ADVERSE REACTIONS

6 WARNINGS AND PRECAUTIONS

• The use of Ximino during tooth development (last half of pregnancy, infancy, and childhood up to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). Enamel hypoplasia has also been reported. Tetracycline antibiotics, including minocycline, should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Patients of childbearing age should be warned of the potential risk of permanent discoloration of the teeth and of enamel hypoplasia. Children and adolescents should be warned of the potential risk of permanent discoloration of developing teeth and of marrow hypoplasia. Children and adolescents need careful monitoring during treatment with Ximino.

7 CLINICAL PHARMACOLOGY

7.1 Anticoagulants

• Increased prothrombin time and bleeding time have been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline antibiotics, including minocycline, should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Patients of childbearing age should be warned of the potential risk of permanent discoloration of the teeth and of enamel hypoplasia. Children and adolescents should be warned of the potential risk of permanent discoloration of developing teeth and of marrow hypoplasia. Children and adolescents need careful monitoring during treatment with Ximino.

7.2 Postmarketing Experience

• Since minocycline has been associated with autoimmune syndromes; discontinue Ximino immediately if symptoms occur. 

7.3 Methoxyflurane

• Methoxyflurane is a fluorinated hydrocarbon anesthetic. Use of Ximino with methoxyflurane may result in severe adverse reactions, including deaths. Methoxyflurane should not be used in patients taking Ximino.

7.4 Low Dose Oral Contraceptives

• Use of Ximino in women using oral contraceptives may result in breakthrough bleeding. Oral contraceptives may be used together with Ximino, if a backup contraceptive method is used.

7.5 Drug/Laboratory Test Interactions

• Increased prothrombin time and bleeding time have been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline antibiotics, including minocycline, should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Patients of childbearing age should be warned of the potential risk of permanent discoloration of the teeth and of enamel hypoplasia. Children and adolescents should be warned of the potential risk of permanent discoloration of developing teeth and of marrow hypoplasia. Children and adolescents need careful monitoring during treatment with Ximino.

8 USE IN SPECIFIC POPULATIONS

• Use of Ximino in children under 12 years of age is not recommended. Use of Ximino in children from birth to 8 years of age has not been studied. Use of Ximino in children 9 to 16 years of age is not recommended. Use of Ximino in children from 9 to 16 years of age has not been studied.

9 HEPATOBILIARY ABNORMALITIES

• Ximino can be taken with or without food.

10 CLINICAL SAFETY INFORMATION

• Patients should be warned of the possibility of developing a photosensitive reaction when using Ximino. Patients should be advised to avoid sun exposure and to use sunscreen and protective clothing when they are taking Ximino.

11 ADVERSE REACTIONS

• When using Ximino, observe for photosensitivity reactions (e.g., pruritus, rash, edema, photosensitivity). Exposure to the sun should be avoided. Sunscreens and protective clothing should be used to prevent photosensitivity reactions during treatment with Ximino.

12 CLINICAL PHARMACOLOGY

• Minocycline has been associated with autoimmune syndromes; discontinue Ximino immediately if symptoms occur. 

13 IMMUNOLOGICAL TOXICOLOGY

• Immunological reactions, including hypereosinophilic syndrome, have been reported in patients treated with Ximino.

16.1 How Supplied

• Ximino is supplied as enteric-coated, delayed-release capsules containing 50 mg, 75 mg, 100 mg, and 150 mg of minocycline hydrochloride. 

16.2 Storage and Handling

• Store at controlled room temperature 20°C to 25°C (68°F to 77°F). 

17 PATIENT PACKAGE INSERT

• Patients should be warned of the possibility of developing a photosensitive reaction when using Ximino. Patients should be advised to avoid sun exposure and to use sunscreen and protective clothing when they are taking Ximino.

18 mMandATORY PATIENT INFORMATION

• Minocycline has been associated with autoimmune syndromes; discontinue Ximino immediately if symptoms occur. 

