

XIMINO™
(minocycline hydrochloride)
extended-release capsules



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use XIMINO safely and effectively. See full prescribing information for XIMINO.

XIMINO™ (minocycline hydrochloride) extended-release capsules, for oral use
Initial U.S. Approval: 1971

INDICATIONS AND USAGE

Ximino is a tetracycline-class drug indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older. (1)

Limitations of Use

Ximino did not demonstrate any effect on non-inflammatory acne lesions. Safety of Ximino has not been established beyond 12 weeks of use. This formulation of minocycline has not been evaluated in the treatment of infections. (14)

DOSAGE AND ADMINISTRATION

The recommended dosage of Ximino is approximately 1 mg/kg once daily for 12 weeks. (2)

DOSAGE FORMS AND STRENGTHS

Extended-Release Capsules: 45 mg, 90 mg, and 135 mg (3)

CONTRAINDICATIONS

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

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). (5.1)
- If pseudomembranous colitis occurs, discontinue Ximino. (5.2)
- If liver injury is suspected, discontinue Ximino. (5.3)
- If renal impairment exists, Ximino doses may need to be adjusted to avoid excessive systemic accumulations of the drug and possible liver toxicity. (5.4)

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- Minocycline may cause central nervous system side effects including light-headedness, dizziness, or vertigo. Advise patients. (5.5)
- Minocycline may cause pseudotumor cerebri (benign intracranial hypertension) in adults and adolescents. Discontinue Ximino if symptoms occur. (5.6)
- Minocycline has been associated with autoimmune syndromes; discontinue Ximino immediately if symptoms occur. (5.7)
- Minocycline has been associated with anaphylaxis, serious skin reactions, erythema multiforme, and DRESS syndrome. Discontinue Ximino immediately if symptoms occur. (5.9)

ADVERSE REACTIONS

The most commonly observed adverse reactions (incidence ≥ 5%) are headache, fatigue, dizziness, and pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sun Pharmaceutical Industries, Inc. at 1-800-406-7984 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)
- The concurrent use of tetracycline and methoxyflurane has been reported to result in fatal renal toxicity. (7.3)
- To avoid contraceptive failure, female patients are advised to use a second form of contraceptive during treatment with minocycline. (7.5)

USE IN SPECIFIC POPULATIONS

- Minocycline like other tetracycline-class drugs can cause fetal harm when administered to a pregnant woman. (5.1, 8.1)

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5.6 Benign Intracranial Hypertension

Pseudotumor cerebri (benign intracranial hypertension) in adults and adolescents has been associated with the use of tetracyclines. Minocycline has been reported to cause or precipitate pseudotumor cerebri, the hallmark of which is papilledema. Clinical manifestations include headache and blurred vision. Bulging fontanels have been associated with the use of tetracyclines in infants. Although signs and symptoms of pseudotumor cerebri resolve after discontinuation of treatment, the possibility for permanent sequelae such as visual loss that may be severe exists. Patients should be questioned for visual disturbances prior to initiation of treatment with tetracyclines. If visual disturbance occurs during treatment, patients should be checked for papilledema. Concomitant use of isotretinoin and minocycline should be avoided because isotretinoin, a systemic retinoid, is also known to cause pseudotumor cerebri.

5.7 Autoimmune Syndromes

Tetracyclines have been associated with the development of autoimmune syndromes. The long-term use of minocycline in the treatment of acne has been associated with drug-induced lupus-like syndrome, autoimmune hepatitis and vasculitis. Sporadic cases of serum sickness have presented shortly after minocycline use. Symptoms may be manifested by fever, rash, arthralgia, and malaise. In symptomatic patients, liver function tests, ANA, CBC, and other appropriate tests should be performed to evaluate the patients. Use of all tetracycline-class drugs should be discontinued immediately.

5.8 Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines, including minocycline. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using minocycline. If patients need to be outdoors while using minocycline, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician.

