

## ADVERSE REACTIONS

Adverse reactions associated with biotin supplementation are rare in the medical literature; however, urticaria and gastrointestinal upset have been reported. As with any oral treatment, if patients experience any adverse reactions or side effects, they should inform their physicians immediately and discontinue use.

## DRUG INTERACTIONS

The anticonvulsants carbamazepine, phenytoin, phenobarbital, and primidone may accelerate biotin metabolism, leading to a reduction in available biotin. Chronic use of these drugs has been associated with decreased plasma concentrations of biotin.<sup>17,18</sup>

The use of antibiotics may reduce the contribution of biotin made by bacteria within the large intestine.

## PRECAUTIONS AND WARNINGS

Pregnant women and nursing mothers should consult their physicians before taking this product. Appearex™ should not be used in patients with known allergy or hypersensitivity to any of its ingredients.

## TOXICITY

No toxic effects have been reported, even at higher doses.<sup>19</sup>

## INDICATION AND USAGE

Appearex™ is recommended for first-line treatment of weak, brittle, splitting, or soft nails.

Appearex™ therapy should be taken regularly as directed to maintain strong, healthy nails. Clinical improvement is generally realized within 3 to 6 months.<sup>3,5,6</sup> Cessation of therapy may result in deterioration of nail health within 6 to 9 months.

## CONTRAINDICATION

Appearex™ is contraindicated in patients allergic or hypersensitive to any of its ingredients.

## DOSAGE AND ADMINISTRATION

Recommended treatment for adults is 1 tablet taken daily with water. For use in children under 12 years of age, consult a physician for guidance regarding proper dosing and administration.

## SUMMARY

Appearex™, for the treatment of weak, brittle, splitting, or soft nails, is pharmaceutical grade oral biotin that restores nail quality by promoting keratinization. It has been clinically proven to increase nail plate thickness, smooth brittle nail ridges, and improve overall nail quality. As a water-soluble essential vitamin, the biotin in Appearex™ is safe and well tolerated. For patients with brittle nails, one Appearex™ tablet taken daily provides the additional biotin needed to manage onychoschizia/onychorrhexis.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

## References

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BIOTIN 2.5 mg

Manufactured for  
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www.appearex.com

For more information  
Please call 1-888-927-8989  
Monday-Friday, 8 AM-9 PM Eastern Time



BIOTIN 2.5 mg

## PRODUCT MONOGRAPH

### INTRODUCTION

Brittle nails (onychoschizia/onychorrhexis) is a familiar complaint seen by physicians that potentially affects up to 40 million Americans.<sup>12</sup> More common in women, the condition involves dystrophic changes of the nail plate such that nails exhibit frailty, breakage, and splitting.<sup>2</sup> The etiology of brittle nails is often occupational; repeated exposure to water, detergents, and solvents such as acetone in nail polish remover causes dehydration of the nail plate keratin.<sup>12</sup> Other etiologies for brittle nails include primary dermatologic conditions, systemic disease, and physical trauma to the nail bed.<sup>2,3</sup>

Because nails protect the distal phalanx from trauma, aid in fine grasping, and have aesthetic value, promoting nail health by treating brittle nails is important.<sup>4</sup> Oral biotin has been demonstrated efficacious for the treatment of brittle nails in humans.<sup>3,5,7</sup> Earlier veterinary studies in which biotin normalized pathologic hoof changes in horses and swine<sup>8,9</sup> led researchers to consider human applications.<sup>5,7</sup> Results demonstrate that in humans oral biotin can increase nail plate thickness and smooth brittle ridges, leading to stronger, firmer nails within 3 to 6 months.<sup>3,5,6</sup> Some patients see improvement within as little as 1 month.<sup>3</sup> Further, the American Academy of Dermatology Association endorses the use of biotin as systemic therapy for brittle nails.<sup>10</sup>

Appearex™ is a once-daily pure oral-biotin preparation that provides 2.5 mg of supplemental biotin to the diet. For patients with brittle nails, Appearex™ provides the additional biotin needed to manage onychoschizia/onychorrhexis.

### DESCRIPTION AND MECHANISM OF ACTION

Appearex™ is a biotin preparation (2.5 mg) available for oral administration as a small, easy-to-swallow tablet. Each Appearex™ tablet contains as its active ingredient 2.5 mg of biotin, a dose clinically proven to improve nail strength and quality.<sup>3,5,7</sup> Inactive ingredients include lactose monohydrate, cornstarch, povidone (K25), and magnesium stearate.

Biotin is a water-soluble vitamin component of the vitamin B complex. As an essential nutrient, biotin acts as a coenzyme for the body's carboxylation reactions and is a factor in maintaining healthy muscle, hair, nails, and skin. Its molecular formula is C<sub>10</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>S and its molecular weight is 244.308. The structural formula of biotin is shown in Figure 1.

