Therapeutic Class Overview
Topical Benzoyl Peroxide and Antibiotic Combinations

Therapeutic Class

Overview/Summary: Acne vulgaris is a chronic inflammatory dermatosis characterized by open and/or closed comedones (blackheads and whiteheads) and inflammatory lesions including papules, pustules, or nodules.[1] The pathogenic factors that produce the various acne lesions include sebum production by the sebaceous gland, *Propionibacterium acnes (P acnes)* follicular colonization, alteration in the keratinization process, and the release of inflammatory mediators to the skin.[2,3]

Several options exist for the treatment of acne vulgaris including topical agents, systemic antibacterial agents, hormonal agents, isotretinoin, laser and light therapies, miscellaneous therapies, complementary/alternative therapies and dietary restrictions.[1] The topical benzoyl peroxide and antibiotic combination products include benzoyl peroxide/clindamycin (Acanya®, Benzaclin® and Duac®) and benzoyl peroxide/erythromycin (Benzamycin® and Benzamycin Pak®). The benzoyl peroxide/clindamycin products primarily differ in their respective strengths. Acanya® contains 2.5% benzoyl peroxide and 1.2% clindamycin, Benzaclin® contains 5% benzoyl peroxide and 1% clindamycin and Duac® contains 5% benzoyl peroxide and 1% (lotion) or 1.2% (gel) clindamycin depending on the formulation. All of these products are Food and Drug Administration approved for the treatment of acne vulgaris. Traditionally, the treatment of acne vulgaris has been directed toward controlling *P acnes* and centered on the use of antibiotics. Current treatment modalities are directed toward as many pathogenic factors as possible. Combination treatment has the ability to target multiple pathogenic factors, including inflammatory and noninflammatory lesions.[2] Data has shown that these agents result in faster and more complete clearing of acne vulgaris lesions compared with monotherapy.[2] Currently, Benzaclin®, Duac® (gel) and Benzamycin® are available generically.

Table 1. Current Medications Available in the Class[4-9]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Benzoyl peroxide/ clindamycin (Acanya®, Benzaclin®*, Duac®*)	Topical treatment of inflammatory acne vulgaris (Duac®), topical treatment of acne vulgaris (Acanya®, Benzaclin®)	Gel: 5%/1% (Benzaclin®) 5%/1.2% (Duac®) 2.5%/1.2% (Acanya®) Gel (pump): 5%/1% (Benzaclin®) Kit (includes cleansing lotion): 5%/1% (Duac CS®) 5%/1%/ hyaluronate liquid (Benzaclin®)	a *
Benzoyl peroxide/ erythromycin (Benzamycin®*, Benzamycin Pak®)	Topical treatment of acne vulgaris	Gel: 5%/3% (Benzamycin®) Pack: 5%/3% (Benzamycin Pak®)	-

*Generic available in at least one dosage form or strength.

Evidence-based Medicine

- There is limited evidence that differentiates the various formulations (gels, lotions, solutions, etc) and strengths of these agents. Clinical studies evaluating combination therapy with benzoyl peroxide and

either clindamycin or erythromycin have consistently demonstrated that these agents are more effective compared to their respective monotherapies.[10-14]

- In a study by Leyden et al (N=492), patients with moderate to severe acne vulgaris were randomized to receive benzoyl peroxide/clindamycin, benzoyl peroxide/erythromycin or benzoyl peroxide alone for 10 weeks. The decrease in the number of inflammatory lesions from baseline, the primary endpoint, was significantly greater for those treated with benzoyl peroxide/clindamycin compared to benzoyl peroxide alone (*P*=0.04). The average decrease in the number of inflammatory lesions was similar in patients treated with benzoyl peroxide/clindamycin and benzoyl peroxide/erythromycin (*P*=0.40).[15]
- In a meta-analysis by Seidler et al, there was a significantly greater percent reduction in noninflammatory acne lesion count with benzoyl peroxide/clindamycin 2.5%/1.2% (-43.4%; 95% CI depicted but not reported) compared to benzoyl peroxide/clindamycin 5%/1% (-38.2%; 95% CI depicted but not reported), benzoyl peroxide alone (-34.2%; 95% CI depicted but not reported), clindamycin alone (-27.9%; 95% CI depicted but not reported) and placebo (-14.9%; 95% CI depicted but not reported) over 10 to 12 weeks of treatment.[16]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - The combination of a topical retinoid and antimicrobial agent remains the preferred treatment approach for the majority of patients with acne vulgaris, especially in the presence of inflammatory lesions.[2]
  - Due to the risk of bacterial resistance, antibiotics should be used for the shortest duration and should only be used in combination with benzoyl peroxide. [2]
  - Topical antibiotics combined with benzoyl peroxide and a topical retinoid may be used in mild to moderate acne vulgaris; oral antibiotics are recommended for moderate to moderately severe acne vulgaris.[2]
  - Topical retinoids alone or in combination with benzoyl peroxide is recommended for the maintenance of acne vulgaris. [2]
  - Long term antibiotic use may be required in the rare cases in which the patient experiences acne vulgaris flares when oral antibiotics are discontinued. [2]
- Other Key Facts:
  - The current benzoyl peroxide/clindamycin products available generically are Benzaclin® and Duac® (gel). Benzoyl peroxide/erythromycin gel (Benzamycin®) is available generically.[17]

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Therapeutic Class Review
Topical Benzoyl Peroxide and Antibiotic Combinations

Overview/Summary

Acne vulgaris is a chronic inflammatory dermatosis characterized by open and/or closed comedones (blackheads and whiteheads) and inflammatory lesions including papules, pustules, or nodules.[1] Four primary pathogenic factors interact in a complex manner to produce the various acne lesions. These four factors include sebum production by the sebaceous gland, *Propionibacterium acnes (P acnes)* follicular colonization, alteration in the keratinization process, and the release of inflammatory mediators to the skin.[2,3]

Several options exist for the treatment of acne vulgaris including topical agents, systemic antibacterial agents, hormonal agents, isotretinoin, laser and light therapies, miscellaneous therapies, complementary/alternative therapies, and dietary restrictions.[1] The focus of this review will be on the benzoyl peroxide and antibiotic combination products. These agents include benzoyl peroxide/clindamycin (Acanya®, Benzaclin® and Duac®) and benzoyl peroxide/erythromycin (Benzamycin® and Benzamycin Pak®). The benzoyl peroxide/clindamycin products primarily differ in their respective strengths. Acanya® contains 2.5% benzoyl peroxide and 1.2% clindamycin, Benzaclin® contains 5% benzoyl peroxide and 1% clindamycin and Duac® contains 5% benzoyl peroxide and 1% (lotion) or 1.2% (gel) clindamycin depending on the formulation. All of these products are Food and Drug Administration approved for the treatment of acne vulgaris. Traditionally, the treatment of acne vulgaris has been directed toward controlling *P acnes* and centered on the use of antibiotics. Current treatment modalities are directed toward as many pathogenic factors as possible. Combination treatment has the ability to target multiple pathogenic factors, including inflammatory and noninflammatory lesions.[2] Data has shown that these agents result in faster and more complete clearing of acne vulgaris lesions compared with monotherapy.[2] Currently, Benzaclin®, Duac® (gel) and Benzamycin® are available generically.