5.9 Serious Skin/Hypersensitivity Reaction

Cases of anaphylaxis, serious skin reactions (e.g. Stevens Johnson syndrome), erythema multiforme, and drug rash with eosinophilia and systemic symptoms (DRESS) syndrome have been reported postmarketing with minocycline use in patients with acne. DRESS syndrome consists of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following visceral complications such as: hepatitis, pneumonitis, nephritis, myocarditis, and pericarditis. Fever and lymphadenopathy may be present. In some cases, death has been reported. If this syndrome is recognized, the drug should be discontinued immediately.

5.10 Tissue Hyperpigmentation

Tetracycline-class antibiotics are known to cause hyperpigmentation. Tetracycline therapy may induce hyperpigmentation in many organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves. Skin and oral pigmentation has been reported to occur independently of time or amount of drug administration, whereas other tissue pigmentation has been reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as over sites of scars or injury.

5.11 Development of Drug-Resistant Bacteria

Bacterial resistance to the tetracyclines may develop in patients using Ximino, therefore, the susceptibility of bacteria associated with infection should be considered in selecting antimicrobial therapy. Because of the potential for drug-resistant bacteria to develop during the use of Ximino, it should be used only as indicated.

5.12 Superinfection

As with other antibiotic preparations, use of Ximino may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, Ximino should be discontinued and appropriate therapy instituted.

5.13 Laboratory Monitoring

Periodic laboratory evaluations of organ systems, including hematopoietic, renal and hepatic studies should be performed. Appropriate tests for autoimmune syndromes should be performed as indicated.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The following table summarizes selected adverse reactions reported in clinical trials at a rate of ≥ 1% for minocycline hydrochloride.

Table 2: Selected Treatment-Emergent Adverse Reactions in at least 1% of Clinical Trial Subjects

Adverse Reactions	Minocycline hydrochloride (1 mg/kg) N = 674 (%)	PLACEBO N = 364 (%)
At least one treatment-emergent event	379 (56)	197 (54)
Headache	152 (23)	83 (23)
Fatigue	62 (9)	24 (7)
Dizziness	59 (9)	17 (5)
Pruritus	31 (5)	16 (4)
Malaise	26 (4)	9 (3)
Mood alteration	17 (3)	9 (3)
Somnolence	13 (2)	3 (1)
Urticaria	10 (2)	1 (0)
Tinnitus	10 (2)	5 (1)
Arthralgia	9 (1)	2 (0)
Vertigo	8 (1)	3 (1)
Dry mouth	7 (1)	5 (1)
Myalgia	7 (1)	4 (1)

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of minocycline hydrochloride. 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.

Adverse reactions that have been reported with minocycline hydrochloride use in a variety of indications include: *Skin and hypersensitivity reactions:* fixed drug eruptions, balanitis, erythema multiforme, Stevens-Johnson syndrome, anaphylactoid purpura, photosensitivity, pigmentation of skin and mucous membranes, hypersensitivity reactions, angioneurotic edema, anaphylaxis, DRESS syndrome [see Warnings and Precautions (5.9)].

Autoimmune conditions: polyarthralgia, pericarditis, exacerbation of systemic lupus, pulmonary infiltrates with eosinophilia, transient lupus-like syndrome.

Central nervous system: pseudotumor cerebri, bulging fontanels in infants, decreased hearing.

Endocrine: brown-black microscopic thyroid discoloration, abnormal thyroid function.

Oncology: thyroid cancer.

Oral: glossitis, dysphagia, tooth discoloration.

FDA-Approved Patient Labeling

PATIENT INFORMATION

XIMINO (Zī-min-ō)

(minocycline hydrochloride)

Extended-Release Capsules

Read this Patient Information leaflet that comes with Ximino before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

What is Ximino?