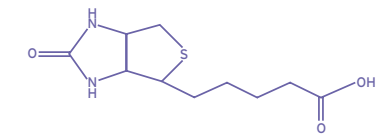


Figure 1. Structural formula of biotin.

The presumed mechanism of action by which Appearex™ affects brittle nails is via the pharmacologic effects of biotin on all keratin structures. Biotin stimulates the differentiation of epidermal cells and is involved in keratinization. It is also believed that biotin increases the quantity of keratin matrix proteins in the nail, thereby improving keratin structure.<sup>5,11</sup>

### PHARMACOKINETICS

#### Absorption and Transport

Biotin is efficiently absorbed in the small intestine sodium-mediated carrier transport.<sup>12,13</sup> Once absorbed, 80% of biotin is free, and the remaining 20% is bound to plasma proteins.<sup>14</sup> Cellular entry of biotin occurs by both diffusion and sodium-dependent transport.

#### Degradation and Excretion

About 43% of biotin is excreted unchanged in the urine.<sup>15</sup> The remainder is excreted as degradation products including bisnorbiotin (30%), biotin sulfoxide (11%), and other small amounts of biotin sulfone, bisnorbiotin methylketone, and tetranorbiotin sulfoxide.<sup>16</sup>



# Clinical Efficacy and Safety of Biotin (the Active Ingredient in Appearex™)

## Study 1<sup>6</sup>

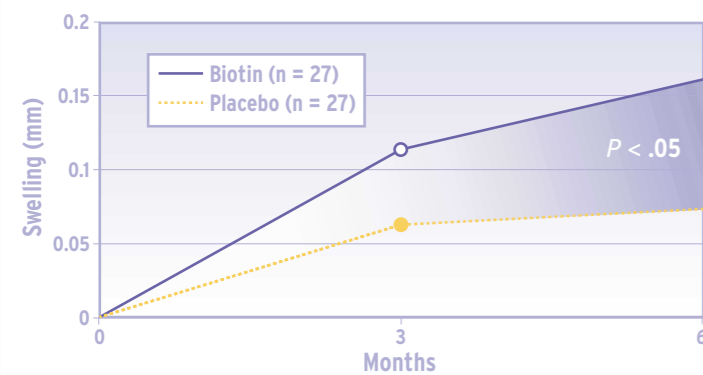
Sixty patients with poor nail quality (brittle, split, or soft nails with a swell factor of <2.5) received either placebo or one 2.5-mg tablet of biotin q.d. in a double-blind placebo-controlled clinical trial. Patients with known nail disease, biotin deficiency, or serious medical conditions were excluded. Concomitant use of other drugs was forbidden. Nail quality was evaluated at baseline and after 3 and 6 months of treatment. Measurements included swell factor (after incubation of the nail in NaOH), transonychia water loss (which correlates with nail plate thickness and is measured via a PeriFlux laser Doppler flowmeter), and subjective ratings of nail quality by the patient and by an observer.

Three patients were excluded from statistical analysis in both the placebo and the biotin groups, leaving a total of 27 evaluable patients in each group. Patients were excluded for a variety of reasons, including study withdrawal; however, none withdrew due to intolerance to study medication. The majority of study participants were female (22 of 27 in the biotin group; 19 of 27 in the placebo group), and ages ranged from 20 to 63 years.

### Efficacy Results

Both the objective and subjective measures of nail quality improved after 6 months of treatment in the biotin-treated group. The swell factor (Figure 2) and the observer ratings of nail quality improved significantly ( $P < .05$  for both) in the biotin group as compared with the placebo group. Measures of transonychia water loss and self-ratings of nail quality also indicated substantial improvement over the course of biotin treatment, but the changes were not statistically significant when compared with the placebo group.

### NAIL SWELLING



**Figure 2.** Improvement in nail quality measured by the swelling of nail keratin in an NaOH medium. Nail swelling was measured on a 10- $\mu$ m-thick cryosection. Adapted from Gehring W. Effect of biotin on poor nail quality: a placebo-controlled double-blind clinical study [in German]. *Aktuelle Dermatol.* 1996;22:20-25. By permission of Georg Thieme Verlag Stuttgart-New York.

### Safety Results

Biotin therapy was very well tolerated over the course of this 6-month study. No patients withdrew due to side effects or reported tolerance problems of any kind.