Treatment recommendations vary based upon the severity and type of acne being treated. Topical treatments are the standard of care for acne treatment.[1] Topical retinoids are the first, or part of the first choice treatment regimens for most types and severities of acne. Other non-retinoid topical agents include, but not limited to, azelaic acid, benzoyl peroxide, clindamycin, and erythromycin. Bacterial resistance is a concern when treating with systemic and topical antibiotics, therefore monotherapy is discouraged. However pairing an antibiotic with benzoyl peroxide is an effective option that targets *P acnes* while minimizing the development of bacterial resistance. Current guidelines strongly recommend adding benzoyl peroxide to retinoids when long-term antimicrobial use is necessary due to its efficient bactericidal properties. Generally topical combination products are indicated in patients with mild to moderate acne vulgaris with an inflammatory component.[2]

Medications

Table 1. Medications Included Within Class Review

Generic Name (Trade name)	Medication Class	Generic Availability
Combination Products		
Benzoyl peroxide/clindamycin (Acanya®, Benzaclin®*, Duac®*)	Topical antibacterial	a
Benzoyl peroxide/erythromycin (Benzamycin®*, Benzamycin Pak®)	Topical antibacterial	a

*Generic available in at least one dosage form or strength.

Indications

Table 2. Food and Drug Administration Approved Indications[4-8]

Generic Name	Topical Treatment of Inflammatory Acne Vulgaris	Topical Treatment of Acne Vulgaris
Combination Products		
Benzoyl peroxide/clindamycin	a (Duac®)	a (Acanya®, Benzaclin®)
Benzoyl peroxide/erythromycin		a

Topical clindamycin/benzoyl peroxide has been used off-label for the treatment of rosacea. Guidelines recognize that topical clindamycin/benzoyl peroxide may be more effective that clindamycin alone.[9]

Pharmacokinetics

Table 3. Pharmacokinetics[4-9]

Generic Name	Absorption (%)	Renal Excretion (%)	Active Metabolites	Serum Half-Life (hours)
Combination Products				
Benzoyl peroxide/ clindamycin	<2/<1-5	As benzoate in the urine (% not available)/ not reported	Benzoic acid/ not reported	Not reported
Benzoyl peroxide/ erythromycin	<2/ Not reported	As benzoate in the urine (% not available)/ not reported	Benzoic acid/ not reported	Not reported

*The kinetics for the combination products listed in Table 1 but not listed here are the same as single entity product(s) that they contain and is listed above.

Clinical Trials

Clinical studies demonstrating the safety and efficacy of the topical benzoyl peroxide and antibiotic combination products in their respective Food and Drug Administration-approved indications are described in Table 4.[10-24]

There is limited evidence that differentiates the various formulations (gels, lotions, solutions, etc) and strengths of these agents. Clinical studies evaluating combination therapy with benzoyl peroxide and either clindamycin or erythromycin have consistently demonstrated that these agents are more effective compared to their respective monotherapies.[10-12,14,19]

In a study by Leyden et al (N=492) patients with moderate to severe acne vulgaris were randomized to receive benzoyl peroxide/clindamycin, benzoyl peroxide/erythromycin or benzoyl peroxide alone for 10 weeks. The decrease in the number of inflammatory lesions from baseline, the primary endpoint, was significantly greater for those treated with benzoyl peroxide/clindamycin compared to benzoyl peroxide alone (*P*=0.04). The average decrease in the number of inflammatory lesions was similar in patients treated with benzoyl peroxide/clindamycin and benzoyl peroxide/erythromycin (*P*=0.40).[20]

In a meta-analysis by Seidler et al, there was a significantly greater percent reduction in noninflammatory acne lesion count with benzoyl peroxide/clindamycin 2.5%/1.2% (-43.4%; 95% CI depicted but not reported) compared to benzoyl peroxide/clindamycin 5%/1% (-38.2%; 95% CI depicted but not reported), benzoyl peroxide alone (-34.2%; 95% CI depicted but not reported), clindamycin alone (-27.9%; 95% CI depicted but not reported) and placebo (-14.9%; 95% CI depicted but not reported) over 10 to 12 weeks of treatment.[23]

Table 4. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Acne Vulgaris – Combination Treatment				
Lookingbill et al[10] Benzoyl peroxide/ clindamycin 5%/1% gel applied QD vs clindamycin 1% gel vs benzoyl peroxide 5% gel vs vehicle gel	AC, DB, MC, PC, PG, VC Patients 13 to 30 years of age with ≥12 inflammatory lesions (papules and pustules) and ≥12 noninflammatory lesions (open and closed comedones) and ≤3 nodulocystic lesions	N=393 11 weeks	Primary: Lesion counts (inflammatory and noninflammatory), global improvement (0 to 4 scale) Secondary: Safety (adverse events and tolerance scores)	Primary: By week 11, significantly greater reductions in inflammatory lesions were observed in patients treated with benzoyl peroxide/clindamycin, clindamycin, and benzoyl peroxide as compared to those treated with vehicle gel ($P \leq 0.002$ for all compared to vehicle). Treatment with benzoyl peroxide/clindamycin resulted in significantly greater average percent reductions than either individual agent alone ($P < 0.02$). Results comparing clindamycin to benzoyl peroxide were similar. Significantly greater average percent reductions in noninflammatory lesions were observed in all treatment groups compared to vehicle, as early as week two for benzoyl peroxide/clindamycin, week five for benzoyl peroxide and week 11 for clindamycin ($P \leq 0.004$, $P \leq 0.005$ and $P = 0.04$ respectively). Treatment with benzoyl peroxide/clindamycin and benzoyl peroxide resulted in significantly greater reductions compared to clindamycin treatment ($P \leq 0.01$); however, the differences between the benzoyl peroxide products were not statistically significant. Significantly more patients treated with benzoyl peroxide/clindamycin, clindamycin and benzoyl peroxide achieved “good” or “excellent” responses on the global improvement scale compared patients treated with vehicle gel ($P \leq 0.001$ for each to vehicle). Treatment with benzoyl peroxide/clindamycin resulted in significantly greater improvement than either individual agent alone ($P \leq 0.001$). Secondary: No significant differences were found between the treatments in terms of local irritant effects. Treatment with benzoyl peroxide/clindamycin and benzoyl peroxide resulted in significantly more peeling compared to clindamycin ($P < 0.02$).
Webster et al[11] Benzoyl peroxide/	DB, MC, PG, RCT Patients ≥12 years	N=2,813 (2,282 with moderate	Primary: Absolute change in the number of	Primary: In patients with moderate acne, the reduction in the median number of inflammatory and noninflammatory lesions was significantly greater at 12 weeks

