**Topical Clindamycin For Acne Vulgaris: Pharmacovigilance Safety Review and Retrospective Analysis of Gastrointestinal Events**

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**SYNOPSIS**

- Clindamycin, a lincosamide antibiotic, was the 125th most prescribed medicine in the US in 2020.
- Topical formulations of clindamycin are combined with topical benzoyl peroxide (BPO) or a retinoid for acne vulgaris (AV) treatment.
- Oral clindamycin carries contraindications regarding the development of gastrointestinal (GI) adverse events (AEs) including Clostridium difficile (C. difficile) colitis.
- While topical formulations have similar warnings and contraindications, the real-world incidence of these AEs has not been studied.

**OBJECTIVE**

To summarize available safety data on topical clindamycin when used for AV treatment.

**METHODS**

- Safety data from published literature, previously unpublished pharmacovigilance data, and two unpublished retrospective case reports were reviewed, with a focus on gastrointestinal AEs following topical administration of clindamycin monotherapy or combination therapy for AV.

**RESULTS**

- **Case Reports**
  - METHODS: Case reports were identified through literature search on GI AEs associated with topical clindamycin use for AV treatment.
  - RESULTS: Only 4 case reports of topical clindamycin-associated GI AEs have been published; none were recent (1987 to 1997).
  - C. difficile pseudomembranous colitis
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  - Clindamycin HCl 1% and BPO 5% (separate formulations) bid
  - Diarrhea
  - Severe abdominal cramping + diarrhea
  - Clindamycin phosphate 1% (dose unknown)

- **Pharmacovigilance Data**
  - METHODS: World-wide pharmacovigilance data were analyzed from Jan 1, 2000 to Jan 31, 2021 for topical clindamycin monotherapy or combination therapy with BPO or tretinoin and GI ADRs.
  - RESULTS: Of the hundreds of millions patients exposed to topical clindamycin, <0.001% of patients reported GI ADRs, including colitis or IBD, over 10% of events were non-serious.
  - Patients worldwide exposed to topical clindamycin = 461,664,932

- **RESULTS: Rates of colitis/pseudomembranous colitis are low in patients with AV prescribed topical clindamycin**
  - Physicians prescribe clindamycin for AV treatment equally to patients with or without IBD history.
  - Study 1: Examined frequency of topical clindamycin prescriptions in patients:
    - With an AV diagnosis in the past year
    - With a history of inflammatory bowel disease (IBD), Crohn’s disease or ulcerative colitis
    - Without any prior topical clindamycin treatment
  - Study 2: Determined incidence of pseudomembranous colitis diagnoses in patients:
    - With an initial topical clindamycin prescription for AV therapy
    - Without a prior diagnosis of colitis

- **Conclusions**
  - A review of published case reports, worldwide pharmacovigilance data, retrospective US prescription data, and clinical trials safety data demonstrate that the incidence of colitis or pseudomembranous colitis in patients with or without IBD exposed to topical clindamycin is extremely low.
  - Global incidence of GI-related AEs (via pharmacovigilance) is estimated at 0.00004%
  - Rates of pseudomembranous colitis within 30 days of initial topical clindamycin prescription for AV (without concurrent oral clindamycin prescription) are <0.02%
  - Rates of GI AEs in pivotal clinical trials were similar to rates of topical clindamycin monotherapy (or combination) versus tretinoin, BPO, or vehicle.

**Clinical Trials**

- METHODS: Safety data for GI AEs were gathered from published articles indexed on PubMed® or from US FDA New Drug Applications® of pivotal clinical trials of topical clindamycin for AV.
  - 2,672 participants (safety populations) with AV treated with:
    - Clindamycin phosphate 1% or 1.2%
    - Clindamycin phosphate 1.2% + BPO 7.5%
    - Clindamycin phosphate 1.2% + tretinoin 0.025%
    - Clindamycin phosphate 1.2% + BPO 2.1%
  - 1,621 participants (safety populations) with AV treated with:
    - Tretinoin 0.025%
    - BPO 1.5%
    - Vehicle

- No severe cases of pseudomembranous colitis were found among patients treated with clindamycin for AV.

**REFERENCES**