

# Novel Lacquer Bests Penlac for Onychomycosis

BY BRUCE JANCIN

BERLIN — A formulation of 8% ciclopirox-medicated nail lacquer for onychomycosis significantly outperformed a commercially available version in a 467-patient, 60-week randomized trial.

The product, 8% ciclopirox hydroxypropyl-chitosan nail lacquer (CicloPoli, Polichem), or P-3051, had an overall 119% greater mycologic cure rate than

the commercially available 8% ciclopirox monoester (Penlac, Sanofi-Aventis).

Penlac significantly outperformed placebo, as expected based on earlier product registration studies in Europe, Dr. Federico Mailland reported at the annual congress of the European Academy of Dermatology and Venereology.

CicloPoli is currently only available in Europe. Penlac is available in Europe and the United States.

The multicenter trial involved patients with toenail onychomycosis of varying severity who were randomized 2:2:1 to P-3051, Penlac, or placebo. They treated themselves for 48 weeks and were followed for another 12 weeks (J. Eur. Acad. Dermatol. Venereol. 2009;23:773-81).

The results varied markedly depending upon baseline severity. Mild disease was defined as baseline involvement of less than 25% of the big toenail, and se-

vere as greater than 65% involvement.

The 60-week cure rate, defined as negative mycology by both KOH (potassium hydroxide) and culture, along with a 100% healthy-appearing nail, was 50% in patients with P-3051-treated mild disease and 0% with Penlac. For patients with moderate disease, the 60-week cure rates were 12.3% with P-3051 and 7.1% for Penlac. And for severe disease, the cure rates were 5.7% and 3.6%, respectively, said Dr. Mailland of Polichem SA in Lugano, Switzerland (manufacturer of CicloPoli).

The same pattern was seen with responder rates as defined by negative mycology and at least a 90% healthy-appearing nail. For patients with baseline mild fungal disease, the 60-week responder rates were 62.5% with P-3051 and 40% with Penlac. For moderate disease, responder rates were 31.6% and 17.7%. For severe disease, response rates were 11.4% with P-3051 and 3.6% with Penlac.

The new topical nail lacquer is an attractive alternative to oral treatment, even in severely affected patients, provided they are prepared for long-term therapy, said Dr. Mailland. ■

## BRIEF SUMMARY - Consult full prescribing information before use.

Tussicaps®  
(Hydrocodone Polistirex and  
Chlorpheniramine Polistirex)  
Extended-Release Capsules

Rx only

### CONTRAINDICATIONS

Tussicaps® extended-release capsules are contraindicated in patients with a known allergy or sensitivity to hydrocodone or chlorpheniramine.

The use of Tussicaps® extended-release capsules are contraindicated in children less than 6 years of age due to the risk of fatal respiratory depression.

### WARNINGS

**Respiratory Depression** – As with all narcotics, Tussicaps® extended-release capsules produce dose-related respiratory depression by directly acting on brain stem respiratory centers. Hydrocodone affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. Caution should be exercised when Tussicaps® extended-release capsules are used postoperatively and in patients with pulmonary disease, or whenever ventilatory function is depressed. If respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride and other supportive measures when indicated (see **OVERDOSAGE**).

**Head Injury and Increased Intracranial Pressure** – The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions, which may obscure the clinical course of patients with head injuries.

**Acute Abdominal Conditions** – The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

**Obstructive Bowel Disease** – Chronic use of narcotics may result in obstructive bowel disease especially in patients with underlying intestinal motility disorder.

**Pediatric Use** – The use of Tussicaps® extended-release capsules are contraindicated in children less than 6 years of age (see **CONTRAINDICATIONS**).

In pediatric patients, as well as adults, the respiratory center is sensitive to the depressant action of narcotic cough suppressants in a dose-dependent manner. Caution should be exercised when administering Tussicaps® extended-release capsules to pediatric patients 6 years of age and older. Overdose or concomitant administration of Tussicaps® extended-release capsules with other respiratory depressants may increase the risk of respiratory depression in pediatric patients. Benefit to risk ratio should be carefully considered, especially in pediatric patients with respiratory embarrassment (e.g., croup) (see **PRECAUTIONS**).

### PRECAUTIONS

#### General

Caution is advised when prescribing this drug to patients with narrow-angle glaucoma, asthma, or prostatic hypertrophy.

**Special Risk Patients** – As with any narcotic agent, Tussicaps® extended-release capsules should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy, or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

#### Information for Patients

As with all narcotics, Tussicaps® extended-release capsules may produce marked drowsiness and impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery; patients should be cautioned accordingly. Tussicaps® extended-release capsules must not be diluted with fluids or mixed with other drugs as this may alter the resin-binding and change the absorption rate, possibly increasing the toxicity.

Keep out of the reach of children.

**Cough Reflex** – Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when Tussicaps® extended-release capsules are used postoperatively, and in patients with pulmonary disease.

#### Drug Interactions

Patients receiving narcotics, antihistamines, antipsychotics, anti-anxiety agents, or other CNS depressants

(including alcohol) concomitantly with Tussicaps® extended-release capsules may exhibit an additive CNS depression. When combined therapy is contemplated, the dose of one or both agents should be reduced.