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
clindamycin 2.0%/1.2% gel applied QD vs clindamycin 1.2% gel applied QD vs benzoyl peroxide 2.5% gel applied QD vs vehicle gel applied QD	of age with moderate to severe acne vulgaris (score of 3 or 4 on the EGSS), with 17 to 40 inflammatory lesions, 20 to 100 noninflammatory lesions and ≤2 nodules	acne and 531 with severe acne) 12 weeks	inflammatory and noninflammatory lesion counts from baseline to week 12, percent of patients with a ≥2-grade improvement on the EGSS (treatment success) Secondary: Absolute change in total lesion counts	for patients treated with benzoyl peroxide/clindamycin (68 and 50%, respectively) compared to those treated with clindamycin alone (55.6 and 41.3%, respectively; *P*<0.001 and *P*=0.001), benzoyl peroxide (57.7% and 43.6%, respectively; *P*<0.001, *P*=0.001) and vehicle (36.4 and 25.0%, respectively; *P*<0.001 for both). In patients with severe acne, the median number of inflammatory and noninflammatory lesions was significantly reduced in patients treated with benzoyl peroxide/clindamycin (48.7 and 45.1%, respectively) compared to those treated with vehicle for 12 weeks (23.9 and 26.6%, respectively; *P*<0.001 for both). At week 12, 32.3% of patients with moderate acne who were treated with benzoyl peroxide/clindamycin had a ≥2-grade improvement in EGSS compared to those treated with clindamycin alone (24.3%; *P*=0.001)), benzoyl peroxide alone (23.5%; *P*<0.001) and vehicle (14.7%; *P*<0.001). At week 12, 32.3% of patients with severe acne who were treated with benzoyl peroxide/clindamycin experienced a ≥2-grade improvement in EGSS, which was significantly greater than those treated with clindamycin (34.6%; *P*=0.040) and vehicle (23.7%; *P*=0.001). Secondary: In patients with moderate acne, there was a significantly greater reduction in total lesion counts at 12 weeks for patients treated with benzoyl peroxide/ clindamycin (54.1%), compared to those treated with clindamycin, (45.2%; *P*<0.001), benzoyl peroxide (47.1%; *P*<0.001) and vehicle (29.7%; *P*<0.001). In patients with severe acne, there was a 44.4% median reduction in total lesion counts at 12 weeks in patients treated with benzoyl peroxide/clindamycin, which was significantly greater than those treated with vehicle (19.4%; *P*<0.001).
Thiboutot et al[12] Benzoyl peroxide/ clindamycin 2.0%/1.2%	DB, MC, PG, RCT Patients ≥12 years of age with	N=2,813 12 weeks	Primary: Absolute change in inflammatory and	Primary: The benzoyl peroxide/clindamycin group had a significantly greater reduction (14.2) in inflammatory lesions compared to each monotherapy treatment group at week 12 (*P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
gel applied QD vs clindamycin 1.2% gel applied QD vs benzoyl peroxide 2.5% gel applied QD vs vehicle gel applied QD	moderate to severe acne vulgaris (score of 3 or 4 on the EGSS), with 17 to 40 inflammatory lesions, 20 to 100 noninflammatory lesions and ≤2 nodules		noninflammatory lesion counts from baseline to week 12, percent of patients with a ≥2-grade improvement on the EGSS (treatment success) Secondary: Percent change in inflammatory and noninflammatory lesion counts, absolute and percent change in total lesion counts, frequency of adverse events	The benzoyl peroxide/clindamycin treatment group experienced a significantly greater reduction (20.5) in noninflammatory lesions compared to the monotherapy treatment groups (*P*<0.001). At week 12, 35% of patients treated with benzoyl peroxide/clindamycin had a ≥2-grade improvement in EGSS which was significantly higher compared to patients treated with clindamycin alone (26%), benzoyl peroxide alone (26%) or vehicle gel (-17.0%; *P*<0.001 for all). Secondary: At week 12, patients treated with benzoyl peroxide/clindamycin experienced a significantly greater reduction in inflammatory lesions (54.6%) compared to clindamycin, benzoyl peroxide and vehicle gel (46.2, 47.5 and 29.0%, respectively; *P*<0.001). At week 12, the benzoyl peroxide/clindamycin group had a significantly greater reduction in noninflammatory lesions (43.2%) compared to clindamycin, benzoyl peroxide and vehicle gel (36.2, 37.4 and 24.0%, respectively; *P*<0.001). Overall adverse events were reported in 5.9% of the benzoyl peroxide/ clindamycin group, 4.3% of the clindamycin group, 5.9% of the benzoyl peroxide group and 6.1% of the vehicle group. Overall, >97.0% of adverse events reported were considered mild to moderate in severity.
Thiboutot et al[13] Benzoyl peroxide/ erythromycin 5%/3% Pak applied BID (BPE Pak) vs vehicle Pak applied BID	DB, MC, PG, RCT Patients ≥12 years of age, with 15 to 80 facial lesions, 20 to 140 comedones, ≤2 nodules or cysts >5 mm and a PGAS score of ≥1.5	N=327 8 weeks	Primary: Lesion counts (total, inflammatory [papules or pustules], noninflammatory [comedones]) Secondary:	Primary: Treatment with benzoyl peroxide/erythromycin Pak resulted in reductions in total, inflammatory and noninflammatory lesions as compared to the vehicle Pak (*P*≤0.001). Significantly more patients in the benzoyl peroxide/erythromycin Pak group achieved treatment success compared to patients in the vehicle Pak group (*P* value not reported). Absolute and percent reductions in total lesions were similar between patients treated with benzoyl peroxide/erythromycin Pak and benzoyl peroxide/erythromycin jar (*P* value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
(VC Pak) vs benzoyl peroxide/ erythromycin 5%/3% jar applied BID (BPE jar) vs vehicle jar applied BID (VC jar)			PGAS, facial-oiliness scores, global improvement and treatment acceptability by patients	Absolute and proportional reductions in inflammatory lesions were similar between patients treated with benzoyl peroxide/erythromycin Pak and benzoyl peroxide/erythromycin jar (*P* value not reported). Proportional reductions in noninflammatory lesions were similar between patients treated with benzoyl peroxide/erythromycin Pak and benzoyl peroxide/erythromycin jar (*P* value not reported). Rates of patients achieving treatment success were similar between treatment with benzoyl peroxide/erythromycin Pak and benzoyl peroxide/erythromycin Jar (*P* values not reported). Secondary: Treatment with benzoyl peroxide/erythromycin Pak resulted in significantly greater improvement on all secondary variables as compared to treatment with vehicle Pak (PGAS; $P \leq 0.002$, facial oiliness scores; $P \leq 0.035$, patient global improvement scores; $P < 0.001$). Evaluation of secondary variable showed that treatment with benzoyl peroxide/erythromycin Pak and benzoyl peroxide/erythromycin Jar resulted in similar results (*P* value not reported).
Chalker et al (abstract)[14] Benzoyl peroxide/ erythromycin 5%/3% gel vs benzoyl peroxide 5% gel vs erythromycin 3% gel	DB, RCT Patients with acne vulgaris	N=165 10 weeks	Primary: Lesion counts Secondary: Not reported	Primary: Benzoyl peroxide and erythromycin treatments were more effective than vehicle treatment alone in reducing lesion counts in patients with acne vulgaris. Combination benzoyl peroxide/erythromycin was more effective than either single agent alone in reducing lesion counts in patients with acne vulgaris. Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs gel vehicle				
Zeichner et al[15] Benzoyl peroxide/ clindamycin 2.5%/1% gel applied QAM plus tretinoin 0.05% gel applied QPM	OL Patients ≥12 years of age with stable, mild acne vulgaris graded as 2 or 3 on a 6-point PGA	N=20 12 weeks	Primary: Treatment success (defined as a score of 0 or 1 on 6-point PGA) Secondary: Tolerability, irritation and safety	Primary: Sixty percent of patients were considered to have a treatment success following 12 weeks of therapy (*P* value not reported). Secondary: The majority of patients reported scores of “none” or “mild” for all tolerability parameters. At week two, 65% and 35% of patients experience “none” or mild burning, respectively. The proportion of patients who reported “none” or “mild” dryness, respectively, was 55% and 45%. Fifty five percent and 40% of patients respectively, reported “none” or “mild” scaling and 75% and 25%, respectively, reported scaling. By week four, 95% of patients reported “none or “mild“ erythema, dryness, scaling, burning or stinging. Tolerability issues were resolved in a majority of patients by week 12. Three adverse events occurred in three patients over the treatment period, all of which were considered mild and treatment-related. Two patients reported mild application site burning while one patient experienced an increase in the number of acne lesions.
Langner et al[16] Benzoyl peroxide/ clindamycin 5%/1% gel applied QD vs adapalene 0.1% gel applied QD	AC, MC, PG, RCT, SB Patients 12 to 39 years of age with mild to moderate acne vulgaris with ≥15 inflammatory and/or noninflammatory lesions but ≤3 nodulocystic	N=130 12 weeks	Primary: Noninflammatory and inflammatory lesion counts, physician and patient reported acne severity and adverse events Secondary: Not reported	Primary: Treatment with benzoyl peroxide/clindamycin was associated with a statistically significant reduction from baseline in total lesion count at week 12 (*P*<0.005). Combination treatment was associated with significantly fewer total lesions at all points evaluated throughout the study (*P*≤0.005 for all time points). Patients receiving treatment with benzoyl peroxide/clindamycin experienced statistically significant reductions in inflammatory lesions throughout the evaluation period compared to adapalene (*P*≤0.001 for all time points). The combination of benzoyl peroxide/clindamycin significantly improved the number of noninflammatory lesions compared to adapalene at week eight and

