

PSORIZIDE® ULTRA

CAUTION: Federal law prohibits dispensing without a prescription.

DESCRIPTION: PSORIZIDE® ULTRA is a biochemical homeopathic medication indicated for the treatment of eczema and seborrhea.²⁴⁻²⁶ The active ingredients in each PSORIZIDE® ULTRA tablet consist of the following: Potassium Bromide (Kali Bromatum) 1X, Nickel Sulphate (Niccolum Sulphuricum) 1X and Zinc Bromide (Zincum Bromatum) 4x. These drug ingredients are listed in the Homeopathic Pharmacopoeia of the United States (HPUS).¹

Inactive ingredients: Lactose and Magnesium Stearate.

Pharmacological class: Homeopathic drug.

Dosage form: Oral 300 mg scored tablet. May be swallowed whole, chewed or dissolved in the mouth and swallowed.

CLINICAL PHARMACOLOGY: The active ingredients in PSORIZIDE® ULTRA are inorganic soluble mineral salts. The exact mechanism of action is unknown; however, it is believed PSORIZIDE® ULTRA addresses a primary genetic biochemical defect.

POTASSIUM BROMIDE dissolves and dissociates in the digestive tract into its ionic constituents. Each tablet contains approximately 15 mg bromide (calculated). Ionic bromide is rapidly and completely absorbed from the intestine and distributed almost exclusively in the extracellular fluids.^{7,8} Bromide is eliminated by the kidneys and the elimination half-life is 11-12 days. "Once a day" dosing will lead to a steady state concentration in about seven weeks.⁷

NICKEL SULPHATE dissolves and dissociates in the digestive tract into its ionic constituents. Each tablet contains approximately 1.5 mg of ionic nickel (calculated). According to studies, 15% to 50% of ionic nickel is absorbed on a fasted stomach.² Food markedly decreases the rate and extent of nickel absorption.^{3,4} Clinical studies show that serum concentrations of nickel are variable among patients after administering the same dosage.⁵ Peak serum nickel concentration is reached about two hours after oral administration. "Once a day" dosing leads to steady state serum concentrations in approximately one week. Nickel is in its highly stable divalent cation state and is therefore not expected to be metabolized to any significant degree in the body. Absorbed nickel is primarily excreted in the urine and elimination half-life is about 21 hours.^{3,5} Renal clearance is rapid and efficient, and nickel does not accumulate in the body.⁶

CLINICAL STUDIES: A variety of controlled clinical studies have been performed using various sources of both nickel and bromide in over 300 subjects. Clinical efficacy and safety have been documented in a significant number of subjects. Published and unpublished reports are available upon request.^{9,22,23}

INDICATIONS: PSORIZIDE® ULTRA is indicated for the treatment of moderate to severe eczema, atopic dermatitis, seborrhea and seborrheic dermatitis. It has been found to work well with a variety of combination therapies. Psoriasis also responds, but generally has a more favorable response to PSORIZIDE® Forte (NDC 61480-255-05.)

CONTRAINDICATIONS: Although there are no known contraindications, patients who are allergic to any PSORIZIDE® ULTRA ingredient should consult a physician prior to taking the medication. (Refer to Section on Hypersensitivity)

WARNING: Do not use if imprinted seal under bottle cap is missing or broken. Do not use if pregnant or nursing. If allergic to nickel or metal objects such as jewelry or if there is a history of blistering hand eczema, see PRECAUTIONS for hypersensitivity information. Lactose intolerant patients may have gastrointestinal difficulty. This has very rarely been reported at the doses used.

PRECAUTIONS: Carefully adjust dosage to weight when treating young children. Do not use in cases of kidney disease. If skin rash appears or if nervous symptoms persist, recur frequently, or are unusual, discontinue use.

Hypersensitivity: Caution should be used when administering to patients with a history of contact sensitivity to nickel (common metal exposure) or if there is a history of vesicular hand eczema (dyshidrosis, pompholyx). Nickel allergy may be confirmed by a positive nickel patch test. Most patients with hand eczema, positive nickel allergy history, or a positive nickel patch test do not have any untoward reaction to administration of PSORIZIDE® ULTRA. If there is a history of nickel sensitivity or dyshidrotic hand eczema, begin with a very low dose and slowly increase to a recommended starting dose over a period of 5 weeks as tolerated, thus allowing progressive GI absorption*.

