HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LYMEPAK safely and effectively. See full prescribing information for LYMEPAK.

LYMEPAK (doxycycline hyclate tablets), for oral use
Initial U.S. Approval: 1967

----------INDICATIONS AND USAGE----------
LYMEPAK is a tetracycline class drug indicated for the treatment of early Lyme disease (as evidenced by erythema migrans) due to *Borrelia burgdorferi* in adults and pediatric patients 8 years of age and older weighing 45 kg and above. (1)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LYMEPAK and other antibacterial drugs, LYMEPAK should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria (1).

----------DOSAGE AND ADMINISTRATION----------
Adults and Pediatric Patients 8 years of age and older weighing 45 kg and above: 100 mg every 12 hours, for 21 days (2.1).

----------DOSAGE FORMS AND STRENGTHS----------
Tablets containing 100 mg of doxycycline as doxycycline hyclate (3)

----------CONTRAINDICATIONS----------
LYMEPAK is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines. (4)

----------WARNINGS AND PRECAUTIONS----------
- The use of LYMEPAK during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown) and enamel hypoplasia. (5.1, 8.1, 8.4)
- The use of LYMEPAK during the second and third-trimester of pregnancy, infancy and childhood up to the age of 8 years may cause reversible inhibition of bone growth (5.2, 8.1, 8.4).
- *Clostridium difficile*-associated diarrhea: Evaluate patients if diarrhea occurs. (5.3)
- Photosensitivity manifested by an exaggerated sunburn reaction has been observed. Limit sun exposure. (5.4)
- Severe skin reactions have been reported. Discontinue use and institute appropriate therapy (5.5).
- Jarisch-Herxheimer reaction may occur in patients with Lyme disease after the initiation of treatment. Inform patients and monitor if a severe reaction occurs. Antipyretics may reduce the severity and the duration of the reaction (5.6).
- Intracranial hypertension has been reported. Avoid concomitant use with isotretinoin Evaluate and monitor visual function if symptoms occur (5.7)

----------ADVERSE REACTIONS----------
Adverse reactions observed in patients receiving tetracycline class drugs including LYMEPAK were: anorexia, nausea, vomiting, diarrhea, rash, photosensitivity, urticaria, and hemolytic anemia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Chartwell RX at 1-845-232-1683 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage (7.1)
- Avoid co-administration of LYMEPAK with penicillin (7.2)
- Absorption of tetracyclines is impaired by antacids containing aluminum, calcium, or magnesium, bismuth subsalicylate and iron-containing preparations (7.3)
- Concurrent use of tetracyclines, including LYMEPAK may render oral contraceptive less effective (7.4)
- Barbiturates, carbamazepine, and phenytoin decrease the half-life of doxycycline (7.6)

----------USE IN SPECIFIC POPULATIONS----------
Lactation: Breastfeeding is not recommended (8.2)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 6/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LYMEPAK is indicated for the treatment of early Lyme disease (as evidenced by erythema migrans) due to *Borrelia burgdorferi* in adults and pediatric patients 8 years of age and older weighing 45 kg and above.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LYMEPAK and other antibacterial drugs, LYMEPAK should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

Adults and Pediatric Patients 8 years of age and older weighing 45 kg and above

Administer LYMEPAK (100 mg) tablet every 12 hours for 21 days.

2.2 Important Administration Instructions

- The usual dosage and frequency of administration of LYMEPAK differs from that of the other tetracyclines. Exceeding the recommended dosage may result in an increased incidence of adverse reactions.
- Administration of adequate amounts of fluid along with the tablets is recommended to wash down the tablet to reduce the risk of esophageal irritation and ulceration *[see Adverse Reactions (6)]*.
- If gastric irritation occurs, LYMEPAK may be given with food or milk. The absorption of doxycycline is not markedly influenced by simultaneous ingestion of food or milk.

3 DOSAGE FORMS AND STRENGTHS

LYMEPAK tablets are green, round, film-coated tablets engraved with LP-1 on one side. Each tablet contains 100 mg of doxycycline (equivalent to 115 mg doxycycline hyclate).