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	lesions and an acne grade of 2 to 7			week 12 (*P*≤0.05). Acne grade improved in both treatment groups; however, this improvement was greater with benzoyl peroxide/clindamycin compared to adapalene as early as week one (*P*=0.013) and was maintained throughout the study (*P*<0.038). Furthermore, there was a statistically significant improvement in physician-assessed severity with benzoyl peroxide/clindamycin as early as week one of treatment compared to adapalene (*P*≤0.007). The percentage of patients that rated themselves as "improved" increased was 90% by the end of the study for both treatment groups. As with physicians rating, the proportion improved was greater early in treatment (weeks 1one through eight) with combination therapy compared to adapalene (*P*<0.005). Overall, 77.0% of patients in the benzoyl peroxide/clindamycin group were rated as having "good" or "excellent" tolerance compared to 52.3% of patients in the adapalene group. The number of patients who reported at least one treatment-emergent adverse event was 32.3% in the benzoyl peroxide/clindamycin group compared to 30.8% of patients receiving adapalene (*P* value not reported).
Ko et al[17] Benzoyl peroxide/ clindamycin 5%/1% gel applied QD vs adapalene 0.1% gel applied QD	AC, OL, PRO, RCT Patients ≥12 years of age with more than 12 inflammatory lesions ≤3 nodules or cysts, ≥12 noninflammatory lesions and an acne grade of ≥2.0 and < 7.0 according to Leeds revised acne grading	N=69 12 weeks	Primary: Change in total lesions, inflammatory lesions, noninflammatory lesions, acne severity, perception of global improvement Secondary: Not reported	Primary: The benzoyl peroxide/clindamycin combination was associated with statistically significant reductions in inflammatory lesions (*P*=0.0165) and total lesions compared to adapalene gel (*P*=0.0258) at 12 weeks. There was no statistically significant difference between the groups at week 12 with regard to the number of noninflammatory lesions (*P* value not reported). Acne grade improved for both treatment groups according to Leeds revised acne grading; however, there was only a statistically significant difference at weeks two and four which favored benzoyl peroxide/clindamycin (*P*≤0.05 for both). Both treatments reduced KSGS-2 scores from baseline; however, the difference between treatments was only statistically significant at week two (*P*≤0.05 favoring benzoyl peroxide/clindamycin gel over adapalene).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				The global improvement scale rated two (much improved) and three (very much improved) in 68% of the benzoyl peroxide/clindamycin group and 61% in adapalene group (*P* value not reported). Both treatments were well tolerated with minimal adverse events, such as erythema, dry skin, desquamation, stinging/burning sensation and pruritus. Most adverse events occurred within a one month of treatment and generally lasts less than one month. Secondary: Not reported
Guerra-Tapia et al[18] Benzoyl peroxide/ clindamycin 5%/1% gel applied QHS vs adapalene 0.1% gel applied QHS	AC, PG, RCT, SB Patients 12 to 39 years of age with ≥15 inflammatory lesions and/or noninflammatory lesions but ≤3 nodulocystic lesions and an acne grade of ≥2.0 and <7.0 on the Leeds Revised Acne Grading System	N=168 12 weeks	Primary: Change in global Skindex-29 QOL scores from baseline to week two Secondary: Change in global Skindex-29 QOL scores from baseline to week 12, correlation between scores and lesion counts at week two, absolute change and percentage change in total lesion counts at all weeks, clinical evaluation of acne at all weeks,	Primary: The mean change in global Skindex-29 score at week two was significantly greater for patients treated with benzoyl peroxide/clindamycin compared to adapalene (-4.9 vs -1.1; *P*<0.001). Secondary: The mean reduction in global Skindex-29 score at week 12 was significantly greater for patients treated with benzoyl peroxide/clindamycin compared to adapalene (-6.8 vs -2.6; *P*<0.001). There was no correlation between inflammatory, noninflammatory or total lesion count and global Skindex-29 score. There was a significant correlation between benzoyl peroxide/clindamycin-treated patients and emotional subdomain scores and total and noninflammatory lesion counts (*P*=0.0307 and *P*=0.0186). Similarly there was a significant correlation between the overall global Skindex-29 score and total lesion count (*P*=0.0429). The reduction from baseline in total and inflammatory lesions was significant with benzoyl peroxide/clindamycin at all time points (*P*≤0.05). Compared to adapalene, the change in lesion count significantly, and favored benzoyl peroxide/clindamycin at week eight (*P*=0.006) and week 12 (*P*=0.010). The change in absolute lesion counts was significantly greater for patients