*Nickel desensitization schedule:

Week	Amount of Time to Take Medication Prior to Breakfast
Week 1	With Breakfast
Week 2	15 min
Week 3	30 min
Week 4	45 min
Week 5 and thereon	1 hour

If new pruritic rashes occur or persist, discontinue PSORIZIDE® ULTRA and treat appropriately. **Do not use if there is a history of extra-cutaneous hypersensitivity to nickel or bromide.**

Information for patients: Patients using PSORIZIDE® ULTRA should receive the following information and instructions:

1. This medication is to be used as directed by a physician.
2. It is important to take orally at the beginning of the day on an empty stomach (or any convenient time after having taken nothing but water for at least 7 hours) and to eat or drink nothing but water for at least one hour afterwards to avoid interference with absorption.

Drug interactions: There are no known drug interactions.

Carcinogenesis, mutagenesis, impairment of fertility: No studies have been done on the carcinogenesis, mutagenesis, or impairment of fertility of PSORIZIDE® ULTRA. No carcinogenesis or mutagenesis has been reported in multiple animal studies for oral administration of soluble nickel and bromide salts (active ingredients) even at very high doses.¹⁰⁻¹⁶

Effects of soluble potassium bromide: KBr is not listed as a carcinogen by the NTP, IARC, and OSHA.¹⁸

Effects of soluble nickel sulphate: Studies on experimental animals have never indicated that nickel, at any dose, is a carcinogen when introduced to the body orally. Furthermore, Nickel sulphate and other highly water soluble nickel salts, have never been known to induce carcinogenesis via any route of introduction including: oral, inhalation, cutaneous, IM, or IP.^{10-12,17} No adverse effects were noted on fertility or reproduction in a 3-generational study of albino Wistar rats fed up to 1000 ppm Ni per day, which is equivalent to 50 mg/kg body weight per day Ni.¹⁷

Pregnancy: Pregnancy category C. Animal reproduction studies have not been conducted with PSORIZIDE® ULTRA. PSORIZIDE® ULTRA should not be given to a pregnant woman.

Nursing mothers: It is not known whether this drug is excreted in human milk. However, since many drugs are excreted in human milk, caution should be exercised when PSORIZIDE® ULTRA is administered to a nursing woman.

Pediatric use: Carefully adjust dosage to weight when treating young children.

ADVERSE REACTIONS: PSORIZIDE® ULTRA contains low doses of active ingredients. Therefore there are minimal known side effects. (see PRECAUTIONS for hypersensitivity information)

OVERDOSAGE: Potassium bromide toxicity: Indications of toxicity due to oral overdosage of bromide may include nausea, vomiting, apathy, disturbed coordination, loss of memory, drowsiness, loss of emotional control, agitation, hallucination, tremors, depressed reflexes, stupor, and coma. Acute toxic reactions in humans have been reported at doses as low as 1000 mg.²¹ This level is 67 times the dose received in one tablet of PSORIZIDE® ULTRA.

Nickel sulphate toxicity: The oral rat LD₅₀ for nickel sulphate hexahydrate is 275 mg/kg.¹⁹ Symptoms of toxicity due to oral overdosage of nickel sulphate may include nausea, vomiting, abdominal discomfort, diarrhea, giddiness, lassitude, headaches, cough, and shortness of breath.²⁰ The lowest observed transitory toxic effects from human ingestion of soluble nickel salts is approximately 8 mg nickel/kg body weight.²⁰ This is 80 times the maximum dose recommended for PSORIZIDE® ULTRA. (See below).

DOSAGE AND ADMINISTRATION: Absorption of nickel sulphate is variable among individuals. For maximum absorption, tablets should be taken orally at the beginning of the day (or any convenient time after having taken nothing but water for at least 7 hours). Take nothing but water for one hour after taking medication to aid absorption.

Weight	Starting Dose	Max. Dose
50-100 lbs	½ tablet	1 tablet
100-150 lbs	1 tablet	2 tablets
150-200 lbs	2 tablets	4 tablets
over 200 lbs	3 tablets	6 tablets

In the setting of renal impairment, dosage should be adjusted and serum nickel and bromide levels should be followed. Steady state trough level should be drawn **prior** to ingesting the day's dose after one week of dosing or at appropriate intervals. Target trough serum nickel level is 20-40 mcg/L. (Warning: post dose peak levels are unreliable.) Treatment duration depends on the individual. Increase dose as needed on a monthly basis.

Maintenance phase: In order to maintain symptomatic relief, medication may be continued at the same or reduced initial phase dose level.

