In Vitro

Benzoyl peroxide has a molecular weight of 242.23 and its chemical name is methyl 3-chloro-7,8-dihydro-5H-dibenzo [c,d]chromene-5-carboxylate. Clindamycin phosphate, C_17H_21ClIN_2O_4, has the following structural formula:

![Clindamycin Phosphate Structure](image)

Drug Resistance

There are reports of an increase of P. acnes resistance to clindamycin in the treatment of inflammatory acne in patients with P. acnes resistant to clindamycin. The clindamycin component may provide no additional benefit beyond benzoyl peroxide alone.

CLINICAL STUDIES

In four randomized, double-blind studies involving 1,139 patients, 397 used Duac, 398 used benzoyl peroxide, 349 used clindamycin, and 177 used vehicle. Patients were instructed to apply the medication once daily for 11 weeks, and then to apply medication twice daily for 4 additional weeks. The percentage of patients achieving 50% or greater reduction in inflammatory lesion counts was higher in the Duac group compared to benzoyl peroxide alone (47% vs. 32%) and clindamycin alone (47% vs. 32%). The clinical superiority of Duac compared to benzoyl peroxide and clindamycin alone was consistent across all studies. The Duac group showed greater overall improvement in the investigator’s global assessment than the benzoyl peroxide group in one of the five studies (Studies 1, 2, and 5).

INDICATIONS AND USAGE

Duac Topical Gel is indicated for the topical treatment of inflammatory acne vulgaris.

CONTRAINDICATIONS

Duac Topical Gel is contraindicated in those individuals who have shown hypersensitivity to any of its components or to its ingredients. It is also contraindicated for those having a history of regional enteritis, ulcerative colitis, pseudomembranous colitis, or other inflammatory intestinal disorders.

WARNINGS

ORAL AND PERORALLY ADMINISTERED CLINDAMYCN HAS BEEN ASSOCIATED WITH SEVERE COLITIS WHICH MAY RESULT IN PATIENT DEATH. USE OF THE TOPICAL FORMULATION OF CLINDAMYCN RESULTS IN ABSORPTION OF THE ANTIBIOTIC FROM THE SKIN SURFACE. DIARRHEA, BLOODY DIARRHEA, AND COLITIS (INCLUDING PSEUDOMEMBRANOUS COLITIS) HAVE BEEN REPORTED IN PATIENTS TREATED WITH THE USE OF TOPICAL CLINDAMYCN. STUDIES INDICATE A TOXIN PRODUCED BY CLOSTRIDIA IS ONE PRIMARY CAUSE OF BACTERIOLOGIC-ASSOCIATED COLITIS. THE COLITIS IS USUALLY CHRONIC, CATARRHAL, SEVERELY DIARRHEAL, AND Frequently associated with abdominal cramps and may be associated with the passage of blood and mucus. ENDOSCOPIC EXAMINATION MAY REVEAL PSEUDOMEMBRANOUS COLITIS. STOOL CULTURE FOR CLOSTRIDIUM CLOSTRIDIUM CLOSTRIDIUM LIVIDUM TOXIN MAY BE HELPFUL DIAGNOSTICALLY. WHEN SIGNIFICANT DIARRHEA OCCURS, THE DRUG SHOULD BE DISCONTINUED. LARGE BOWEL ENDOSCOPY SHOULD BE CONSIDERED TO ESTABLISH A DEFINITIVE DIAGNOSIS IN CASES OF SEVERE DIARRHEA. ANTIBIOTIC AGENTS SUCH AS AMpicillin AND DISOPhyldine WITH AMPRINE MAY PROLONG AND/OR WORSEN THE CONDITION. DIARRHEA, COLITIS AND PSEUDOMEMBRANOUS COLITIS HAVE BEEN REPORTED IN PATIENTS TREATED FOR SEVERAL WEEKS FOLLOWING CESSATION OF ORAL AND PARENTERAL THERAPY WITH CLINDAMYCN.

Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolyte substitution and treatment with an anti-bacterial drug clinically effective against Clostridium difficile infections.

PRECAUTIONS

General:

For dermatological use only; not for opthalmic use. Concomitant topical acne therapy should be used with caution because a possible cumulative irritant contact dermatitis effect may occur with the use of peeling, desquamating, or abrasive agents.

The use of antibiotics may be associated with the overgrowth of non- susceptible bacteria, particularly yeasts. If this occurs, discontinue use of this medication and take appropriate measures.

Advise contact with eyes and mucous membranes.

Clindamycin and erythromycin-containing products should not be used in combination with topical or systemic vitamin A derivatives. Use of the topical formulation of clindamycin results in antibiotic levels in the skin that may inhibit vitamin A action in these two antihormones. The clinical significance of this in vitro antibacterial action is not known.

Information for Patients: Patients using Duac Topical Gel should receive the following information and instructions:

1. Duac Topical Gel is to be used as directed by the physician. It is for external use only.

2. This medication should not be used for any disorder other than that for which it was prescribed.

3. Patients should not use any other acne topical preparation unless otherwise directed by their physician.

4. Patients should report any signs of local adverse reactions to their physician.

5. Duac Topical Gel may stain hair or colored fabric.

6. Duac Topical Gel can be stored at room temperature up to 25°C (77°F) for up to 2 months. Do not freeze. Keep out of the reach of small children. Discard any unused product after 2 months.

7. Before applying Duac Topical Gel to affected areas, wash the skin gently, rinse with warm water, and pat dry.

8. Excoriation or prolonged exposure to sunlight should be limited. To minimize exposure to sunlight, a hat or other clothing should be worn.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Benzoyl peroxide has been shown to be a very weak mutagen and a potential carcinogen in animal studies. The clinical significance of this is unknown.

Benzoyl peroxide is in solution at doses of 5 and 10 mg administered twice per week induced squamous cell skin tumors in transgenic Tg.AC mice in a study using 20 weeks of topical benzoyl peroxide treatment.

Genotoxicity studies were not conducted with Duac Topical Gel. Clindamycin phosphate was not genotoxic in Salmonella typhimurium or in rat micronucleus test. Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types, to be mutagenic in Salmonella typhimurium/Extraneous and mouse testes, and to inhibit micronucleus induction.

Mildly increased serum alkaline phosphatase and SGPT and SGOT levels in those having a history of regional enteritis, ulcerative colitis, or other inflammatory intestinal disorders. Absorption of the antibiotic from the skin surface. Diarrhea, blood dyscrasias, reduced bone mass, and pseudomembranous colitis have been reported in patients treated with the use of oral and parenteral therapy with clindamycin.

Severe. The percentage of patients that had symptoms present before treatment (at Baseline) were:

- 52% with symptom present
- 48% with symptom present

Use of antibiotic agents may be associated with the overgrowth of non-susceptible bacteria, particularly yeasts. If this occurs, discontinue use of this medication and take appropriate measures.

Adverse Effects:

1. Duac Topical Gel may cause skin irritation or burning.

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