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			change in acne grade, subject self evaluation of improvement and tolerability	treated with benzoyl peroxide/clindamycin compared to adapalene at weeks 4, 8 and 12 ($P \leq 0.008$). Inflammatory lesions were significantly improved with benzoyl peroxide/clindamycin compared to adapalene at all time points evaluated with the exception of week two ($P \leq 0.012$). Noninflammatory lesions were significantly reduced from baseline with benzoyl peroxide/clindamycin compared to adapalene at weeks four ($P=0.032$) and eight ($P=0.032$). Statistically significant differences in investigator ratings scores favored benzoyl peroxide/clindamycin compared to adapalene at week eight ($P=0.0022$) and week 12 ($P=0.0103$). Patient reported improvement in acne severity was significantly higher with benzoyl peroxide/clindamycin compared to adapalene at week one and week eight ($P<0.01$ for both). Patient acne grade improved in both treatment groups over time; however, the improvement was significantly greater with benzoyl peroxide/clindamycin compared to adapalene at week eight ($P=0.0158$) and week 12 ($P=0.0031$). At week 12, a significantly higher proportion of patients treated with benzoyl peroxide/clindamycin reported "excellent" tolerability compared to patients treated with adapalene (42 vs 20%; $P<0.0001$). Investigator-rated and patient-rated tolerability was significantly higher in patients treated with benzoyl peroxide/clindamycin with regard to peeling ($P \leq 0.0036$), erythema ($P \leq 0.0127$) and dryness ($P \leq 0.0286$). Sixteen percent of patients treated with benzoyl peroxide/clindamycin experienced at least one treatment-emergent adverse event compared to 26% of patients receiving adapalene. The most commonly reported adverse events include erythema, exfoliation, pruritus, irritation and eczema. No serious adverse events or deaths were reported.
Cunliffe et al[19] Benzoyl peroxide/	DB, PG, RCT, SB Patients 13 to 30	N=790 16 weeks	Primary: Percent change in lesion counts	Primary: Both treatments resulted in significant reductions from baseline in total lesion counts, number of inflammatory lesions and number of comedones.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
clindamycin 5%/1% gel applied BID vs clindamycin 1% gel applied BID	years of age with mild to moderate acne, 15-100 comedones, 15-100 inflammatory lesions, ≤2 nodules/cysts on the face and *P acnes* counts ≥10^4 CFU/cm^2 of skin		(total, inflammatory and comedones), physician's CGI score Secondary; Antimicrobial assessment (counts of total and clindamycin-resistant *P acnes* and coag-neg *S aureus),* patient CGI score, tolerability; association between bacterial counts and efficacy (post-hoc)	The use of benzoyl peroxide/clindamycin resulted in significantly greater reductions in median total lesion counts compared to clindamycin alone (*P*=0.013). The median percent reductions in inflammatory lesions (*P*=0.014) and comedones (*P*=0.018) from baseline were significantly greater in the combination group compared to the monotherapy group. Average physician CGI scores were significantly greater in the benzoyl peroxide/clindamycin group compared to the monotherapy group at week 16 (*P*=0.041). Secondary: Benzoyl peroxide/clindamycin resulted in significantly better antimicrobial efficacy compared to clindamycin at week 16 (*P*≤0.004). The use of benzoyl peroxide/clindamycin resulted in significantly fewer resistant *P acnes* counts (*P*=0.018). The use of benzoyl peroxide/clindamycin resulted in significantly fewer resistant coag-neg *S aureus* counts (*P*≤0.003). There were no significant differences between the benzoyl peroxide/clindamycin treatment group and monotherapy treatment in patient CGI scores or treatment acceptability scores. Significant associations were observed between percent change from baseline in total lesion counts and comedone counts with a change in baseline in total *P acnes* counts (*P*<0.001 for both).
Leyden et al[20] Benzoyl peroxide/ clindamycin 5%/1% applied BID	MC, PG, RCT, SB Patients 13 to 30 years of age, with moderate to	N=492 10 weeks	Primary: Reduction from baseline in the number of inflammatory	Primary: All treatments resulted in a decrease in average number of inflammatory lesions (*P* value not reported). The average decrease in the number of inflammatory lesions was significantly

