevated liver enzymes and jaundice have occurred during Fucidin[®] ~~systemically~~ therapy but are usually reversible on discontinuation of the drug.

Fucidin[®] ~~tablets administered systemically~~ should be given with caution and ~~periodic~~ liver function ~~tests~~ should be ~~carried out~~ monitored ~~when high oral doses are used, when the drug is given for prolonged periods,~~ if used in patients with ~~liver~~ hepatic dysfunction, in patients given potentially hepato-toxic drugs, and if used ~~with other antibiotics which have similar~~ in patients with biliary tract obstruction or in patients on concurrent drugs with similar excretion pathway.

~~biliary excretion pathways, e.g. lincomycin and rifampicin.~~

~~Fucidin[®] Fusidic acid administered systemically~~ competitively inhibits binding of bilirubin to albumin. Caution is necessary if Fucidin[®] ~~tablets~~ are administered ~~systemically~~ to patients with impaired transport and metabolism of bilirubin. Particular care should be taken in neonates (especially if premature) due to the theoretical risk of kernicterus.

~~The use of Fucidin[®] in combination with drugs that are CYP 3A4 biotransformed should be avoided. See section "Interaction with Other Medicinal Products and Other Forms of Interaction".~~

~~Prolonged administration of an anti infective may result in the development of superinfection with organisms resistant to that anti infective.~~

~~Fucidin[®] filmcoated tablets contain lactose.~~ Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine due to the content of lactose.

Each tablet contains 11 mg of sodium. To be taken into consideration by patients on a controlled sodium diet.

Bacterial resistance has been reported to occur with the use of fusidic acid. As with all antibiotics, extended or recurrent use may increase the risk of developing antibiotic resistance.

4.5 Interaction with other medicinal products and other forms of interaction

HMG-CoA reductase inhibitors

Co-administration of Fucidin[®] tablets ~~systemically~~ and HMG-CoA reductase inhibitors such as statins may cause increased plasma concentrations of both agents. This may result in an elevation of creatine kinase level and risk of rhabdomyolysis, muscle weakness and pain. Concomitant treatment with statins is therefore contraindicated, see section 4.3.

CYP-3A4 biotransformed drugs

Specific pathways of ~~Fucidin[®]~~ fusidic acid metabolism in the liver are not known, however, an interaction between ~~Fucidin[®]~~ fusidic acid and drugs being CYP-3A4 biotransformed can be suspected. The mechanism of this interaction is presumed to be a mutual inhibition of metabolism. ~~There is insufficient data to characterize the effect of fusidic acid on CYPs in vitro.~~ The use of Fucidin[®] tablets systemically should be avoided in patients treated with CYP-3A4 biotransformed drugs.

Oral anticoagulants

Fucidin[®] tablets administered ~~systemically and~~ concomitantly with oral anticoagulants such as coumarin derivatives or anticoagulants with similar actions may increase the plasma concentration of these agents enhancing the anticoagulant effect. ~~Anticoagulation should be closely monitored and a decrease of the oral anticoagulant dose.~~ Adjustment of the oral anticoagulant dose may be necessary in order to maintain the desired level of anticoagulation. ~~Similarly, discontinuation of Fucidin[®] may require the maintenance dose of anticoagulant to be re-assessed.~~

The mechanism of this suspected interaction ~~remains~~ is unknown.

HIV protease inhibitors

Co-administration of Fucidin[®] tablets systemically and HIV protease inhibitors such as ritonavir and saquinavir causes increased plasma concentrations of both agents which may result in hepatotoxicity.

Ciclosporin

Co-administration of Fucidin[®] tablets systemically and ciclosporin has been reported to cause increased plasma concentration of ciclosporin.

4.6 Fertility, pregnancy and lactation

Pregnancy

~~There is inadequate evidence of safety in human pregnancy.~~

There are no adequate data from the use of fusidic acid administered systemically in pregnant women.

~~There is evidence to suggest that when given systemically, fusidic acid can cross the placental barrier and therefore should be avoided during the third trimester due to the theoretical risk of kernicterus. If the administration of Fucidin[®] to pregnant patients is considered essential, its use requires that the potential benefits be weighed against the possible hazards to the fetus.~~

Animal studies are insufficient with respect to effects on pregnancy.

The potential risk for humans is unknown.

Fucidin[®] administered systemically should not be used during pregnancy unless clearly necessary.

