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.

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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. Renal clearance is rapid and efficient, and nickel does not accumulate in the body.

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.

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.

Nickel desensitization schedule:

<table>
<thead>
<tr>
<th>Week</th>
<th>Amount of Time to Take Medication Prior to Breakfast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>1 tablet With Breakfast</td>
</tr>
<tr>
<td>Week 2</td>
<td>1 tablet 15 min Prior</td>
</tr>
<tr>
<td>Week 3</td>
<td>1 tablet 30 min Prior</td>
</tr>
<tr>
<td>Week 4</td>
<td>1 tablet 45 min Prior</td>
</tr>
<tr>
<td>Week 5</td>
<td>1 tablet 1 hour Prior</td>
</tr>
</tbody>
</table>
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. 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. 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. 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. The lowest observed transitory toxic effects from human ingestion of soluble nickel salts is approximately 8 mg nickel/kg body weight. 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.

<table>
<thead>
<tr>
<th>Weight</th>
<th>Starting Dose</th>
<th>Max Daily Dose</th>
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<tbody>
<tr>
<td>40-80 lbs</td>
<td>½ tablet</td>
<td>1 ½ tablet</td>
</tr>
<tr>
<td>80-120 lbs</td>
<td>1 tablet</td>
<td>3 tablets</td>
</tr>
<tr>
<td>120-160 lbs</td>
<td>1 ½ tablets</td>
<td>4 ½ tablets</td>
</tr>
<tr>
<td>160-200 lbs</td>
<td>2 tablets</td>
<td>6 tablets</td>
</tr>
<tr>
<td>200-240 lbs</td>
<td>2 ½ tablets</td>
<td>7 ½ tablets</td>
</tr>
<tr>
<td>Over 240 lbs</td>
<td>3 tablets</td>
<td>9 tablets</td>
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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 tamper-resistant bottles of 90. NDC 61480-255-05

REFERENCES
21. Thio, HB, et al, Fumaric Acid Derivatives... Inhibit the proliferation of Human Keratinocytes, Br J


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

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<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
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<tr>
<td>Nickel Sulfate (UNII: 4FLT4T3WUN) (NICKEL CATION - UNII:OIS2CXW7AM)</td>
<td>Nickel Sulfate</td>
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<tr>
<td>Potassium Bromide (UNII: OSD78555ZM) (BROMIDE ION - UNII:952902IX06)</td>
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<tr>
<td>Fumaric Acid (UNII: 88XHZ13131) (Fumaric Acid - UNII:88XHZ13131)</td>
<td>Fumaric Acid</td>
<td>1 [hp_X]</td>
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Product Characteristics

Color: WHITE (Off-White with Green Speckles)
Shape: ROUND
Size: 11mm
Flavor: Contains
Imprint Code: LL
Score: 2 pieces

Packaging

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<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
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<tr>
<td>1</td>
<td>NDC:61480-255-05</td>
<td>90 in 1 BOTTLE</td>
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Marketing Information

Marketing Category: Unapproved homeopathic
Application Number or Monograph Citation: |
Marketing Start Date: 11/15/2001
Marketing End Date: |

Labeler - PLYMOUTH HEALTHCARE PRODUCTS LLC (079330314)
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<th>Name</th>
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<tr>
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<td>102783016</td>
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Revised: 1/2015

PLYMOUTH HEALTHCARE PRODUCTS LLC