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs benzoyl peroxide 5% applied BID vs benzoyl peroxide/ erythromycin 5%/3% applied BID	moderately severe acne, with 10 to 80 inflammatory lesions (papules and pustules) and 10 to 100 comedones in the facial area		lesions, physician evaluation of overall improvement as percent change from baseline, patient assessment of efficacy and adverse events Secondary: Not reported	greater in those treated with benzoyl peroxide/clindamycin compared to benzoyl peroxide alone (*P*=0.04). The average decrease in the number of inflammatory lesions was similar in patients treated with benzoyl peroxide/clindamycin and benzoyl peroxide/erythromycin (*P*=0.40). Physician assessment indicated improvement with all treatments. At week 10, physician assessment of improvement was significantly greater for those treated with benzoyl peroxide/clindamycin compared to those treated with benzoyl peroxide (*P*=0.04); however, there was no difference compared to benzoyl peroxide/clindamycin (*P* value not reported). Patient assessment at week 10 indicated that benzoyl peroxide/clindamycin was associated with a statistically significant improvement in acne compared to with benzoyl peroxide alone (*P*<0.001); however, there was no difference compared to benzoyl peroxide/clindamycin (*P* value not reported). Dry skin was the most frequently reported adverse event and was reported at a similar rate across the benzoyl peroxide/clindamycin (4.8%), benzoyl peroxide/erythromycin (4.3%) and benzoyl peroxide (7.3%) groups (*P* values not reported). Secondary: Not reported
Jackson et al[21] Benzoyl peroxide/ clindamycin 5%/1% gel applied QPM vs clindamycin/ tretinoin 1.2%/0.025% gel applied QPM	MC, PG, RCT, SB Patients ≥12 years of age with moderate to severe facial acne vulgaris and 15 to 100 facial inflammatory lesions, 15 to 100 noninflammatory lesions and ≤2 facial nodules	N=54 16 weeks	Primary: Antimicrobial efficacy, lesion counts, IGA and overall disease severity Secondary: Not reported	Primary: At 16 weeks, there was a significantly greater reduction in *P. acnes* count with benzoyl peroxide/clindamycin compared to clindamycin/tretinoin (-1.84 vs -0.78 $\log_{10}$ CFU/cm^2; *P*=0.003). There was a similar change from baseline in inflammatory lesions between patients receiving benzoyl peroxide/clindamycin compared to clindamycin/tretinoin at 16 weeks (-74.1 vs 70.7%; *P* value not reported). The reduction in noninflammatory lesions was also similar between the benzoyl peroxide/clindamycin and clindamycin/tretinoin treatment groups (53.3 vs 52.8%; *P* value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				The percentage change in the total number of inflammatory lesions was similar between patients randomized to receive benzoyl peroxide/clindamycin compared to those receiving clindamycin/tretinoin for 16 weeks (-52.4 vs -54.3%; *P* value not reported). The IGA results were similar between the benzoyl peroxide/clindamycin and the clindamycin/tretinoin treatment groups with regard to patients who showed improvement in at least one category (60.0 vs 62.5%; *P* value not reported). Overall disease severity was considered to be comparable between the two treatment groups with 80 and 87.55 of patients showing improvement, respectively.
Draelos et al[22] Benzoyl peroxide/ clindamycin 5%/1% gel applied BID plus tretinoin 0.025% cream applied QHS vs benzoyl peroxide 5.5% applied BID plus tretinoin 0.025% cream applied QHS	AC, DB, MC, RCT Patients 18 to 50 years of age with mild to moderate acne	N=66 12 weeks	Primary: Lesion counts, tolerability, skin appearance, skin irritation Secondary: Not reported	Primary: Both treatments significantly reduced noninflammatory and inflammatory lesion counts at treatment weeks 4, 8, 12 and 16 as compared to baseline (*P*<0.05 for both). The benzoyl peroxide/clindamycin /tretinoin combination demonstrated a statistically significant reduction in open comedones at week two (*P*<0.05); however, there was no significant difference in the benzoyl peroxide/tretinoin treatment group. Treatment with benzoyl peroxide/tretinoin demonstrated a statistically significant reduction in pustules at week two (*P*<0.05); however, there was no statistically significant difference in the benzoyl peroxide/clindamycin/tretinoin treatment group. Treatment with benzoyl peroxide/tretinoin significantly increased investigator-assessed erythema compared with baseline at week two (*P*=0.042); however, no change was observed with benzoyl peroxide/clindamycin/tretinoin. Compared to baseline, a statistically significant increase in dryness and peeling was noted in both treatment groups at week two and week four (*P*<0.05 for all). Participant reported a statistically significant increase with both treatments in stinging (*P*<0.001 for both), tingling (*P*≤0.007 for both), itching (*P*<0.05 for both), and burning (both *P*<0.001) at week two compared to baseline. Symptoms persisted at week four, with the exception of an insignificant difference in itching in both treatments and in tingling for benzoyl

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				peroxide/tretinoin. Participant-assessed irritation had largely resolved by week eight in both groups.
Seidler et al[23] Benzoyl peroxide/ clindamycin 5%/1% vs benzoyl peroxide/ clindamycin 2.5%/1.2% vs benzoyl peroxide 2.5% or 5% vs clindamycin 1% or 1.2%	MA (16 RCTs) Randomized controlled trials of patients treated with combination benzoyl peroxide/ clindamycin 1%/5% or 1.2%/2.5% and included end points of actual reduction and/or percent reduction of inflammatory and/or noninflammatory lesion counts	N=5,737 Up to 12 weeks	Primary: Percent reduction and absolute reduction in noninflammatory and inflammatory lesion counts Secondary: Not reported	At weeks 10 through 12, there was a significantly greater percent reduction in noninflammatory lesion count with benzoyl peroxide/clindamycin 2.5%/1.2% (-43.4%; 95% CI depicted but not reported) compared to benzoyl peroxide/clindamycin 5%/1% (-38.2%; 95% CI depicted but not reported), benzoyl peroxide (-34.2%; 95% CI depicted but not reported), clindamycin (-27.9%; 95% CI depicted but not reported) and placebo (-14.9%; 95% CI depicted but not reported). In inflammatory lesion count, benzoyl peroxide/clindamycin 2.5%/1.2% and benzoyl peroxide/clindamycin 5%/1% had similar percent reductions in lesions (-54.2 vs -56.3%, respectively) with overlapping confidence intervals and were not statistically different. The reductions in inflammatory lesion count were -46.0% with benzoyl peroxide, 41.7% with clindamycin and -22.0% with placebo. The weighted mean reductions in noninflammatory lesion count were -38.2% benzoyl peroxide/clindamycin 5%/1%, -43.4% with benzoyl peroxide/ clindamycin 2.5%/1.2%, -34.2% with benzoyl peroxide, -27.9% with clindamycin and -14.9% with placebo. Weighted absolute reductions in inflammatory lesion count were -14.81 with benzoyl peroxide/clindamycin 5%/1%, -25.37 with benzoyl peroxide/clindamycin 2.5%/1.2%, -11.60 with benzoyl peroxide, -11.03 with clindamycin and -5.89 with placebo. Weighted absolute reductions in noninflammatory lesion count were -16.83 with benzoyl peroxide/clindamycin 5%/1%, -20.83 with benzoyl peroxide/clindamycin 2.5%/1.2%, -15.07 with benzoyl peroxide, -12.50 with clindamycin and -7.61 with placebo. Secondary: Not reported
Seidler et al[24]	MA (23 RCTs)	N=7,309	Primary:	Primary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Benzoyl peroxide/ clindamycin (both 5%/1% and 2.5%/1.2%) vs benzoyl peroxide/ salicylic acid 5%/2% vs benzoyl peroxide 5% vs clindamycin 1% or 1.2%	Studies with at least one treatment arm with 5%benzyl peroxide (either with or without salicylic acid), 1% to 1.2% clindamycin, or combination benzoyl peroxide/ clindamycin as part of a RCT for acne vulgaris and efficacy end points of actual lesion reduction and/or percent lesion reduction at 2 to 4 weeks and/or 10 to 12 weeks	Up to 12 weeks	Percent reduction in inflammatory lesions and noninflammatory lesions at two to four weeks and 10 to 12 weeks Secondary: Not reported	At two to four weeks, the mean percent reduction in inflammatory lesions was 55.22% (95% CI, 50.72 to 59.72) with benzoyl peroxide/salicylic acid, 40.74% (95% CI, 37.3 to 44.24) with benzoyl peroxide/clindamycin, 33.38% (95% CI, 29.37 to 37.40) with benzoyl peroxide, 21.52% (95% CI, 17.47 to 25.57) with clindamycin and 7.26% (95% CI, -3.03 to 17.55) with placebo. At two to four weeks, the mean percent reduction in noninflammatory lesions was 42.71% (95% CI, 39.33 to 46.10) with benzoyl peroxide/salicylic acid, 26.21% (95% CI, 22.16 to 30.26) with benzoyl peroxide/clindamycin, 19.12% (95% CI, 14.06 to 24.18) with benzoyl peroxide, 9.99% (95% CI, 5.01 to 14.96) with clindamycin and 6.65% (95% CI, -0.68 to 13.98) with placebo. At weeks 10 to 12 the mean percent reduction in inflammatory lesions was 55.58% (95% CI, 53.59 to 57.56) with benzoyl peroxide/clindamycin, 51.77% (95% CI, 43.08 to 60.45) with benzoyl peroxide/salicylic acid, 45.91% (95% CI, 42.77 to 49.05) with clindamycin, 43.72% (95% CI, 41.13 to 46.32) with benzoyl peroxide and 26.76% (95% CI, 21.65 to 31.88) with placebo. At weeks 10 to 12 the mean percent reduction in noninflammatory lesions was 47.75% (95% CI, 40.49 to 55.01) with benzoyl peroxide/salicylic acid, 40.30% (95% CI, 37.02 to 43.58) with benzoyl peroxide/clindamycin, 32.60% (95% CI, 27.86 to 37.35) with clindamycin, 30.88% (95% CI, 25.61 to 36.16) with benzoyl peroxide and 17.04% (95% CI, 11.70 to 22.38) with placebo. Secondary: Not reported

