ONEXTON® (clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/3.75% is indicated for the topical treatment of acne vulgaris in patients 12 years of age and older. (1)

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**INDICATIONS AND USAGE**

ONEXTON Gel is a combination of clindamycin phosphate (a lincosamide antibacterial) and benzoyl peroxide indicated for the topical treatment of acne vulgaris in patients 12 years of age and older. (1)

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**CONTRAINDICATIONS**

- Patients who have demonstrated hypersensitivity (e.g., anaphylaxis) to clindamycin, benzoyl peroxide, any components of the formulation, or lincomycin. (4.1)
- Patients with a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis. (4.2)

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**ADVERSE REACTIONS**

The most common adverse reactions are: burning sensation (0.4%); contact dermatitis (0.4%); pruritus (0.4%); and rash (0.4%). (6.1)

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**WARNINGS AND PRECAUTIONS**

- Colitis: Clindamycin can cause severe colitis, which may result in death. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of clindamycin. ONEXTON Gel should be discontinued if significant diarrhea occurs. (5.1)
- Ultraviolet Light and Environmental Exposure: Minimize sun exposure following drug application. (5.2)

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**DRUG INTERACTIONS**

- Avoid using ONEXTON Gel in combination with topical or oral erythromycin-containing products because of its clindamycin component. (7.1)

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**USE IN SPECIFIC POPULATIONS**

- Pregnancy
- Lactation
- Pediatric Use
- Geriatric Use

---

**DESCRIPTION**

12 CLINICAL PHARMACOLOGY
- 12.1 Mechanism of Action
- 12.3 Pharmacokinetics
- 12.4 Microbiology

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**NONCLINICAL TOXICOLOGY**

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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**SIDE EFFECTS**

- Burning sensation (0.4%); contact dermatitis (0.4%); pruritus (0.4%); and rash (0.4%). (6.1)

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**CLINICAL STUDIES**

16.1 How Supplied/STORAGE AND HANDLING
- 16.2 Dispensing Instructions for the Pharmacist
- 16.3 Storage and Handling

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**PATIENT COUNSELING INFORMATION**

*Sections or subsections omitted from the full prescribing information are not listed.*
Table 1: Percent of Subjects with Local Skin Reactions. Results from the Phase 3 Trial (N = 243)

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Before Treatment (Baseline)</th>
<th>During Treatment</th>
<th>End of Treatment (Week 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Mod.</td>
<td>Severe</td>
</tr>
<tr>
<td>Erythema</td>
<td>20</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Scaling</td>
<td>10</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Itching</td>
<td>14</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Burning</td>
<td>5</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Soreness</td>
<td>5</td>
<td>&lt;1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Mod. = Moderate

6.2 Postmarketing Experience
Because postmarketing adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Anaphylaxis, as well as allergic reactions leading to hospitalizations, has been reported in postmarketing use of products containing clindamycin phosphate/benzoyl peroxide.

7 DRUG INTERACTIONS
7.1 Erythromycin
Avoid using ONEXTON Gel in combination with topical or oral erythromycin-containing products due to its clindamycin component. In vitro studies have shown antagonism between erythromycin and clindamycin. The clinical significance of this in vitro antagonism is not known.

7.2 Neuromuscular Blocking Agents
Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. ONEXTON Gel should be used with caution in patients receiving such agents.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy

Risk Summary
There are no available data on ONEXTON Gel use in pregnant women to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. The limited published data on use of clindamycin in pregnant women with exposure during the first trimester are insufficient to inform a drug-associated risk of pregnancy-related adverse outcomes (see Data). In limited published clinical trials with pregnant women, the systemic administration of clindamycin during the second and third trimesters has not been associated with an increased frequency of major birth defects. In animal reproduction studies, clindamycin did not cause malformations or embryo-fetal development toxicity in pregnant rats and mice when administered during the period of organogenesis at systemic doses up to 240 times the maximum recommended human dose (MRHD) of 2.5 g ONEXTON Gel, based on body surface area (BSA) comparisons (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of major birth defects, loss, and other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data
Human Data
In limited published trials in pregnant women administered clindamycin during the first trimester of pregnancy, there was no difference in the rate of major birth defects reported among in utero exposed infants compared to unexposed infants. These data cannot definitively establish or exclude any clindamycin-associated risk during pregnancy.