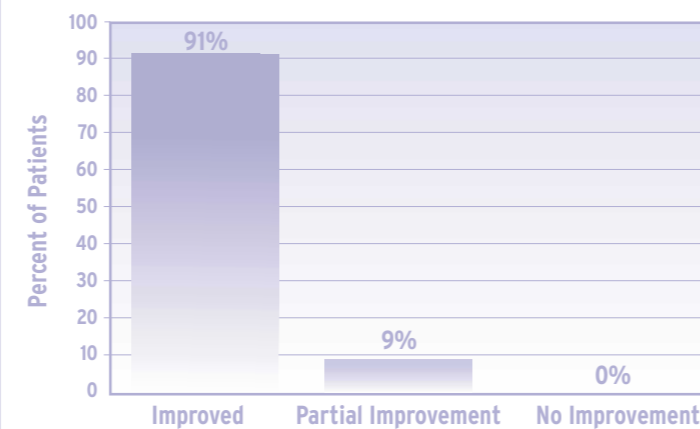
## Study 2<sup>5</sup>

Forty-five patients with brittle, splitting, or soft fingernails were treated with biotin (2.5 mg q.d.) for 6 to 10 months in an open-label study. Patients were screened at baseline and determined to be free of any deficiency of zinc, iron, calcium, magnesium, triiodothyronine, thyroxine, folic acid, protein, albumin/globulin ratio, or hemoglobin. Efficacy measures were based on patients' subjective reports of improvement in nail firmness and reduction in chipping and cracking. Most patients were female (43 of 45) and the mean age was 51.1  $\pm$  16.1 years.

### Efficacy Results

Improvement in nail quality was reported by 41 of 45 patients (91%). The mean time to first mention of improvement was 5.5  $\pm$  2.3 months, which approximates the period of time required for nail renewal. The 4 remaining patients reported partial improvement (Figure 3). In addition, 7 of 9 patients with concomitant alopecia or effluvium spontaneously reported improvement of their hair.

### PATIENT ASSESSMENT OF NAIL QUALITY



**Figure 3.** Improvement in nail quality after 6 to 10 months of biotin therapy.

### Safety Results

Biotin was very well tolerated, and no side effects were reported.

## Study 3<sup>3</sup>

The efficacy of biotin for brittle nails was examined via an analysis of retrospective survey data collected on patients who had attended a nail consultation clinic over a 6-month period. Forty-four patients (3 males; 41 females) were identified, but complete information was obtained on only 35 patients. These 35 patients had dry, splitting nails with signs of onychorrhexis or onychoschizia and were offered biotin therapy (2.5 mg q.d.) as treatment. Efficacy assessment was based on patient reports of clinical improvement.

The median patient age was 57 years (range = 21 to 74 years), and duration of symptoms ranged from 2 months to 30 years, with 3 patients claiming their nail condition had always existed. Most patients had tried a variety of treatments without success before receiving biotin therapy. Duration of biotin treatment ranged from 1.5 to 7 months.

### Efficacy Results

Clinical improvement was reported by 22 of 35 patients (63%) and was first evident after about 2 months of therapy on average (range = 1 to 4 months). In the group of responders, actual biotin doses ranged from 1.0 to 3.0 mg per day with a mean dose of 2.04 mg per day.

### PATIENT ASSESSMENT OF IMPROVEMENT\*

(N = 35)	
<b>Efficacy Results</b>	<b>n (%)</b>
No Improvement	13 (37%)
Improved	22 (63%)
<b>Time to Improvement</b>	
< 2 Months	9 (41%)
2-4 Months	12 (55%)
Unknown	1 (5%)

\*Adapted with permission from Hochman.<sup>3</sup> ©Quadrant HealthCom, Inc.

### Safety Results

Biotin was well tolerated by this group of patients. Only one patient reported any adverse effect possibly related to biotin. That patient experienced gastrointestinal upset and so discontinued therapy after 6 weeks.

## Study 4<sup>7</sup>

Eight women with a diagnosis of brittle nails of unknown origin were treated with 2.5 mg of oral biotin (open label) for 6 to 15 months. Nine nails were collected from these 8 women at baseline and after biotin treatment. Scanning electron microscopy (SEM) was used to evaluate nail thickness, nail splitting, and nail topography at both time points. Ten subjects with normal fingernails served as nontreated controls. SEM evaluations were performed under blinded conditions.

Six of the 8 patients exhibited nail splitting at baseline, and all 8 patients exhibited abnormal nail topography at baseline (irregular and multidirectional orientation of dorsal nail cells). Mean duration of biotin therapy was 9.3  $\pm$  3.6 months.

### Efficacy Results

All efficacy parameters improved after biotin treatment. Nail thickness increased by 25% on average, and nail splitting resolved completely in 3 nails and partially in one nail (of the 6 nails with splitting at baseline). Nail topography improved in all 8 patients: 5 nails normalized completely, and 4 nails became more homogeneous in topography.

### IMPROVEMENT IN NAIL THICKNESS

Baseline	Posttreatment	Change From Baseline
256 $\pm$ 53 $\mu$ m	319 <sup>†</sup> $\pm$ 86 $\mu$ m	25% improvement

<sup>†</sup> $P < .05$ , baseline vs posttreatment.

### Safety Results

No safety results were reported.