

ACUNOL- nickel sulfate, potassium bromide, sodium bromide, zinc sulfate anhydrous, and sulfur 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.

Acunol™

CAUTION

Federal law prohibits dispensing without a prescription.

DESCRIPTION

Acunol™ is a biochemical homeopathic medication indicated for the **treatment of acne**.³²⁻³⁴ The active ingredients in each Acunol™ tablet consist of the following: Potassium Bromide (Kali Bromatum) 1X, Sodium Bromide (Natrum Bromatum) 1X, Zinc Sulphate (Zincum Sulphuricum) 1X, Sulphur 1X, and Nickel Sulphate (Niccolum Sulphuricum) 1X. These drug ingredients are listed in the Homoeopathic Pharmacopoeia of the United States (HPUS).¹

Inactive ingredients: Lactose, Magnesium Stearate, and Copper (II) Oxide.

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 Acunol™ are simple biochemical compounds. The exact mechanism of action is unknown; however, it is known that bromide enhances phagocytic and bactericidal activity of neutrophils.³¹

POTASSIUM BROMIDE & SODIUM BROMIDE dissolve and dissociate in the digestive tract into their ionic constituents. Each tablet contains approximately 30 mg of 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.

ZINC SULPHATE dissolves and dissociates in the digestive tract into its ionic constituents. Each tablet contains approximately 5 mg of zinc (calculated). Zinc is an essential trace mineral necessary for protein synthesis, enzyme stimulation, and alkaline balance.^{27,28} It is primarily absorbed from the duodenum and excreted via feces, urine, and sweat.²⁶

SULPHUR is a naturally occurring mineral that is an essential part of the human body. It exhibits anti-bacterial, anti-parasitic, fungicidal, and keratolytic properties.²⁶ Each tablet contains approximately 5 mg of sulphur (calculated). Sulphur is highly water soluble and

contains approximately 0.5 mg of sulphur (calculated). Sulphur is highly water soluble and as a result is easily excreted by the body via sweat and urine. ²² Since the sulphur found in Acunol™ is a naturally occurring mineral, it is radically different from sulfa drugs (sulfonamide antibiotics). Therefore, **patients who are allergic to sulfa drugs CAN safely take Acunol™**.

NICKEL SULPHATE dissolves and dissociates in the digestive tract into its ionic constituents. Each tablet contains approximately 0.5 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. 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. ^{9,20,21}

INDICATIONS

Acunol™ is indicated for the treatment of mild to moderate acne vulgaris, acne rosacea, peri-oral dermatitis, and folliculitis. It has been found to work well with a variety of combination therapies.

CONTRAINDICATIONS

Although there are no known contraindications, patients who are allergic to any Acunol™ 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) 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 Acunol™. 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 Prior
Week 3	30 min Prior
Week 4	45 min Prior
Week 5 and thereon	1 hour Prior

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

Information for patients

Patients using Acunol™ 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 and at the end of the day before bed; take nothing but water for one hour afterwards to avoid interference with absorption.

Drug interactions

There are no known drug interactions. Since copper deficiency in human nutrition has occasionally been induced by supplemental zinc therapy, copper has been added in order to minimize this rare occurrence. (see Inactive ingredients) For Tetracycline or Quinolones co-administration with Acunol, see Dosage and Administration

Carcinogenesis, mutagenesis, impairment of fertility

No studies have been done on the carcinogenesis, mutagenesis, or impairment of fertility of Acunol™. 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. ¹⁰⁻¹⁴

Effects of soluble potassium bromide

KBr is not listed as a carcinogen by the NTP, IARC, and OSHA. ¹⁶

Effects of sodium bromide

NaBr is not listed as a carcinogen by the IARC, NTP, or OSHA. ³⁵

Effects of zinc sulphate

ZnSO₄ is not listed as a carcinogen by the ACGIH, IARC, NTP, or CA Prop 65. ²⁹

Effects of sulphur

Sulphur is not listed as a carcinogen by the ACGIH, IARC, NIOSH, NTP, or OSHA. ²⁵

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 has never been known to induce carcinogenesis via any route of introduction including: oral, inhalation, cutaneous, IM, or IP. ^{10-12,15} 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 per day Ni. ¹⁵

Pregnancy

Pregnancy category C

Animal reproduction studies have not been conducted with Acunol™. Acunol™ 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 Acunol™ is administered to a nursing woman.

Pediatric use

Carefully adjust dosage to weight when treating young children.

ADVERSE REACTIONS

Acunol™ contains low doses of active ingredients. Therefore there are minimal known side effects. (see PRECAUTIONS for hypersensitivity information)

OVERDOSAGE

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. ¹⁹ This level is 33 times the dose received in one tablet of Acunol™.