4 CONTRAINDICATIONS

LYMEPAK is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.

5 WARNINGS AND PRECAUTIONS

5.1 Tooth Discoloration and Enamel Hypoplasia

The use of LYMEPAK during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term use of the drugs of the tetracycline class, but it has been observed following repeated short-term courses. Enamel hypoplasia has also been reported with drugs of the tetracycline class. Advise the patient of the potential risk to the fetus if LYMEPAK is used during the second or third trimester of pregnancy *[see Use in Specific Populations (8.1, 8.4)]*.

5.2 Inhibition of Bone Growth

The use of LYMEPAK during the second and third trimester of pregnancy, infancy and childhood up to the age of 8 years may cause reversible inhibition of bone growth. All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. Advise the patient of the potential risk to the fetus if LYMEPAK is used during the second or third trimester of pregnancy *[see Use in Specific Populations (8.1, 8.4)]*.

5.3 *Clostridium Difficile* Associated Diarrhea

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including LYMEPAK, and may range in severity from mild diarrhea 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 diarrhea following the use of antibacterial drugs. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing use of antibacterial drugs not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

5.4 Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with LYMEPAK, and treatment should be discontinued at the first evidence of skin erythema.

5.5 Severe Skin Reactions

Severe skin reactions, such as exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in patients receiving doxycycline *[see Adverse Reactions (6)]*. If severe skin reactions occur, discontinue LYMEPAK immediately and initiate appropriate therapy.

5.6 Jarisch-Herxheimer Reaction

The Jarisch-Herxheimer reaction is a self-limiting systemic reaction that has been reported after the initiation of doxycycline therapy in up to 30% of patients with early Lyme disease. The reaction begins one to two hours after initiation of therapy and disappears within 12 to 24 hours. It is characterized by fever, chills, myalgias, headache, exacerbation of cutaneous lesions, tachycardia, hyperventilation, vasodilation with flushing, and mild hypotension. The pathogenesis of the Jarisch-Herxheimer reaction is unknown, but thought to be due to the release of spirochetal heat-stable pyrogen. Advise the patient of this reaction before starting LYMEPAK. Administer fluids and antipyretics to alleviate symptoms and duration of the reaction if severe.

5.7 Intracranial Hypertension

Intracranial hypertension (IH, pseudotumor cerebri) has been associated with the use of tetracyclines including doxycycline. Clinical manifestations of IH include headache, blurred vision, diplopia, and vision loss; papilledema can be found on fundoscopy. Women of childbearing age who are overweight or have a history of IH are at greater risk for developing tetracycline associated IH. Concomitant use of isotretinoin and LYMEPAK should be avoided because isotretinoin is also known to cause pseudotumor cerebri.

Although IH may improve after discontinuation of treatment, the possibility for permanent visual loss exists. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Since intracranial pressure can remain elevated for weeks after drug cessation patients should be monitored until they stabilize.

5.8 Antianabolic Action

The antianabolic action of the tetracyclines, including LYMEPAK may cause an increase in BUN. Studies to date indicate that this does not occur with the use of doxycycline in patients with renal impairment.

5.9 Development of Drug Resistant Bacteria

Prescribing LYMEPAK in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria

5.10 Potential for Microbial Overgrowth

As with other antibacterial drugs, use of LYMEPAK may result in overgrowth of non-susceptible organisms, including fungi. If such infections occur, discontinue doxycycline and institute appropriate therapy.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Tooth Discoloration and Enamel Hypoplasia *[see Warnings and Precautions (5.1)]*
- Inhibition of Bone Growth *[see Warnings and Precautions (5.2)]*
- *Clostridium Difficile* Associated Diarrhea *[see Warnings and Precautions (5.3)]*
- Photosensitivity *[see Warnings and Precautions (5.4)]*
- Severe Skin Reactions *[see Warnings and Precautions (5.5)]*
- Jarisch-Herxheimer reaction *[see Warnings and Precautions (5.6)]*

