TOPICAL CLINDAMYCIN PRODUCTS:
ACANYA® (clindamycin phosphate-benzoyl peroxide) gel
BENZA CLIN® (clindamycin phosphate-benzoyl peroxide) gel
CLEOCIN-T® (clindamycin phosphate) gel, lotion, solution, swab
CLINDAGEL® (clindamycin phosphate) gel
DUAC® (clindamycin phosphate-benzoyl peroxide) gel
EVOCLIN® (clindamycin phosphate 1%) foam
NEUAC™ (clindamycin phosphate-benzoyl peroxide) gel (kit is a plan exclusion)
ONEXTON™ (clindamycin phosphate-benzoyl peroxide) gel

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:
Clindamycin phosphate alone or in combination with benzoyl peroxide is indicated for the topical treatment of acne vulgaris.
The pathogenesis of acne is multifactorial and includes hyperkeratinization of follicles, bacterial infectious process, production of sebum, androgens, and inflammation. Acne vulgaris is a chronic inflammatory dermatologic condition notable for open and/or closed comedones (blackheads – dark or blackish bumps; and whiteheads – tiny white bumps) and inflammatory lesions including papules (small, firm, may be painful pink bumps), pustules (small, may be painful bumps with pus), or nodules/cysts (large, hard, inflamed and painful bumps). Acne pimples occur on the face, neck, chest, shoulders, back, and upper arms caused by clogged pores due to excessive sebum (oil) production.

The prevalent bacterium implicated in acne is *Propionibacterium acnes* (*P acnes*), a gram-positive anaerobe that is normally found on the skin and is implicated in the inflammatory phase of acne. *P acnes* promotes lesions by secreting chemotactic factors that attract leukocytes to the follicle resulting in inflammation.

All anti-acne agents are effective in reducing inflammatory and non-inflammatory lesions when compared to placebo based on many years of clinical experience, multiple systematic reviews, and clinical practice guidelines. There is no evidence that confirms superiority of any one branded option over available brand or generic alternatives, including available over-the-counter (OTC) products. All anti-acne products have adequate track records of safety; most are generally well tolerated, but all cause skin irritation.

Published guidelines on the treatment of acne consistently recommend the use of topical antimicrobial, topical retinoid, azeleic acid, benzoyl peroxide, dapsone, and combination topical products, oral antibiotics or oral isotretinoin. The guidelines do not differentiate between branded options over other brand or generic options.

The American Academy of Dermatology has published guidelines for the care of acne vulgaris. The guidelines indicate that topical therapy is a standard of care in treatment and that topical retinoids and topical antibiotics are effective treatments. The effectiveness of topical retinoids in the treatment of acne is well documented. These agents act to reduce obstruction within the follicle and are useful in the management of both comedonal and inflammatory acne. The value of topical antibiotics in the treatment of acne has been investigated in many clinical trials. Topical erythromycin and clindamycin have been demonstrated to be effective and well tolerated. A combination of topical retinoids and topical erythromycin or clindamycin is more effective than either agent used alone.

Both Veltin® and Ziana® are topical acne products with 1.2% clindamycin phosphate and 0.025% tretinoin in an aqueous based gel. Each gram contains, as dispensed, 10mg (1%) clindamycin and 0.25mg (0.025%) tretinoin. Clindamycin phosphate and tretinoin are also available separately as topical preparations for the treatment of acne. (For coverage criteria for Veltin and Ziana see Topical Retinoid and Combination Products Pharmacy Coverage Guidelines.)

There are many acne medications that are available as generic products in a variety of different formulations (gels, lotions, creams, ointments, solutions, and foams). The choice of delivery system (formulation) can be dependent on skin type (dry versus oily), site of application, and preference. Creams and lotions are useful for dry skin, gels and solutions are generally better for oily skin.
Definitions:

Drug related events:

**Ineffective / failure**
Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

**Adverse Drug Event: Allergic reaction / Hypersensitivity / Intolerance**
Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record.

*Allergic reaction / hypersensitivity* – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline.

*Intolerance* – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record.

**Contraindication**
Use of a drug that is not recommended by the manufacturer or FDA labelling

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer’s labelled recommendation and is considered investigational or experimental.

**Non-adherence**
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record.
Precertification:

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states’ Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Criteria:

- Cleocin-T (clindamycin phosphate) gel, lotion, solution, swab
- Clindagel (clindamycin phosphate) gel
- Evoclin (clindamycin phosphate 1%) foam

See “Resources” section for FDA-approved dosage.

- Precertification for Cleocin-T, Clindagel, and Evoclin requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.

- **Initial therapy:** FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Cleocin-T, Clindagel, and Evoclin is considered *medically necessary* when ALL of the following criteria are met:

1. Individual is 12 years of age or older

2. Medical record documentation of a confirmed diagnosis of acne vulgaris

3. Individual is unable to use ALL of the following *topical acne products* due to either inadequate response, hypersensitivity or intolerance:
   - One topical over-the-counter acne product
   - All covered topical clindamycin products
   - All covered topical erythromycin or topical sulfacetamide products
   - All covered topical adapalene or topical tretinoin products

4. Absence of ALL of the following contraindications:
   - Hypersensitivity to clindamycin or lincomycin
   - History of antibiotic-associated colitis (including pseudomembranous colitis)
TOPICAL CLINDAMYCIN PRODUCTS (cont.)