Zinc sulphate toxicity

Symptoms of acute toxicity of zinc due to oral overdose can include dehydration, stomach pain, lethargy, dizziness, muscular incoordination, and in severe cases renal failure. ²⁶ Chronic zinc toxicity can occur at levels of 100-300 mg/d. ³⁰

Sulphur toxicity

The oral rat LD₅₀ for sulphur is reported to be greater than 5,000 mg/kg. ²³ This is more than 11,000 times the maximum dose recommended for Acunol™. Ingestion of toxic levels of sulphur can cause sore throat, nausea, headache, gastrointestinal irritation, and possibly unconsciousness in severe cases. ^{24,25} Sulphur poses such a remote risk that is placed in the lowest toxic category possible, EPA Toxicity Category IV. ²³

Nickel sulphate toxicity

The oral rat LD₅₀ for nickel sulphate hexahydrate is 275 mg/kg. ¹⁷ 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. ¹⁸ The lowest observed transitory toxic effects from human ingestion of soluble nickel salts is approximately 8 mg nickel/kg body weight. ¹⁸ This is 180 times the maximum dose recommended for Acunol™. (See below)

DOSAGE AND ADMINISTRATION

Take tablets twice a day (b.i.d.) for best results. Absorption of nickel sulphate is variable among individuals. **For maximum nickel absorption, tablets should be taken orally upon rising at the beginning of the day and at the end of the day before bed.** Take nothing but water for one hour after taking medication to aid nickel absorption. If taking Tetracycline or Levofloxacin allow at least two hours after taking Acunol. If taking a different Quinolone antibiotic, consult manufacturer's information.

Kg	lbs	Starting dose	Max Daily dose
23-45	51-100	½ • b.i.d.	1 • b.i.d.
46-68	101-150	1 • b.i.d.	2 • b.i.d.
69-90	151-200	1½ • b.i.d.	3 • b.i.d.
91+	201+	2 • b.i.d.	4 • b.i.d.

Increase dose only if needed on a monthly basis up to the max daily dose. Treatment dose and duration depends on the individual.

In the setting of significant renal impairment

Dosage should be adjusted and serum nickel and bromide levels should be followed. Steady state trough nickel 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 10-40 mcg/L. (Caution: post dose peak levels are unreliable.) Serum bromide assay by spectrophotometry is the historic standard. ³⁶ Concentrations higher than 50 mg/dl may

be compatible with toxicity. No therapeutic target levels exist for bromide.

HOW SUPPLIED

Scored tablets, off white in color with green speckles, with  **imprinted on one side and a score on the other side**, in child-resistant and tamper-resistant bottles of 90.
NDC 61480-137-05

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Revised 09.13.06 TDS

PRINCIPAL DISPLAY PANEL - 90 Tablet Label

NDC 61480-137-05

Homeopathic Medication

Acunol®

Indicated for treatment of
ACNE

600mg

90 Tablets

Rx only

For Oral Use Only

<p>Directions: See product insert for full prescribing information. Consume at the beginning of the day and at bed time with water. Take nothing but water for 60 minutes before and after taking medication.</p> <p>Dosage: Rx only Over 50 lbs. 1/2 tablet b.i.d. Over 100 lbs. 1 tablet b.i.d. Over 150 lbs. 1 1/2 tablets b.i.d. Over 200 lbs. 2 tablets b.i.d. <i>Unless otherwise prescribed.</i></p> <p>Adverse Reactions: Patients allergic to nickel or jewelry may experience temporary skin rashes.</p> <p><small>U.S. Patents Pending. Rev. 1/05</small></p>	<p>NDC 61480-137-05 Homeopathic Medication</p> <h1>Acunol</h1> <p>Indicated for treatment of ACNE</p> <p>600mg</p> <p>90 Tablets Rx only For Oral Use Only</p>	<p>Each 600 mg tablet contains: Kali Bromatum 1X / Potassium Bromide; Natrium Bromatum 1X / Sodium Bromide; Sulphur 1X; Zincum Sulphuricum 1X / Zinc Sulphate; & Nicotinum Sulphuricum 1X / Nickel Sulphate. <i>Inactive Ingredients:</i> Lactose, Magnesium Stearate and Copper (II) Oxide.</p> <p>Plymouth pharmaceuticals</p> <p>Manufactured for and distributed by: Plymouth Pharmaceuticals™ P.O. Box 702418 Tulsa, OK 74170-2418 PlymouthPharmaceuticals.com</p>
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ACUNOL

nickel sulfate, potassium bromide, sodium bromide, zinc sulfate anhydrous, and sulfur tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:61480-137
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
NICKEL SULFATE (UNII: 4FLT4T3WJN) (NICKEL CATION - UNII:OIS2CXW7AM)	NICKEL SULFATE	1 [hp_X]
POTASSIUM BROMIDE (UNII: OSD78555ZM) (BROMIDE ION - UNII:952902IX06)	POTASSIUM BROMIDE	1 [hp_X]
SODIUM BROMIDE (UNII: LC1V549NOM) (BROMIDE ION - UNII:952902IX06)	SODIUM BROMIDE	1 [hp_X]
ZINC SULFATE ANHYDROUS (UNII: 0J6Z13X3WO) (ZINC CATION - UNII:13S1S8SF37)	ZINC CATION	1 [hp_X]
SULFUR (UNII: 70FD1KFU70) (SULFUR - UNII:70FD1KFU70)	SULFUR	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:61480-137-05	90 in 1 BOTTLE; Type 0: Not a Combination Product	04/18/2006	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
unapproved homeopathic		04/18/2006		

Labeler - PLYMOUTH HEALTHCARE PRODUCTS LLC (079330314)

Revised: 11/2022

PLYMOUTH HEALTHCARE PRODUCTS LLC