Study abbreviations: AC=active-controlled, CCT=controlled clinical trial, DB=double-blind, IB=investigator-blind, MC=multicenter, OL=open-label, PC=placebo-controlled, PG=parallel group, RCT=randomized controlled trial, SB=single-blind, SC=single-center, VC=vehicle-controlled
Miscellaneous abbreviations: CGI=Clinical Global Improvement, CII=Cumulative irritancy Index (sum of the irritation score/number of readings), EGSS=Evaluator Global Severity Score, GAAS=Global Acne Assessment Score, PGAS=Physician's Global Acne Severity score

Special Populations

Table 5. Special Populations[4-9]

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Combination Products					
Benzoyl peroxide/ clindamycin	Safety and efficacy in elderly patients have not been established. Safety and efficacy in patients under the age of 12 have not been established.	Not reported	Not reported	C	Unknown; use with caution.
Benzoyl peroxide/ erythromycin	Safety and efficacy in elderly patients have not been established. Safety and efficacy in patients under the age of 12 have not been established.	Not reported	Not reported	C	Unknown; use with caution.

*The impact on special populations for the combination products listed in Table 1 but not listed here are the same as the single entity product(s) that they contain and is listed above.

Adverse Drug Events

Table 6. Adverse Drug Events (%)[4-9]

Adverse Event(s)	Combination Products*	
	Benzoyl peroxide/ Clindamycin (%)	Benzoyl peroxide/ Erythromycin (%)
Dermatological		
Allergic reaction	-	-
Application site pain	0.1*	-
Application site exfoliation	0.1*	-
Blepharitis	-	<2
Burning	<1 to 5‡	0.8 to 2.5
Dry skin/dryness	12 to 15†‡	5.0 to 7.6
Edema	-	a
Erythema	1†, 5 to 26‡	0.8 to 2.5
Inflammation	-	a
Irritation	0.1*	a
Itching	6 to 15*	a
Oily skin/oiliness	-	a
Peeling	2 to 17‡	<1
Photosensitivity	-	<2
Pruritus	2†	<2
Scaling	8 to 18*	-
Skin discoloration	-	a
Stinging	1 to 6*	0.8 to 2.5
Sun burn	1†	-
Tenderness	-	a

- Event not reported
a % not specified.
*Acanya®

Contraindications

Table 7. Contraindications[4-9]

Contraindication	Benzoyl peroxide/ Clindamycin	Benzoyl peroxide/ Erythromycin
History of hypersensitivity to erythromycin, clindamycin, linomycin, benzoyl peroxide, or to any of its components	a	a
Patients with a history of regional enteritis, ulcerative colitis or antibiotic-associated colitis.	a	-

Warnings/Precautions

Table 8. Warnings and Precautions[4-9]

Warning/Precaution	Benzoyl peroxide/ Clindamycin	Benzoyl peroxide/ Erythromycin
Orally and parenterally administered antibacterial agents, including erythromycin and clindamycin have been associated with severe colitis, which may result in patient death	a	a
Use concomitant topical acne therapy with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents	a	a
Use externally only	a	a
The use of antibiotic agents (especially prolonged or repeated therapy) may be associated with the overgrowth of nonsusceptible organisms including fungi.	a	a
Benzoyl peroxide has been shown to be a tumor promoter and progression agent in a number of animal studies. The clinical significance of this is unknown.	a	-
Minimized sun exposure following drug application	a	-

Drug Interactions

Table 9. Drug Interactions[4-9]

Generic Name	Interacting Medication or Disease	Potential Result
Benzoyl peroxide/ clindamycin	Erythromycin	Clindamycin should not be used in combination with topical or oral erythromycin-containing products *In vitro* studies have shown antagonism between erythromycin and clindamycin.