- Colitis
- History of regional enteritis or Crohn’s disease
- Ulcerative colitis

5. Absence of ALL of the following exclusions:
   - Use in combination with erythromycin-containing products

- **Continuation of coverage (renewal request):** Cleocin-T, Clindagel, and Evoclin is considered *medically necessary* with documentation of ALL of the following:

   1. The individual has benefited from therapy but remains at high risk
   2. The condition has not progressed or worsened while on therapy
   3. Individual has not developed any contraindications or other exclusions to its continued use

- **Cleocin-T, Clindagel, and Evoclin** for all other indications not previously listed is considered *experimental or investigational* based upon:

   1. Lack of final approval from the Food and Drug Administration, and
   2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
   3. Insufficient evidence to support improvement of the net health outcome, and
   4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
   5. Insufficient evidence to support improvement outside the investigational setting.

**Criteria:**
- Acanya (clindamycin phosphate-benzoyl peroxide) gel
- Benzaclin (clindamycin phosphate-benzoyl peroxide) gel
- Duac (clindamycin phosphate-benzoyl peroxide) gel
- Neuac (clindamycin phosphate-benzoyl peroxide) gel (kit is a plan exclusion)
- Onexton (clindamycin phosphate-benzoyl peroxide) gel

See “Resources” section for FDA-approved dosage.

- Precertification for Acanya, Benzaclin, Duac, Neuac and Onexton requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.

- **Initial therapy:** FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Acanya, Benzaclin, Duac, Neuac and Onexton is considered *medically necessary* when ALL of the following criteria are met:

   1. Individual is 12 years of age or older
   2. Medical record documentation of a confirmed diagnosis of acne vulgaris
TOPICAL CLINDAMYCIN PRODUCTS (cont.)

3. Individual is unable to use **ALL** of the following **topical acne products** due to either inadequate response, hypersensitivity or intolerance to:
   - One topical over-the-counter acne product
   - All covered topical clindamycin products
   - All covered topical erythromycin or topical sulfacetamide products
   - All covered topical adapalene or topical tretinoin products
   - All covered topical clindamycin products used simultaneously with topical benzoyl peroxide

4. Absence of **ALL** of the following contraindications:
   - Hypersensitivity to clindamycin or lincomycin
   - Hypersensitivity to benzoyl peroxide
   - History of antibiotic-associated colitis (including pseudomembranous colitis)
   - Colitis
   - History of regional enteritis or Crohn’s disease
   - Ulcerative colitis

5. Absence of **ALL** of the following exclusions:
   - Use in combination with erythromycin-containing products

**Continuation of coverage (renewal request):** Acanya, Benzaclin, Duac, Neuac and Onexton is considered **medically necessary** with documentation of **ALL** of the following:

1. The individual has benefited from therapy but remains at high risk
2. The condition has not progressed or worsened while on therapy
3. Individual has not developed any contraindications or other exclusions to its continued use

**Acanya, Benzaclin, Duac, Neuac and Onexton** for all other indications not previously listed is considered **experimental or investigational** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

**Resources:**


TOPICAL CLINDAMYCIN PRODUCTS (cont.)


FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<tbody>
<tr>
<td>ACANYA Gel is a lincosamide antibiotic and benzoyl peroxide indicated for</td>
<td>• Apply a pea-sized amount of ACANYA Gel to the face once daily.</td>
</tr>
<tr>
<td>the topical treatment of acne vulgaris.</td>
<td>• Not for oral, ophthalmic, or intravaginal use.</td>
</tr>
<tr>
<td>BENZACLIN Topical Gel is indicated for the topical treatment of acne</td>
<td>BenzaCln Topical Gel should be applied twice daily, morning and evening, or as</td>
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<tr>
<td>vulgaris.</td>
<td>directed by a physician, to affected areas after the skin is gently washed,</td>
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<tr>
<td></td>
<td>rinsed with warm water and patted dry.</td>
</tr>
<tr>
<td>CLEOCIN T Topical Solution, CLEOCIN T Topical Gel and CLEOCIN T Topical</td>
<td>Apply a thin film of CLEOCIN T Topical Solution, CLEOCIN T Topical Lotion,</td>
</tr>
<tr>
<td>Lotion are indicated in the treatment of acne vulgaris.</td>
<td>CLEOCIN T Topical Gel, or use a pledge for the application of CLEOCIN T twice</td>
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<tr>
<td></td>
<td>daily to affected area. More than one pledge may be used. Each pledge should be</td>
</tr>
<tr>
<td></td>
<td>used only once and then be discarded.</td>
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<tr>
<td></td>
<td>Lotion: Shake well immediately before using.</td>
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<tr>
<td></td>
<td>Pledge: Remove pledge from foil just before use. Do not use if the seal is</td>
</tr>
<tr>
<td></td>
<td>broken. Discard after single use.</td>
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<tr>
<td></td>
<td>Keep all liquid dosage forms in containers tightly closed.</td>
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</table>
**CLINDAGEL** is indicated for topical application in the treatment of acne vulgaris.

- Apply a thin film of Clindagel once daily to the skin where acne lesions appear. Use enough to cover the entire affected area lightly.
- Keep container tightly closed.

**DUAC Gel** is a combination of clindamycin phosphate (a lincosamide antibacterial) and benzoyl peroxide indicated for the topical treatment of inflammatory acne vulgaris.

**Limitation of Use:**
DUAC Gel has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

- Apply a thin layer of DUAC Gel to the face once daily, in the evening.
- Not for oral, ophthalmic, or intravaginal use.

**EVOCLIN Foam** is a lincosamide product indicated for acne vulgaris in patients 12 years and older.

- For topical use only; not for oral, ophthalmic, or intravaginal use.
- Apply EVOCLIN Foam once daily to affected areas.
- Flammable; avoid fire, flame and/or smoking during and immediately following application.

**NEUAC (clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/5%** is indicated for the topical treatment of inflammatory acne vulgaris.

- Apply a pea-sized amount of ONEXTON Gel to the face once daily.
- Not for oral, ophthalmic, or intravaginal use.