Lactation

Safety in nursing mothers has not been established. When fusidic acid (as the sodium salt) has been given systemically, negligible levels have been detected in the breast milk.

Fusidic acid is excreted in breast milk in negligible amounts. The clinical relevance of this is unknown. Caution is required when Fucidin[®] is used in nursing mothers who wish to breast feed.

A bilirubin-displacing effect of Fucidin[®] has been demonstrated in vitro. Although kernicterus has not been observed in newborns receiving Fucidin[®], this effect should be borne in mind when giving Fucidin[®] to infants, especially icteric, prematurely born, jaundiced, acidotic or very ill neonates.

4.7 Effects on ability to drive and use machines

~~Presumed to be safe or unlikely to produce an effect.~~

Fusidic acid has no or negligible influence on the ability to drive and to use machines.

4.8 Undesirable effects

Very common —————>1/10

~~Common —————>1/100 and <1/10~~

~~Uncommon —————>1/1,000 and <1/100~~

~~Rare —————>1/10,000 and <1/1,000~~

Very rare —————<1/10,000

Based on clinical trial data, undesirable effects occurred in approximately 15% of patients receiving Fucidin[®] orally.

The most frequently reported undesirable effects to Fucidin[®] administered orally are gastrointestinal disorders ~~and symptoms of general disorders~~. Gastrointestinal system disorders are dose dependant. Various skin reactions, reversible jaundice, haematological disorders and generalised hypersensitivity reactions have been reported.

~~Based on clinical data in the indication skin and subcutaneous tissue infection, undesirable effects occurred in approximately 15% of patients receiving Fucidin[®] film-coated tablets. Nausea, dyspepsia, vomiting, diarrhoea, abdominal pain or discomfort were common. Gastrointestinal system disorders are dose dependent. General disorders such as lethargy, drowsiness, fatigue, anorexia and headache were uncommon. Rash, urticaria, pruritus and allergic reaction were all rare.~~

Post market data on Fucidin[®] administered systemically:

~~Raised bilirubin, raised liver enzymes such as alkaline phosphatase or transaminases and jaundice have been reported and are considered to be rare. These undesirable effects are usually reversible on discontinuation of the drug. Haematological undesirable effects mainly describing affection of the white cell line have been reported and is considered to~~

~~be very rare. These have especially been observed in cases of more than 15 days of treatment and are reversible upon drug withdrawal.~~

~~Based on post-marketing data on Fucidin[®] administered systemically, the total 'reporting rate' of undesirable effect is very rare being approximately 3:10,000 treatment courses.~~

~~The~~ Undesirable effects are listed by MedDRA SOC and the individual undesirable effects are listed starting with the most frequently reported.

Blood and lymphatic system disorders

Frequency not known:

Pancytopenia

Leukopenia*

Thrombocytopenia

Anaemia

* Haematological disorders affecting the white cell line (neutropenia, granulocytopenia, agranulocytosis) and more rarely disorders affecting the other two cell lines have been reported, either as isolated events or associated. This has been observed especially in case of treatment with duration of more than 15 days and is reversible upon drug withdrawal.

Immune system disorders

Rare ($\geq 1/10,000$ and $< 1/1,000$):

Allergic reaction

Frequency not known:

Anaphylactic reaction

Metabolism and nutrition disorders

Uncommon ($\geq 1/1,000$ and $< 1/100$):

Anorexia

Nervous system disorders

Common ($\geq 1/100$ and $< 1/10$):

Drowsiness/dizziness

Uncommon ($\geq 1/1,000$ and $< 1/100$):

Headache

Gastrointestinal disorders

Common ($\geq 1/100$ and $< 1/10$):

Diarrhoea

Vomiting

Abdominal pain

Dyspepsia

Nausea

Hepatobiliary disorders

Frequency not known:

Hyperbilirubinaemia

Jaundice

Hepatic enzymes increased

Hepatorenal syndrome

Cholestasis

Liver function abnormalities like hyperbilirubinaemia with or without jaundice and increase in hepatic enzymes such as alkaline phosphatase and transaminases should lead to withdrawal of treatment. Return of laboratory parameters to normal is usual and generally rapid.

Hepatorenal syndrome, cf. 'Renal disorders'.

Skin and subcutaneous tissue disorders

Uncommon ($\geq 1/1,000$ and $< 1/100$):

Rash*

Urticaria

Pruritus

*Rash includes various types of rash reactions such as erythematous, maculo-papular and pustular.