19 HOW SUPPLIED

• Ximino is supplied as enteric-coated, delayed-release capsules containing 50 mg, 75 mg, 100 mg, and 150 mg of minocycline hydrochloride.
Serious liver problems. Ximino should not be used by individuals of either gender who are attempting to conceive a child. Exposed male or female reproductive organs were examined in male rabbits, male mice, and female rats treated with minocycline HCl under conditions of toxicological studies that did not result in the overt appearance of adverse effects. Male rabbits were given minocycline HCl dosages of up to 400 mg/kg/day for 4 weeks, male mice were given dosages of up to 200 mg/kg/day for 4 weeks, and female rats were given dosages of up to 100 mg/kg/day for 2 weeks. No evidence of reproductive damage was observed in these studies.

Minocycline caused impaired fertility in rats in a dose-dependent manner (tested in male and female rats) and in male rabbits (tested in male rabbits; there was no evidence of impairment of fertility in female rabbits). The combined incidence of adenomas and carcinomas in females. In a carcinogenicity study in which minocycline hydrochloride was administered orally to male and female rats at dosages up to 200 mg/kg/day (which resulted in up to approximately 40 times the level of systemic exposure to minocycline observed in patients as a result of use of Ximino) adversely affected spermatogenesis.

Minocycline hydrochloride is a semi-synthetic tetracycline antibiotic derived from the naturally occurring tetracycline derivative, oxytetracycline. Minocycline hydrochloride is chemically designated as 10-(4-methyl-1-piperazinyl)undecyl-7-[(2R)-2-8-hydroxy-8-quinolinyl]-1,4,5,6,7,8-hexahydro-1,2-diazepine hydrochloride.

The structural formula is represented below:

In common with other tetracyclines, minocycline is a broad-spectrum antibiotic, acting on Gram-positive and Gram-negative organisms and on some mycobacteria, Rickettsia, and Chlamydia. It is effective against most strains of Gram-positive bacteria and is highly effective against many strains of Gram-negative organisms. Differences in activity against bacteria of the same genus and species are minor, but variations in activity against different strains in a single species are considerable. Minocycline is active against the following narrow-spectrum tetracyclines: staphylococci, Neisseria, meningitidis, gonococci, meningococci, and H. influenzae. Its activity against Escherichia coli, Proteus, and Pseudomonas aeruginosa is similar to that of the narrow-spectrum tetracyclines.

Minocycline is used to treat a variety of infections caused by susceptible organisms, including acne, acneiform dermatitis, and certain soft-tissue infections. It is also used to treat certain syphilis infections and pelvic inflammatory disease. Minocycline is available in the form of extended-release capsules. Minocycline is also available as an injectable form.

Minocycline is mainly excreted unchanged in the urine. It is metabolized in the liver to a limited extent to a minor degree. Tetracycline-class antibiotics are excreted in human milk. Because of the potential for serious adverse effects (including arthralgia, osteoporosis, and possible osteoporotic fractures) to the infant, Ximino is not recommended for use during breastfeeding. Minocycline is not recommended for use during pregnancy in postmarketing experience. Only limited information is available regarding these reports; however, tetracycline was generally given for a very short period of time in these reports in postmarketing experience. Ximino is not recommended for use during pregnancy in postmarketing experience. Only limited information is available regarding these reports; however, tetracycline was generally given for a very short period of time in these reports in postmarketing experience.

Minocycline is structurally related to the tetracycline antibiotics and has been used extensively in the treatment of acne vulgaris. Minocycline is also administered by injection for the treatment of certain syphilis infections and pelvic inflammatory disease. Minocycline is not recommended for use during breastfeeding because of the potential for serious adverse effects (including arthralgia, osteoporosis, and possible osteoporotic fractures) to the infant. Minocycline is not recommended for use during pregnancy in postmarketing experience. Only limited information is available regarding these reports; however, tetracycline was generally given for a very short period of time in these reports in postmarketing experience.

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