PSORIZIDE FORTE- nickel sulfate, potassium bromide, and fumaric acid tablet
PLYMOUTH HEALTHCARE PRODUCTS LLC

Disclaimer: This homeopathic product has not been evaluated by the Food and Drug Administration for safety or efficacy. FDA is not aware of scientific evidence to support homeopathy as effective.

PSORIZIDE ® Forte

CAUTION

Federal law prohibits dispensing without a prescription.

DESCRIPTION

PSORIZIDE ® Forte is a biochemical homeopathic medication indicated for the **treatment of contact dermatitis due to nickel (metal/jewelry allergy), dyshidrotic hand/foot eczema, and mild to severe psoriasis**. [1-3] The active ingredients in each *PSORIZIDE ® Forte* tablet consist of the following: Fumaric Acid (Fumaricum Acidum) 1X, Potassium Bromide (Kali Bromatum) 1X, and Nickel Sulphate (Niccolum Sulphuricum) 1X. These drug ingredients are listed in the Homoeopathic Pharmacopoeia of the United States (HPUS). [4]

Inactive ingredients: Lactose and Magnesium Stearate.

Pharmacological Class: Homeopathic drug.

Dosage form: Oral 600 mg scored tablet. May be swallowed whole, chewed or dissolved in the mouth and swallowed.

CLINICAL PHARMACOLOGY

The active ingredients in *PSORIZIDE ® Forte* are simple biochemical compounds. The exact mechanism of action is unknown; however, it is believed *PSORIZIDE ® Forte* addresses a primary genetic biochemical defect. [5]

FUMARIC ACID is a naturally occurring four carbon organic acid important in the Krebs cycle. This biochemical pathway is of central importance to energy production. Each tablet contains approximately 30 mg fumaric acid (calculated). Fumaric Acid has many uses, including use as a food additive (GRAS) and as a chelating agent. [13] The use of fumaric acid and its derivatives (esters) as a treatment for psoriasis is increasing worldwide. [14-20] Very little is known about its clinical pharmacology; however, dose dependant inhibitory effects on keratinocyte proliferation have been demonstrated. [16,21]

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 into the extracellular fluids. [11,12] 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. [11]

NICKEL SULPHATE dissolves and dissociates in the digestive tract into its ionic constituents. Each tablet contains approximately 1.0 mg of ionic nickel (calculated). According to studies, 15% to 50% of ionic nickel is absorbed on a fasted stomach. [6] Food markedly decreases the rate and extent of nickel absorption. [7,8] Clinical studies show that serum concentrations of nickel are variable among patients after administering the same dose. [9] 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. [7,9] Renal clearance is rapid and efficient, and nickel does not accumulate in the body. [10]

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. [22,23,32]

INDICATIONS

PSORIZIDE ® Forte is indicated for the treatment of contact dermatitis due to nickel (metal/jewelry allergy,) dyshidrotic hand/foot eczema, and mild to severe psoriasis. It has been found to work well with a variety of combination therapies. Eczema, seborrhea and a variety of chronic pruritic inflammatory dermatoses generally respond well also.

CONTRAINDICATIONS

Although there are no known contraindications, patients who are allergic to any *PSORIZIDE ® Forte* 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, 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. Use cautiously in setting of kidney disease. (see Dosage and Administration) 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). Nickel allergy may be confirmed by a positive nickel patch test. Most patients with positive nickel allergy history or a positive nickel patch test **do not** have any untoward reaction to administration of *PSORIZIDE ® Forte.* However, if there is a history of nickel sensitivity, begin with a very low dose and slowly increase over a period of six weeks as tolerated. Progressive G.I. absorption allows desensitization to occur. [8]

Nickel desensitization schedule:

Week	Amount of Time to Take Medication Prior to Breakfast
Week 1	**1 tablet With Breakfast**
Week 2	1 tablet 15 min Prior
Week 3	1 tablet 30 min Prior
Week 4	1 tablet 45 min Prior
Week 5	1 tablet 1 hour Prior
Week 6 and thereon	2 tablets 1 hour Prior

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

Information for patients

Patients using *PSORIZIDE ® Forte* should receive the following information and instructions:

1. This medication is to be used only 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 one hour afterwards to avoid interference with absorption.

Drug Interactions

There are no known drug interactions.

Carcinogenesis, mutagenesis, and impairment of fertility

No studies have been done on the carcinogenesis, mutagenesis, or impairment of fertility of *PSORIZIDE ® Forte.* No carcinogenesis or mutagenesis has been reported in multiple animal studies for oral administration of fumaric acid and soluble nickel and bromide salts (active ingredients) even at very high doses. [24-27]

Effects of fumaric acid

It is not listed as a carcinogen by ACGIH, IARC, NIOSH, NTP, or OSHA. [26] It is a GRAS substance (generally recognized as safe) and is commonly used in food processing.

Effects of soluble potassium bromide

KBr is not listed as a carcinogen by the NTP, IARC, and OSHA. [28]

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. [10-12,27] 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. [27]

Pregnancy

Pregnancy category C

Animal reproduction studies have not been conducted with *PSORIZIDE ® Forte. PSORIZIDE ® Forte* should not be given to a pregnant woman.

Nursing mothers

It is not known whether this drug is secreted in human milk. However, since many drugs are secreted in human milk, caution should be exercised when *PSORIZIDE ® Forte* is administered to a nursing woman.