Dosage and Administration

Table 10. Dosing and Administration[4-9]

Generic Name	Adult Dose	Pediatric Dose	Availability
Combination Products			

Generic Name	Adult Dose	Pediatric Dose	Availability
Benzoyl peroxide/ clindamycin	Topical treatment of acne vulgaris: 5%/1% gel (Benzaclin®): Apply twice daily, morning and evening after skin is gently washed, rinsed and dried 5%/1.2% gel (Duac®): Apply to the face once-daily in the evening 2.5%/1.2% gel (Acanya®): Apply to the face once-daily	Safety and efficacy in patients under the age of 12 have not been established.	Gel: 5%/1% (Benzaclin®) 5%/1.2% (Duac®) 2.5%/1.2% (Acanya®) Gel (pump): 5%/1% (Benzaclin®) Kit (includes cleansing lotion): 5%/1% (Duac CS®) 5%/1%/ hyaluronate liquid (Benzaclin®)
Benzoyl peroxide/ erythromycin	Topical treatment of acne vulgaris: 5%/3% gel, packs: Apply twice daily, morning and evening after skin is gently washed, rinsed and dried	Safety and efficacy in patients under the age of 12 have not been established.	Gel: 5%/3% (Benzamycin®) Pack: 5%/3% (Benzamycin Pak®)

Clinical Guidelines

Table 11. Clinical Guidelines

Clinical Guideline	Recommendations
American Academy of Dermatology (AAD): **New Insights into the Management of Acne: An Update from the Global Alliance to Improve Outcomes in Acne Group (2009)**[2]	· Acne vulgaris should be managed early and aggressively as a chronic disease to limit scarring. The disease is self-limiting in only 60% of cases. · Oral isotretinoin, the most effective acne vulgaris treatment, is administered during a 20-week period and sometimes must be given in repeated courses. · The combination of a topical retinoid and antimicrobial agent remains the preferred treatment approach for the majority of patients with acne vulgaris, especially in the presence of inflammatory lesions. · Due to the risk of bacterial resistance, antibiotics should be used for the shortest duration and should only be used in combination with benzoyl peroxide. · Topical antibiotics combined with benzoyl peroxide and a topical retinoid may be used in mild to moderate acne vulgaris; oral antibiotics are recommended for moderate to moderately severe acne vulgaris. · Topical retinoids alone or in combination with benzoyl peroxide is recommended for the maintenance of acne vulgaris. · Long term antibiotic use may be required in the rare cases in which the patient experiences acne vulgaris flares when oral antibiotics are discontinued. Global alliance acne vulgaris treatment algorithm · Topical retinoids are considered first-line treatment for mild acne vulgaris (comedonal). Treatment alternatives include azelaic acid or salicylic acid are considered alternatives. · For mild acne vulgaris (mixed and papular/pustular), treatment with a topical retinoid and a topical antimicrobial is considered first-line; treatment with alternative topical retinoid and alternative topical antimicrobial, or azelaic acid are considered alternatives. · For moderate acne vulgaris (mixed and papular/pustular), treatment with an oral antibiotic and a topical retinoid with or without benzoyl peroxide is

Clinical Guideline	Recommendations
	considered first-line therapy. Treatment with an alternative oral antibiotic and alternative topical retinoid with or without benzoyl peroxide are considered alternatives. · For moderate acne vulgaris vulgaris (nodular), treatment with an oral antibiotic and a topical retinoid and benzoyl peroxide is considered first-line treatment; treatment with oral isotretinoin or alternate oral antibiotic and an alternate topical retinoid (with or without) benzoyl peroxide/azelaic acid are considered alternatives. · For severe acne (nodular/conglobate), treatment with oral isotretinoin is considered initial treatment. Treatment with high dose oral antibiotic and a topical retinoid and benzoyl peroxide are considered alternative. · For maintenance therapy (mild to severe acne vulgaris), treatment with a topical retinoid with or without benzoyl peroxide is considered first–line treatment.
AAD: **Guidelines of Care for Acne Vulgaris Management (2007)[3]**	<u>Standard of care</u> · Topical therapy is the standard of care in acne vulgaris treatment. · Systemic antibiotics are used in moderate to severe acne vulgaris and treatment-resistant forms of inflammatory acne vulgaris. · Intralesional corticosteroid injections are effective for large inflammatory lesions. <u>Topical therapy</u> · Topical retinoids reduce obstruction within the follicle and are useful in the management of both comedonal and inflammatory acne vulgaris. · The relative efficacy between topical retinoids (i.e., tretinoin, adapalene, tazarotene, isotretinoin [not available topically in the United States]) is unclear. · Benzoyl peroxide is a bactericidal agent with the ability to prevent or eliminate the development of *P acnes* resistance, and is therefore used in combination with oral or topical antibiotics. · Topical antibiotics (erythromycin and clindamycin) are effective in the treatment of acne vulgaris but are more effective when used in combination with benzoyl peroxide due to a synergy as well as the resulting elimination or reduction of bacterial resistance. · Salicylic acid has moderately effective and less potent comedolytic properties than topical retinoids and is therefore used in patients intolerant to dermatological effects caused by topical retinoids. · Azelaic acid has shown to be effective, with comedoyltic and antibacterial properties. · The role of aluminum chloride, resorcinol, sodium sulfacetamide, sulfur and zinc in the management of acne vulgaris is unclear due to limited clinical evidence and/or peer-reviewed literature. <u>Systemic antibiotics</u> · Doxycycline and minocycline are more effective than tetracycline. · Minocycline has been shown to be superior to doxycycline in reducing *P acnes*. · Erythromycin is effective but associated with bacterial resistance and therefore its use should be limited to those who cannot tolerate tetracyclines (i.e., pregnant women and children <8 years old due to the potential damage to the skeleton or teeth). <u>Hormonal agents</u>

Clinical Guideline	Recommendations
	· Oral contraceptives containing norgestimate with ethinyl estradiol and norethindrone acetate with ethinyl estradiol are Food and Drug Administration (FDA)-approved for the management of acne vulgaris. Isotretinoin · Isotretinoin, a vitamin A derivative, is approved for the treatment of severe recalcitrant nodular acne vulgaris and possibly effective in treatment-resistant acne vulgaris or acne vulgaris producing physical or psychological scarring. · Since isotretinoin is a potent teratogenic, females of child-bearing age must only be treated if they are participating in the approved pregnancy prevention and management program (iPLEDGE).

Conclusions

The topical benzoyl peroxide and antibiotic combination products include benzoyl peroxide/clindamycin (Acanya®, Benzaclin® and Duac®) and benzoyl peroxide/erythromycin (Benzamycin® and Benzamycin Pak®).[4-8] All of these products are Food and Drug Administration-approved for the topical treatment of acne vulgaris. The benzoyl peroxide/clindamycin products primarily differ in their respective strengths. Acanya® contains 2.5% benzoyl peroxide and 1.2% clindamycin, Benzaclin® contains 5% benzoyl peroxide and 1% clindamycin and Duac® contains 5% benzoyl peroxide and 1% (lotion) or 1.2% (gel) clindamycin depending on the formulation. Currently Benzaclin®, Duac® (gel) and Benzamycin® are available generically.[25]

The benzoyl peroxide and antibiotic combination agents are effective for the treatment of acne vulgaris. Combination treatment, with benzoyl peroxide and either clindamycin or erythromycin has been shown to be more effective than treatment with each individual agent alone.[10-12,14,19] In addition, clinical studies have not demonstrated one agent to be more effective than another with regard to improvements in the number of acne lesions.[20] Current clinical guidelines support the use of combination treatment in order to limit the development of bacterial resistance.[2,3]

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