INACTIVE INGREDIENTS: Lactose and magnesium stearate.

HOW SUPPLIED: Scored tablets, off white in color with green speckles, with LL and score imprinted on same side, in child-resistant and tamper-resistant bottles of 100. NDC 61480-124-05.

REFERENCES:

1. The Homoeopathic Pharmacopoeia of the United States (HPUS), 8th Edition, Falls Church, Virginia, 1979.
2. Sunderman FW jr., Biological monitoring of nickel in humans. Scand J Work Environ Health 1993; 19 suppl 1:34-38.
3. Sunderman FW jr., Hopfer SM, Sweeny KR, Marcus AH, Most BM, Creason J. Nickel absorption and kinetics in human volunteers, P.S.E.B.M. 1989; 191:5-11.
4. Solomons NW, Viteri F, Shuler TR, Nielsen FH. Bioavailability of nickel in man: Effects of foods and chemically-defined dietary constituents on the absorption of inorganic nickel. J Nutr 1982; (2); 112: 39-50.
5. Christensen OB, Iagesson V. Nickel concentration of blood and urine after oral administration. Annals of Clinical and Laboratory Science 1981;2(2):119-125.
6. Nielsen FH. Is nickel nutritionally important? Nutrition Today 1993;28(1):14-19.
7. Vaiseman N, Koren G, Pencharz P. Pharmacokinetics of oral and intravenous bromide in normal volunteers. Clinical Toxicology 1986;24(5):403-413.
8. Van Leeuwen FXR, Sangster B. The toxicology of bromide ion. CRC Critical Reviews in Toxicology 1987; 18(3):189-213.
9. Smith SA. Oral supplementation of nickel and bromide in psoriasis vulgaris using nickel sulfate and sodium bromide. 1995 (unpublished report).
10. Miller MJ, Bogdan KG, Leach JF, and Gray AJ. Ambient air criteria document, Bureau of Toxic Substance Assessment, New York Department of Health, Albany, NY 1989.
11. US EPA, Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, health assessment document for nickel and nickel compounds. Washington DC, EPA/600/8-83/012FF.
12. US EPA, Environmental Criteria and Assessment Office, Office of health and Environmental Assessment. Drinking water quantification of toxicological effects for nickel. ECAO-CIN-443.1991
13. US FDA, Center for Food Safety and Applied Nutrition. Guidance document for nickel in shellfish. 1993.
14. Buselmaier W. von, Rohrborn G, and Propping G. Mutagenitäts – Untersuchungen mit Pestiziden im Host – Mediated Assay und mit dem Dominanten Letaltest an der Maus. Biol Zbl 1972; 91:311-325.
15. IARC Monograph on the Evaluation of Carcinogenic Risk of Chemicals to Man. IRC Publication #11, Lyon, France 1976.
16. Corbett TH, Heidelberger C, and Dove WF. Determination of mutagenic activity to bacteriophage T4 or carcinogenic and non-carcinogenic compounds. Mol Pharmacol 1970;6:667-669.
17. Ambrose AM, Larson PS, Borselleca JF, and Hennigar GR, Jr. Long term toxicologic assessment of nickel in rats and dogs. Journal of Food Science and Technology 1976;13:181-187.
18. MSDS Sheet No. 247 Potassium Bromide. Schenectady, NY: Genium Publishing Corp 1991.
19. MSDS Sheet No. 37 Nickel Sulfate. Schenectady, NY: Genium Publishing Corp 1993.
20. Sunderman FW Jr., Dingle B, Hopfer SM, and Swift T. Acute nickel toxicity in electroplating workers who accidentally ingested a solution of nickel sulfate and nickel chloride. American Journal of Industrial Medicine 1988;14:257-266.
21. Martindale: The Extra Pharmacopoeia 27th ed. Wade A, editor. The Pharmaceutical Press: London, 1977, pp273-274.
22. Smith SA, et al, Improvement of Psoriasis Vulgaris with Oral Nickel Dibromide. Archives of Dermatology 1997; 133:661-663.
23. Smith SA, Baker AE, et al. Effective Treatment of Seborrheic Dermatitis Using a Low Dose, Oral Homeopathic Medication... Alt Med Rev 2002; 7, pp59-67
24. Reckeweg, Hans-Heinrich, Materia Medica, 1983, first English edition.
25. Boericke, William, Materia Medica with Reperatory, 1927, ninth edition.
26. Clarke, John Henry, A Dictionary of Practical Materia Medica, 1921, reprint edition 1996.