The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone.

The concurrent use of other anticholinergics with hydrocodone may produce paralytic ileus.

#### Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity and reproductive studies have not been conducted with Tussicaps® extended-release capsules.

#### Pregnancy

**Teratogenic Effects.** *Pregnancy Category C* – Hydrocodone has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. Tussicaps® extended-release capsules should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nonteratogenic Effects** – Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. The intensity of the syndrome does not always correlate with the duration of maternal opioid use or dose.

#### Labor and Delivery

As with all narcotics, administration of Tussicaps® extended-release capsules to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.

#### Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Tussicaps® extended-release capsules, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

#### Pediatric Use

The use of Tussicaps® extended-release capsules are contraindicated in children less than 6 years of age (see **CONTRAINDICATIONS and ADVERSE REACTIONS, Respiratory, Thoracic and Mediastinal Disorders**).

Tussicaps® extended-release capsules should be used with caution in pediatric patients 6 years of age and older (see **WARNINGS, Pediatric Use**).

#### Geriatric Use

Clinical studies of hydrocodone polistirex and chlorpheniramine polistirex extended-release did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

#### ADVERSE REACTIONS

##### Gastrointestinal Disorders

Nausea and vomiting may occur; they are more frequent in ambulatory than in recumbent patients. Prolonged administration of Tussicaps® extended-release capsules may produce constipation.

##### General Disorders and Administration Site Conditions

Death

##### Nervous System Disorders

Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, euphoria, dizziness, psychic dependence, mood changes.

##### Renal and Urinary Disorders

Ureteral spasm, spasm of vesical sphincters, and urinary retention have been reported with opiates.

##### Respiratory, Thoracic and Mediastinal Disorders

Dryness of the pharynx, occasional tightness of the chest, and respiratory depression (see **CONTRAINDICATIONS**).

Tussicaps® extended-release capsules may produce

dose-related respiratory depression by acting directly on brain stem respiratory centers (see **OVERDOSAGE**). Use of Tussicaps® in children less than 6 years of age has been associated with fatal respiratory depression. Overdose with Tussicaps® extended-release capsules in children 6 years of age and older, in adolescents, and in adults has been associated with fatal respiratory depression.

#### Skin and Subcutaneous Tissue Disorders

Rash, pruritus.

#### DRUG ABUSE AND DEPENDENCE

Tussicaps® extended-release capsules are Schedule III narcotics. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of narcotics; therefore, Tussicaps® extended-release capsules should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when Tussicaps® extended-release capsules are used for a short time for the treatment of cough. Physical dependence, the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome, assumes clinically significant proportions only after several weeks of continued oral narcotic use, although some mild degree of physical dependence may develop after a few days of narcotic therapy.

#### OVERDOSAGE

**Signs and Symptoms** – Serious overdosage with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. Although miosis is characteristic of narcotic overdose, mydriasis may occur in terminal narcosis or severe hypoxia. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur. The manifestations of chlorpheniramine overdosage may vary from central nervous system depression to stimulation.


**Treatment** – Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote for respiratory depression which may result from overdosage or unusual sensitivity to narcotics including hydrocodone. Therefore, an appropriate dose of naloxone hydrochloride should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of hydrocodone in this formulation may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration. For further information, see full prescribing information for naloxone hydrochloride. An antagonist should not be administered in the absence of clinically significant respiratory depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated. Gastric emptying may be useful in removing unabsorbed drug.

A Schedule CIII Narcotic.

#### For Medical Information

Contact: Product Monitoring Department  
Phone: 800-778-7898

Manufactured by:  
Mallinckrodt Inc.  
Hazelwood, Missouri  
63042 U.S.A.

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## Adapalene Advised for Mild, Moderate Acne

WASHINGTON — The newer topical retinoid adapalene is often the best front-line agent for the management of mild to moderate acne because it can be applied along with benzoyl peroxide, according to Dr. Richard J. Antaya.

Adapalene (Differin) “is a much more stable molecule, so you can apply it with other medications like benzoyl peroxide,” said Dr. Antaya, director of pediatric dermatology at Yale University in New Haven, Conn. “Retin-A gets broken down much more easily.”

Although a topical retinoid alone is effective for mild acne that is primarily comedonal, benzoyl peroxide (a topical antibacterial) should be added when the acne has a papulopustular component, he explained at the annual meeting of the American Academy of Pediatrics.

A topical antibiotic also should be part of the regimen if the acne is more severe at presentation or if it does not improve in 6-12 weeks of treatment with a retinoid and benzoyl peroxide.

Moisturizers are a critical part of acne management since all medications cause some degree of erythema, drying, or peeling. “With Tazorac [tazarotene, another newer-generation topical retinoid], because it’s so irritating, we’ve actually realized that if you put moisturizer on before the Tazorac, it actually slows the [drug’s] absorption and softens the blow so you get less irritation,” he noted.

Dr. Antaya said that he has had no financial relationships in the past year with any manufacturers of these products.

—Christine Kilgore