Ximino is a tetracycline-class drug. Ximino is prescription medicine used to treat pimples and red bumps (non-nodular inflammatory lesions) that happen with moderate to severe acne vulgaris in people 12 years and older. Ximino is not effective for acne that is not red-looking (this means acne that is not inflammatory).

It is not known if Ximino is:

- safe for use longer than 12 weeks.
- safe and effective for the treatment of infections.
- safe and effective in children under the age of 12 years.

Who should not take Ximino?

Do not take Ximino if you are allergic to tetracycline class medicines. Ask your doctor or pharmacist for a list of these medicines if you are not sure.

What should I tell my doctor before taking Ximino?

Before you take Ximino, tell your doctor if you:

- have kidney problems. Your doctor may prescribe a lower dose of medicine for you
- have liver problems
- have diarrhea or watery stools
- have vision problems

- plan to have surgery with general anesthesia
- have any other medical conditions

- are a male, and you and your female partner are trying to conceive a baby. You should not take Ximino.

- are pregnant or plan to become pregnant. Ximino may harm your unborn baby. Taking Ximino while you are pregnant may cause serious side effects on the growth of bone and teeth of your baby. Talk to your doctor before taking Ximino if you plan to become pregnant, or if you are already taking Ximino and plan to become pregnant. Stop taking Ximino and call your doctor right away if you become pregnant while taking Ximino.

- are breastfeeding or plan to breastfeed. Ximino passes into your milk and may harm your baby. You and your doctor should decide if you will take Ximino or breastfeed. You should not do both.

Tell your doctor about all the other medicines you take including prescription and nonprescription medicines, vitamins and herbal supplements. Ximino may affect the way other medicines work, and other medicines may affect how Ximino works.

Especially tell your doctor if you take:

- birth control pills.** Ximino may make your birth control pills less effective. You could become pregnant. You should use a second form of birth control while taking Ximino.

- a blood thinner medicine.**

- a penicillin antibiotic medicine.** Ximino and penicillins should not be used together.

- antacids that contain aluminum, calcium, or magnesium or iron-containing products.**

- an acne medication that contains isotretinoin.** Ximino and isotretinoin should not be used together.

Ask your doctor or pharmacist if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take Ximino?

- Take Ximino exactly as your doctor tells you.

- Skipping doses or not taking all doses of Ximino may:

- make the treatment not work as well.
- increase the chance that the bacteria will become resistant to Ximino.

- Ximino can be taken with or without food.** Taking Ximino with food may lower your chances of getting irritation or ulcers in your esophagus. Your esophagus is the tube that connects your mouth to your stomach.

- Swallow Ximino whole. Do not chew, crush, or split the capsules.**

If you take too much Ximino, call your doctor or poison control center right away. Your doctor may do blood tests to check you for side effects during treatment with Ximino.

What should I avoid while taking Ximino?

- Avoid sunlight, sunlamps, and tanning beds. Ximino can make your skin sensitive to the sun and the light from sunlamps and tanning beds. You could get severe sunburn.

- Wear loose-fitting clothes that protect your skin from sun exposure. Talk to your doctor about other ways to protect your skin while out in sunlight.

- You should not drive or operate dangerous machinery until you know how Ximino affects you. Ximino may cause you to feel dizzy or lightheaded, or have a spinning feeling (vertigo).

What are possible side effects of Ximino?

Ximino may cause serious side effects, including:

- Harm to an unborn baby.** See “What should I tell my doctor before taking Ximino?”

- Permanent teeth discoloration.** Ximino may permanently turn a baby or child’s teeth yellow-gray-brown during tooth development. Ximino should not be used during tooth development. Tooth development happens in the last half of pregnancy, and from birth to 8 years of age. See “What should I tell my doctor before taking Ximino?”

- Intestine infection** (pseudomembranous colitis). Pseudomembranous colitis can happen with most antibiotics, including Ximino. Call your doctor right away if you get watery diarrhea, diarrhea that does not go away, or bloody stools. You may have stomach cramps and a fever.