Animal Data
Animal reproductive/developmental toxicity studies have not been conducted with ONEXTON Gel or benzoyl peroxide. Developmental toxicity studies of clindamycin performed in pregnant rats and mice administered during the period of organogenesis at oral doses of up to 600 mg/kg/day (240 and 120 times the MRHD for clindamycin, respectively, based on BSA comparisons) or subcutaneous doses of up to 200 mg/kg/day (80 and 40 times the MRHD for clindamycin, respectively, based on BSA comparisons) revealed no malformations or embryo-fetal development toxicity.

8.2 Lactation

Risk Summary
There are no data on the presence of clindamycin or benzoyl peroxide in human milk, the effects on the breastfed child, or the effects on milk production following topical administration. However, clindamycin has been reported to be present in breast milk in small amounts following oral and parenteral administration. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ONEXTON Gel and any potential adverse effects on the breastfed child from ONEXTON Gel or from the underlying maternal condition.

Clinical Considerations
If used during lactation and ONEXTON Gel is applied to the chest, care should be taken to avoid accidental ingestion by the infant.

8.4 Pediatric Use
Safety and effectiveness of ONEXTON Gel in pediatric patients under the age of 12 years have not been evaluated.

8.5 Geriatric Use
Clinical trials of ONEXTON Gel did not include sufficient numbers of subjects age 65 years and older to determine whether they respond differently from younger subjects.

11 DESCRIPTION
ONEXTON Gel is a combination product with two active ingredients in a white to off-white, opaque, smooth, aqeous gel formulation intended for topical use. Clindamycin phosphate is a water-soluble ester of the semisynthetic antibiotic produced by a 7-(3-chloro-substitution of the 7(R)-hydroxy group of the parent antibiotic lincomycin. The chemical name for clindamycin phosphate is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-trans-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-threo-octopyranoside 2-(dihydrogen phosphate). The structural formula for clindamycin phosphate is represented below:

Clindamycin phosphate:

Molecular Formula: C_{36}H_{54}Cl_{2}O_{9}PS
Molecular Weight: 504.97

Benzoyl peroxide is an antibacterial and keratolytic agent. The structural formula for benzoyl peroxide is represented below:

Benzoyl peroxide:

Molecular Formula: C_{10}H_{12}O_{4}
Molecular Weight: 242.23

ONEXTON Gel contains the following inactive ingredients: carboxer 980, potassium hydroxide, propylene glycol, and purified water. Each gram of ONEXTON Gel contains 12 mg (1.2%) clindamycin phosphate, equivalent to 10 mg (1%) clindamycin, and 37.5 mg (3.75%) benzoyl peroxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Clindamycin: Clindamycin is a lincosamide antibacterial (see Microbiology (12.4)).

Benzoyl Peroxide: Benzoyl peroxide is an oxidizing agent with bactericidal and keratolytic effects but the precise mechanism of action is unknown.

12.3 Pharmacokinetics
The systemic absorption of ONEXTON Gel has not been evaluated. The systemic absorption of clindamycin was investigated in an open-label, multiple-dose trial in 16 adult subjects with moderate to severe acne vulgaris treated with 1 gram of a marketed gel containing clindamycin 1%/benzoyl peroxide 2.5% applied to the face once daily for 30 days. This product has the same formulation as ONEXTON Gel but with a lower concentration of benzoyl peroxide. Twelve subjects (75%) had at least one quantifiable clindamycin plasma concentration above the lower limit of quantification (LOQ = 0.5 ng/mL) on Day 1 or Day 30. On Day 1, the mean (± standard deviation) peak plasma concentrations (C_{max}) was 0.78 ± 0.22 ng/mL (n=9 with measurable concentrations), and the mean AUC_{0-24} was 5.29 ± 0.81 h ng/mL (n=4). On Day 30, the mean C_{max} was 1.22 ± 0.88 ng/mL (n=10), and the mean AUC_{0-24} was 8.42 ± 6.01 h ng/mL (n=6). Clindamycin plasma concentrations were below LOQ in all subjects at 24 hours post-dose on the three tested days (Day 1, 15, and 30).

Benzoyl peroxide has been shown to be absorbed by the skin where it is converted to benzoic acid.

12.4 Microbiology
Clindamycin binds to the 50S ribosomal subunits of susceptible bacteria and prevents elongation of peptide chains by interfering with peptidyl transfer, thereby suppressing bacterial protein synthesis.

Clindamycin and benzoyl peroxide individually have been shown to have in vitro activity against Propionibacterium acnes, an organism which has been associated with acne vulgaris. In an in vitro study, the minimum inhibitory concentration (MIC) for benzoyl peroxide against Propionibacterium acnes is 128 mg/L. The clinical significance of this activity against P. acnes is not known.