Musculoskeletal, connective tissue and bone disorders

Frequency not known:

Rhabdomyolysis (examples of signs and symptoms are: muscle weakness, swelling and pain, dark urine, myoglobinuria, elevated serum creatine kinase, acute renal failure, cardiac arrhythmia), see section 4.5.

Rhabdomyolysis may be fatal.

Renal and urinary disorders

Frequency not known:

Renal failure

Acute renal failure has been described in patients with jaundice, in particular in the presence of other factors predisposing for renal failure.

General disorders and application site conditions

Uncommon ($\geq 1/1,000$ and $< 1/100$):

Asthenia

Fatigue

Malaise

Drowsiness

Anorexia

○ ~~Skin and subcutaneous tissue disorders~~

~~Rash*~~

~~Pruritus~~

~~Urticaria~~

~~* Rash includes various types of rash reactions such as erythematous, maculo-papular and pustular.~~

○ ~~Hepatobiliary disorders~~

~~Hyperbilirubinaemia~~

~~Jaundice~~

~~Hepatic enzymes increased~~

~~Hepatorenal syndrome~~

~~Liver function abnormalities like hyperbilirubinaemia with or without jaundice and increase in hepatic enzymes such as alkaline phosphatase and transaminases should lead to withdrawal of treatment. Return of laboratory parameters to normal is usual and generally rapid.~~

~~Hepatorenal syndrome, cf. 'Renal and urinary disorders'.~~

○ ~~Blood and lymphatic system disorders~~

~~Leukopenia*~~

~~Thrombocytopenia~~

~~Pancytopenia~~

~~Anaemia~~

~~* Haematological disorders affecting the white cell line (neutropenia, granulocytopenia, agranulocytosis) and more rarely disorders affecting the other two cell lines have been reported, either as isolated events or associated. This has been observed especially in case of treatment with a duration of more than 15 days and is reversible upon drug withdrawal.~~

○ ~~Renal and urinary disorders~~

~~Renal failure~~

~~Acute renal failure has been described in patients with jaundice in particular in the presence of other factors predisposing for renal failure.~~

○ ~~Immune system disorders~~

~~Allergic reaction~~

~~Anaphylactic~~

~~Isolated cases have been reported within the immune system disorders.~~

○ ~~Musculoskeletal, connective tissue and bone disorders~~

~~Rhabdomyolysis (examples of signs and symptoms are: muscle weakness, swelling and pain, dark urine, myoglobinuria, elevated serum creatine kinase, acute renal failure, cardiac arrhythmia), see Interaction with other medicinal products and other forms of interaction.~~

4.9 Overdosage

Acute symptoms of overdose include gastrointestinal disturbances and possible effect on liver function. ~~Treatment should be restricted to symptomatic and supportive measures. Dialysis is of no benefit, since the drug is not significantly dialysed.~~ Management should be directed towards alleviation of symptoms. Dialysis will not increase the clearance of fusidic acid.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: General anti-infective for systemic use

ATC code: J01XC01

Fucidin® exerts powerful activity against a number of gram-positive organisms. Staphylococci including the strains resistant to penicillin and other antibiotics are particularly susceptible to Fucidin®. Concentrations of 0.03 - 0.12 mcg/ml inhibit nearly all strains of *Staphylococcus aureus*.

5.2 Pharmacokinetic properties

Fucidin® readily penetrates tissue. Bactericidal levels have been assayed in bone and necrotic tissue. Blood levels are cumulative, reaching concentrations of 50-100 mcg/ml after oral administration of 1.5 g daily for three to four days. Fucidin® is excreted mainly in the bile, little or none being excreted in the urine.

5.3 Preclinical safety data

Animal studies have indicated that Fucidin® is practically atoxic.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:

microcrystalline cellulose
lactose monohydrate
crospovidone
talc
magnesium stearate
colloidal anhydrous silica
all-rac-α-tocopherol

Filmcoating:

hypromellose
titanium dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

3 years

6.4 Special precautions for storage

The medicinal product does not require any special storage conditions ~~store in a cool place.~~

6.5 Nature and contents of container

Aluminium/aluminium blister packs and packs of 12 tablets, 36 tablets and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

Any unused product or waste material should be disposed of in accordance with local Requirements.