- Intracranial Hypertension *[see Warnings and Precautions (5.7)]*

The following adverse reactions have been observed during clinical trials or post-approval use of tetracycline-class drugs, including LYMEPAK. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal: Anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, and inflammatory lesions (with monilial overgrowth) in the anogenital region, and pancreatitis. Hepatotoxicity has been reported. These reactions have been caused by both the oral and parenteral administration of tetracyclines. Superficial discoloration of the adult permanent dentition, reversible upon drug discontinuation and professional dental cleaning has been reported. Permanent tooth discoloration and enamel hypoplasia may occur with drugs of the tetracycline class when used during tooth development *[see Warnings and Precautions (5.1)]*. Esophagitis and esophageal ulcerations have been reported in patients receiving capsule and tablet forms of drugs in the tetracycline-class. Most of these patients took medications immediately before going to bed *[see Dosage and Administration (2.2)]*.

Skin: Toxic epidermal necrolysis, Stevens-Johnson syndrome, erytherma multiforme, maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Photosensitivity is discussed above *[see Warnings and Precautions (5.4)]*.

Renal: Rise in BUN has been reported and is apparently dose-related *[see Warnings and Precautions (5.8)]*.

Immune: Hypersensitivity reactions including urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, serum sickness, pericarditis, exacerbation of systemic lupus erythematosus and drug reaction with eosinophilia and systemic symptoms (DRESS). Jarisch-Herxheimer reaction has been reported in patients treated with doxycycline for early Lyme disease *[see Warnings and Precautions (5.6)]*.

Blood: Hemolytic anemia, thrombocytopenia, neutropenia, and eosinophilia have been reported.

Intracranial Hypertension: Intracranial hypertension (IH, pseudotumor cerebri) in adults and bulging fontanels in infants has been associated with the use of tetracycline *[see Warnings and Precautions (5.7)]*.

Thyroid Gland Changes: When given over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands. No abnormalities of thyroid function are known to occur.

7 DRUG INTERACTIONS

7.1 Anticoagulant Drugs

Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

7.2 Penicillin

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracyclines, including LYMEPAK in conjunction with penicillin.

7.3 Antacids and Iron Preparations

Absorption of tetracyclines is impaired by antacids containing aluminum, calcium, or magnesium, bismuth subsalicylate, and iron-containing preparations. Absorption of tetracyclines is impaired by bismuth subsalicylate.

7.4 Oral Contraceptives

Concurrent use of tetracycline, including LYMEPAK, may render oral contraceptives less effective.

7.5 Isotretinoin

There have been reports of intracranial hypertension associated with the concomitant use of isotretinoin and doxycycline. Avoid the concomitant use of isotretinoin and LYMEPAK because isotretinoin is also known to cause pseudotumor cerebri (benign intracranial hypertension *[see Warnings and Precautions (5.7)]*.

7.6 Barbiturates and Anti-Epileptics

Barbiturates, carbamazepine, and phenytoin decrease the half-life of doxycycline.

7.7 Drug/Laboratory Test Interactions

False elevations of urinary catecholamines may occur due to interference with the fluorescence test.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

LYMEPAK, like other tetracycline-class antibacterial drugs, may cause discoloration of deciduous teeth and reversible inhibition of bone growth when administered during the second and third trimester of pregnancy *[see Warnings and Precautions (5.1, 5.2), Data, Use in Specific Populations (8.4)]*. Available data from published studies over decades have not shown a difference in major birth defect risk compared to unexposed pregnancies with doxycycline

exposure in the first trimester of pregnancy *(see Data).* There are no available data on the risk of miscarriage following exposure to doxycycline in pregnancy.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

A retrospective cohort study of 1,690 pregnant patients who received doxycycline prescriptions in the first trimester of pregnancy compared to an unexposed pregnant cohort showed no difference in the major malformation rate. There is no information on the dose or duration of treatment, or if the patients actually ingested the doxycycline that was prescribed.

Other published studies on exposure to doxycycline in the first trimester of pregnancy have small sample sizes; however, these studies have not shown an increased risk of major malformations.