P. acnes resistance to clindamycin has been documented. Resistance to clindamycin is often associated with resistance to erythromycin.
The results of the trial at Week 12 are presented in Table 3:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>Normal, clear skin with no evidence of acne</td>
</tr>
<tr>
<td>Almost Clear</td>
<td>Rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red)</td>
</tr>
<tr>
<td>Mild</td>
<td>Some non-inflammatory lesions are present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)</td>
</tr>
<tr>
<td>Moderate</td>
<td>Non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and there may or may not be one small nodulocystic lesion</td>
</tr>
<tr>
<td>Severe</td>
<td>Inflammatory lesions are more apparent, many comedones and papules/pustules, there may or may not be up to 2 nodulocystic lesions</td>
</tr>
<tr>
<td>Very Severe</td>
<td>Highly inflammatory lesions predominate, variable number of comedones, many papules/pustules and more than 2 nodulocystic lesions</td>
</tr>
</tbody>
</table>

The EGS scoring scale used in the clinical trial for ONEXTON Gel is as follows:

Table 2: EGS Scoring Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>Normal, clear skin with no evidence of acne</td>
</tr>
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<td>Rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red)</td>
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</tr>
</tbody>
</table>

The results of the trial at Week 12 are presented in Table 3:

<table>
<thead>
<tr>
<th></th>
<th>ONEXTON Gel N = 293</th>
<th>Vehicle Gel N = 245</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EGSS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear or Almost Clear</td>
<td>29%</td>
<td>15%</td>
</tr>
<tr>
<td>2-grade reduction from baseline</td>
<td>35%</td>
<td>17%</td>
</tr>
<tr>
<td><strong>Inflammatory Lesions:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean absolute reduction</td>
<td>16.3</td>
<td>8.2</td>
</tr>
<tr>
<td>Mean percent (%) reduction</td>
<td>60.4%</td>
<td>31.3%</td>
</tr>
<tr>
<td><strong>Non-Inflammatory Lesions:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean absolute reduction</td>
<td>19.2</td>
<td>9.6</td>
</tr>
<tr>
<td>Mean percent (%) reduction</td>
<td>51.8%</td>
<td>27.6%</td>
</tr>
</tbody>
</table>
**Important information:** ONEXTON Gel is for use on skin only (topical use). Do not use ONEXTON Gel in your mouth, eyes, or vagina.

**What is ONEXTON Gel?**
ONEXTON Gel is a prescription medicine used on the skin (topical) to treat acne vulgaris in people 12 years of age and older.

It is not known if ONEXTON Gel is safe and effective for use longer than 12 weeks.

It is not known if ONEXTON Gel is safe and effective in children under 12 years of age.

**Do not use ONEXTON Gel if you have:**
- had an allergic reaction to clindamycin, benzoyl peroxide, lincomycin, or any of the ingredients in ONEXTON Gel. See the end of this leaflet for a complete list of ingredients in ONEXTON Gel.
- Crohn’s disease or ulcerative colitis.
- had inflammation of the colon (colitis) or severe diarrhea with past antibiotic use.

Talk with your doctor if you are not sure if you have any of the conditions listed above.

**Before using ONEXTON Gel, tell your doctor about all of your medical conditions, including if you:**
- plan to have surgery. ONEXTON Gel may affect how certain medicines work that may be given during surgery.
- are pregnant or plan to become pregnant. It is not known if ONEXTON Gel will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ONEXTON Gel passes into your breast milk. Clindamycin when taken by mouth or by injection has been reported to appear in breast milk. Talk to your doctor about the best way to feed your baby during treatment with ONEXTON Gel.

**Tell your doctor about all the medicines you take,** including prescription and over-the-counter medicines, vitamins and herbal supplements. ONEXTON Gel may affect the way other medicines work and other medicines may affect how ONEXTON Gel works.

- Especially tell your doctor if you take medicine by mouth that contains erythromycin or use products on your skin that contain erythromycin. ONEXTON Gel should not be used with products that contain erythromycin.
- Tell your doctor about any skin products you use. Other skin and topical acne products may increase the irritation of your skin when used with ONEXTON Gel.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

**How should I use ONEXTON Gel?**
- Use ONEXTON Gel exactly as your doctor tells you to use it. See the detailed “Instructions for Use” for directions about how to apply ONEXTON Gel.
- Your doctor will tell you how long to use ONEXTON Gel.
- Apply ONEXTON Gel to your face 1 time each day.
  Before you apply ONEXTON Gel, wash your face gently with a mild soap, rinse with warm water, and pat your skin dry.