Pediatric use

Carefully adjust dosage to weight when treating young children.

ADVERSE REACTIONS

PSORIZIDE ® Forte contains low doses of active ingredients. Therefore there are minimal known side effects.

(see PRECAUTIONS for hypersensitivity information)

OVERDOSAGE

Fumaric acid toxicity

The oral rat LD_{50} is 9300mg/kg. [26] This is 3800 times the maximum dose recommended for *PSORIZIDE ® Forte.*

Potassium bromide toxicity

Indications of toxicity due to oral overdosage of bromide may include nausea and 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 1000mg. [31] This level is 67 times the dose received in one tablet of *PSORIZIDE ® Forte.*

Nickel sulphate toxicity

The oral rat LD_{50} for nickel sulphate hexahydrate is 275mg/kg. [29] 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. [30] The lowest observed transitory toxic effects from human ingestion of soluble nickel salts is approximately 8 mg nickel/kg body weight. [30] This is 138 times the maximum dose recommended for *PSORIZIDE ® Forte* (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 Daily Dose
40-80 lbs	½ tablet	1 ½ tablet
80-120 lbs	1 tablet	3 tablets
120-160 lbs	1 ½ tablets	4 ½ tablets
160-200 lbs	2 tablets	6 tablets
200-240 lbs	2 ½ tablets	7 ½ tablets
Over 240 lbs	3 tablets	9 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 30-60 mcg/L. (Caution: post dose peak levels are unreliable.)

Maintenance phase

In order to maintain symptomatic relief, medication may be continued at the same or reduced initial phase dose level. Treatment duration depends on the individual. **For allergic nickel dermatitis, continue 2 tablets 1 hour prior to breakfast for weeks 7 – 16. (Refer to Hypersensitivity section above). Some patients may require continued or intermittent repeated treatment to maintain nickel desensitization.**

INACTIVE INGREDIENTS

Lactose and magnesium stearate.

HOW SUPPLIED

Scored tablets, off white in color with green speckles, with **imprinted on one side and a score on the other**, in child-resistant and tamperresistant bottles of 90 **. NDC**

61480-255-05

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Revised 1.10.07 TS

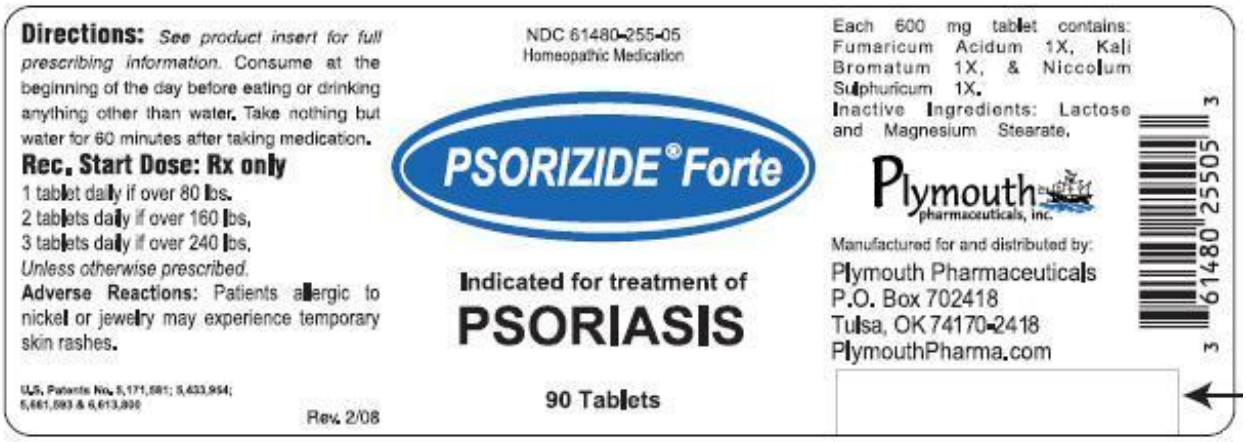
PRINCIPAL DISPLAY PANEL - 90 Tablet Label

NDC 61480-255-05
Homeopathic Medication

PSORIZIDE ® Forte

Indicated for treatment of
PSORIASIS

90 Tablets



PSORIZIDE FORTE

nickel sulfate, potassium bromide, and fumaric acid tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:61480-255
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NICKEL SULFATE (UNII: 4FLT4T3WUN) (NICKEL CATION - UNII:OIS2CXW7AM)	NICKEL SULFATE	1 [hp_X]
POTASSIUM BROMIDE (UNII: OSD78555ZM) (BROMIDE ION - UNII:952902IX06)	POTASSIUM BROMIDE	1 [hp_X]
FUMARIC ACID (UNII: 88XHZ13131) (FUMARIC ACID - UNII:88XHZ13131)	FUMARIC ACID	1 [hp_X]

Product Characteristics			
Color	white (Off-White with Green Speckles)	**Score**	2 pieces
Shape	ROUND	**Size**	11mm
Flavor		**Imprint Code**	LL
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:61480-255-05	90 in 1 BOTTLE; Type 0: Not a Combination Product	11/15/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved homeopathic		11/15/2001	

Labeler - PLYMOUTH HEALTHCARE PRODUCTS LLC (079330314)

Revised: 11/2022 PLYMOUTH HEALTHCARE PRODUCTS LLC