The use of tetracyclines during tooth development (second and third trimester of pregnancy) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term use of the drug but has been observed following repeated short-term courses.

Animal Data

Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryotoxicity also has been noted in animals treated early in pregnancy *[see Warnings and Precautions (5.1, 5.2)]*.

8.2 Lactation

Risk Summary

Based on available published data, doxycycline is present in human milk. There are no data that inform the levels of doxycycline in breastmilk, the effects on the breastfed infant, or the effects on milk production. Because there are other antibacterial drug options available to treat Lyme disease in lactating women and because of the potential for serious adverse reactions, including tooth discoloration and inhibition of bone growth, advise patients that breastfeeding is not recommended during treatment with LYMEPAK and for 5 days after the last dose.

8.4 Pediatric Use

The safety and efficacy of LYMEPAK has been established in pediatric patients 8 years of age and older, weighing 45 kg and greater.

Because of the effects of the tetracycline-class of drugs on tooth development and growth, use of LYMEPAK in pediatric patients younger than 8 years of age, weighing less than 45 kg is not recommended *[see Warnings and Precautions (5.1, 5.2)]*.

8.5 Geriatric Use

Clinical studies of LYMEPAK did not report specific treatment outcomes of patients aged 65 and over to determine whether they respond differently from younger subjects.

8.6 Hepatic Impairment

The use of tetracyclines has been associated with hepatotoxicity.

8.7 Renal Impairment

Studies have shown no significant difference in the serum half-life of doxycycline *[see Clinical Pharmacology (12.3)]*. No dosage adjustment is warranted in patients with renal impairment.

10 OVERDOSAGE

In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures. Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of overdosage.

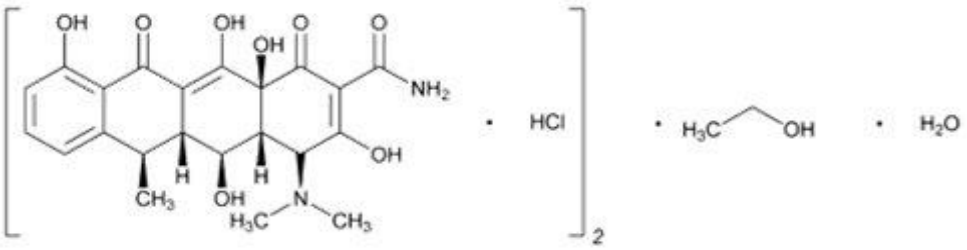
11 DESCRIPTION

LYMEPAK contains doxycycline hyclate, USP which is the hyclate salt form of doxycycline, a tetracycline class antibacterial drug derived from oxytetracycline.

The chemical name of doxycycline hyclate is 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2- naphthacenecarboxamide monohydrochloride, compound with ethyl alcohol (2:1), monohydrate. The molecular formula for doxycycline hyclate is $(C_{22}H_{24}N_2O_8 \cdot HCl)_2 \bullet C_2H_6O \bullet H_2O$ and the molecular weight is 1025.89. Doxycycline is a light-yellow crystalline powder. Doxycycline hyclate is soluble in water.

Doxycycline has a high degree of lipid solubility and a low affinity for calcium binding. It is highly stable in normal human serum. Doxycycline will not degrade into an epianhydro form. The chemical structure of doxycycline hyclate is shown in Figure 1.

Figure 1: Structure of Doxycycline Hyclate



LYMEPAK tablets, for oral administration, contain 100 mg of doxycycline (equivalent to 115 mg doxycycline hyclate). Inert ingredients in the tablet formulation are: anhydrous lactose, colloidal silicon dioxide, D&C yellow #10, FD&C blue #1, FD&C yellow #6, hypromellose, magnesium stearate, methylcellulose, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, stearic acid, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

LYMEPAK is an antibacterial drug *[see Microbiology (12.4)]*.