**What should I avoid while using ONEXTON Gel?**
- Limit your time in sunlight. You should avoid using tanning beds or sun lamps during treatment with ONEXTON Gel. If you have to be in sunlight, wear a wide-brimmed hat or other protective clothing, and use sunscreen to cover the treated areas.
- Avoid getting ONEXTON Gel in your hair or on colored fabric. ONEXTON Gel may bleach hair or colored fabric.

**What are possible side effects of ONEXTON Gel?**
ONEXTON Gel can cause serious side effects including:
- Inflammation of the colon (colitis). Stop using ONEXTON Gel and call your doctor right away if you have severe stomach (abdominal) cramps, watery diarrhea, or bloody diarrhea during treatment, and within several weeks after treatment with ONEXTON Gel.
- Allergic reactions. Stop using ONEXTON Gel, call your doctor and get help right away if you have any of the following symptoms during treatment with ONEXTON Gel:
  - severe itching
  - swelling of your face, eyes, lips, tongue or throat
  - trouble breathing

**The most common side effects of ONEXTON Gel include** burning sensation, skin redness or swelling, itching and rash. Stop using ONEXTON Gel and call your doctor if you have a skin rash or your skin becomes very red, itchy or swollen. Talk to your doctor about any side effect that bothers you or that does not go away.

These are not all of the possible side effects with ONEXTON Gel.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
**How should I store ONEXTON Gel?**
- Store ONEXTON Gel at room temperature at or below 77°F (25°C).
- Do not freeze ONEXTON Gel.
- Throw away (discard) ONEXTON Gel that has passed the expiration date.
- Store pump upright.
- Keep the container tightly closed.

**Keep ONEXTON Gel and all medicines out of the reach of children.**

**General information about the safe and effective use of ONEXTON Gel.**
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ONEXTON Gel for a condition for which it was not prescribed. Do not give ONEXTON Gel to other people, even if they have the same condition you have. It may harm them. You can also ask your doctor or pharmacist for information about ONEXTON Gel that is written for healthcare professionals.

**What are the ingredients in ONEXTON Gel?**
**Active Ingredients:** clindamycin phosphate and benzoyl peroxide
**Inactive Ingredients:** carbomer 980, potassium hydroxide, propylene glycol, and purified water.

**Distributed by:** Bausch Health US, LLC, Bridgewater, NJ 08807 USA
**Manufactured by:** Bausch Health Companies Inc., Laval, Quebec H7L 4A8, Canada

U.S. Patent Numbers: 8,288,434; 9,504,704; 9,561,208; 10,137,142 and 10,220,049
ONEXTON is a trademark of Bausch Health Companies Inc. or its affiliates.
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This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 04/2020

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**INSTRUCTIONS FOR USE**
**ONEXTON® (ON-EX-TUN)**
(clindamycin phosphate and benzoyl peroxide) gel, 1.2%/3.75%

**Important Information:** ONEXTON Gel is for use on skin only (topical use). ONEXTON Gel is not for use in your mouth, eyes or vagina.

Read this Instructions for Use before you start using ONEXTON Gel and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment.

- Apply ONEXTON Gel to your face 1 time each day as prescribed.
- Before you apply ONEXTON Gel, wash your face gently with a mild soap, rinse with warm water, and pat your skin dry.
- To apply ONEXTON Gel to your face, use the pump to dispense one pea-sized amount of ONEXTON Gel onto your fingertip. See Figure 1.
- One pea-sized amount of ONEXTON Gel should be enough to cover your entire face.

**Figure 1**

- Dot the one pea-sized amount of ONEXTON Gel onto six areas of your face (chin, left cheek, right cheek, nose, left forehead, right forehead). See Figure 2.

**Figure 2**

- Spread the gel over your face and gently rub it in. **It is important to spread the gel over your entire face.** If your doctor tells you to put ONEXTON Gel on other areas of your skin with acne, be sure to ask how much you should use.
- Wash your hands with soap and water after applying ONEXTON Gel.

**How should I store ONEXTON Gel?**
- Store ONEXTON Gel at room temperature at or below 77°F (25°C).
- Do not freeze ONEXTON Gel.
- Throw away (discard) ONEXTON Gel that has passed the expiration date.
- Store pump upright.
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The Patient Information and Instructions for Use have been approved by the U.S. Food and Drug Administration. Issued: April 2020

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