12.3 Pharmacokinetics

Tetracyclines are readily absorbed and are bound to plasma proteins in varying degrees. They are concentrated by the liver in the bile, and excreted in the urine and feces at high concentrations and in a biologically active form.

Absorption

Doxycycline is virtually completely absorbed after oral administration. Following a 200 mg dose, normal adult volunteers averaged peak serum levels of 2.6 mcg/mL of doxycycline at 2 hours, decreasing to 1.45 mcg/mL at 24 hours.

Elimination

Excretion of doxycycline by the kidney is about 40%/72 hours in individuals with normal function (creatinine clearance about 75 mL/min.). This percentage excretion may fall as low as 1–5%/72 hours in individuals with severe renal insufficiency (creatinine clearance below 10 mL/min.).

Specific Populations

Studies have shown no significant difference in serum half-life of doxycycline (range 18–22 hours) in individuals with normal and severely impaired renal function. Hemodialysis does not alter serum half-life.

12.4 Microbiology

Mechanism of Action

Doxycycline inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit. Doxycycline has bacteriostatic activity against a broad range of gram-positive and gram-negative bacteria.

Resistance

Cross resistance with other tetracyclines is common.

Antimicrobial Activity

Culture and susceptibility testing are not routinely performed to establish the diagnosis of early Lyme disease; standard methods for susceptibility testing of *Borrelia burgdorferi* have not been established. The in vitro susceptibility of *Borrelia burgdorferi* to doxycycline has been reported in the literature; however, the clinical significance of these findings is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential of doxycycline have not been conducted. However, there has been evidence of oncogenic activity in rats in studies with the related antibacterial drugs, oxytetracycline (adrenal and pituitary tumors), and minocycline (thyroid tumors).

Likewise, although mutagenicity studies of doxycycline have not been conducted, positive results using in vitro mammalian cell assays have been reported for related antibacterial drugs (tetracycline, oxytetracycline).

Doxycycline administered orally at dosage levels as high as 250 mg/kg/day had no apparent effect on the fertility of female rats. Effect on male fertility has not been studied.

13.2 Animal Toxicology and/or Pharmacology

Hyperpigmentation of the thyroid has been produced by members of the tetracycline class in the following species: in rats by oxytetracycline, doxycycline, tetracycline PO_4, and methacycline; in minipigs by doxycycline, minocycline, tetracycline PO_4, and methacycline; in dogs by doxycycline and minocycline; in monkeys by minocycline.

Minocycline, tetracycline PO_4, methacycline, doxycycline, tetracycline base, oxytetracycline HCl, and tetracycline HCl were goitrogenic in rats fed a low iodine diet. This goitrogenic effect was accompanied by high radioactive iodine uptake. Administration of minocycline also produced a large goiter with high radioiodine uptake in rats fed a relatively high iodine diet.

Treatment of various animal species with this class of drugs has also resulted in the induction of thyroid hyperplasia in the following: in rats and dogs (minocycline); in chickens (chlortetracycline); and in rats and mice (oxytetracycline). Adrenal gland hyperplasia has been observed in goats and rats treated with oxytetracycline.

14 CLINICAL STUDIES

14.1 Clinical Trial Experience

Doxycycline has been used in clinical practice for early stages of Lyme disease for several decades. Thorough search of the published literature identified 31 studies in which doxycycline treatment was used for the treatment of Lyme disease. Of these 31, three randomized studies evaluating doxycycline treatment in patients with erythema migrans and associated symptoms were identified[1-3]. In addition, two natural history studies of Lyme disease evaluated disease progression in patients presenting with erythema migrans and associated symptoms[4,5]. Over 200 patients from Lyme-disease hyperendemic areas were enrolled in these five studies, and more than 100 received doxycycline. Evidence of efficacy was derived by comparing the doxycycline treatment in studies using doxycycline 100 mg twice daily for 20-21 days with no treatment in the natural history studies. Clinical resolution of symptoms was defined as absence of objective late manifestations of Lyme disease, specifically those related to the musculoskeletal, nervous, and cardiac systems at 6 months. In comparison to untreated patients, doxycycline-treated

patients had a higher response rate at 6 months. Doxycycline-treated patients had a response rate of 75-95% compared to 56-66% in untreated patients.

15 REFERENCES

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4. Steere AC, Hardin JA, Ruddy S, Mummaw JG, Malawista SE. Lyme arthritis: correlation of serum and cryoglobulin IgM with activity, and serum IgG with remission. Arthritis Rheum 1979b; 22(5):471-483.
5. Steere AC, Malawista SE, Newman JH, Spieler PN, Bartenhagen NH. Antibiotic therapy in Lyme disease. Ann Intern Med 1980; 93(1):1-8.

16 HOW SUPPLIED/STORAGE AND HANDLING

LYMEPAK tablets contain 100 mg of doxycycline (equivalent to 115 mg doxycycline hyclate). The tablets are green, round, film-coated tablets engraved with LP-1 on one side.

• NDC # 62135-596-01: is supplied as a child-resistant blister card containing 14 tablets

• NDC # 62135-596-87: carton containing 3 blister cards

Store at 20°C to 25°C (68°F to 77°F) excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature]. Protect from light and moisture.

17 PATIENT COUNSELING INFORMATION

Important Administration and Safety Information for Patients and Caregivers

Advise all patients taking LYMEPAK:

- to avoid excessive sunlight or artificial ultraviolet light while receiving LYMEPAK and to discontinue therapy if phototoxicity (e.g., skin eruption, etc.) occurs. Sunscreen or sunblock should be considered *[see Warnings and Precautions (5.4)]*.
- to drink fluids liberally along with LYMEPAK to reduce the risk of esophageal irritation and ulceration *[see Adverse Reactions (6)]*.
- that the absorption of tetracyclines is reduced when taken with foods, especially those which contain calcium. However, the absorption of LYMEPAK is not markedly

influenced by simultaneous ingestion of food or milk *[see Dosage and Administration (2.2)]*.

- that the absorption of tetracyclines is reduced when taken with antacids containing aluminum, calcium or magnesium, bismuth subsalicylate, and iron-containing preparations *[see Drug Interactions (7.3)]*.
- that the use of LYMEPAK might increase the incidence of vaginal candidiasis *[see Warnings and Precautions (5.10)]*.
- that LYMEPAK can make birth control pills less effective *[see Drug Interactions (7.3)]*.

Tooth Discoloration and Inhibition of Bone Growth

Advise patients that LYMEPAK, like other tetracycline-class drugs, may cause permanent tooth discoloration of deciduous teeth and reversible inhibition of bone growth when administered during the second and third trimesters of pregnancy. Tell your healthcare provider right away if you become pregnant during treatment *[see Warnings and Precautions (5.1,5.2) and Use in Specific Populations (8.1, 8.4)]*.

Lactation

Advise women not to breastfeed during treatment with LYMEPAK and for 5 days after the last dose *[see Use in Specific Populations (8.2)]*.

Jarisch-Herxheimer Reaction

Inform patients that a systemic reaction known as the Jarisch–Herxheimer reaction (JHR) may occur within 24 hours of starting LYMEPAK. Symptoms include shaking chills, fever, and intensification of skin rash and usually resolve within several hours. Advise patients to contact their health care provider if symptoms occur *[see Warnings and Precautions 5.6]*.

Development of Resistance

Patients should be counseled that antibacterial drugs, including LYMEPAK should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When LYMEPAK is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by LYMEPAK or other antibacterial drugs in the future *[see Warnings and Precautions 5.9]*.

Diarrhea

Diarrhea is a common problem caused by antibacterial drugs, including LYMEPAK, which usually ends when the antibacterials are discontinued. Sometimes after starting treatment with antibacterial drugs, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterial drug. If this occurs, advise patients to contact their physician as soon as possible *[see Warnings and Precautions 5.3]*.

Manufactured By:

Chartwell Pharmaceuticals, LLC.

Congers, NY 10920 USA

Manufactured For:

Chartwell RX, LLC.

Congers, NY 10920 USA

Made in USA