ONEXTON®
(clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/3.75%

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ONEXTON Gel safely and effectively. See full prescribing information for ONEXTON Gel.

ONEXTON® (clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/3.75% for topical use
Initial U.S. Approval: 2000

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)

Dosage and Administration
Apply a pea-sized amount of ONEXTON Gel to the face once daily. (2)

For oral, ophthalmic, or intravaginal use. (2)

DOSAGE FORMS AND STRENGTHS
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. (3)

CONTRAINDICATIONS
ONEXTON Gel is contraindicated in:
• Patients who have demonstrated hypersensitivity (e.g., anaphylaxis) to clindamycin, benzoyl peroxide, any components of the formulation, or lincomycin. (4.1)

ADVERSE REACTIONS
The following adverse reactions are described in more detail in the Warnings and Precautions (4.1)

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)

• Pseudomembranous colitis: Pseudomembranous colitis has been reported with the use of clindamycin. ONEXTON Gel should be discontinued if diarrhea occurs, ONEXTON Gel should be discontinued if significant diarrhea occurs. (5.1)

• Ultraviolet Light and Environmental Exposure: Minimize sun exposure following drug application. (5.2)

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

To report SUSPECTED ADVERSE REACTIONS, contact Valeant Pharmaceuticals North America LLC at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2018
These adverse reactions occurred in less than 0.5% of subjects treated with ONEXTON Gel: burning sensation (0.4%); contact dermatitis (0.4%); pruritus (0.4%); and rash (0.4%). During the clinical trial, subjects were assessed for local cutaneous signs and symptoms of erythema, scaling, itching, burning, and stinging. Most local skin reactions either were the same as baseline or increased and peaked around Week 4 and were near or improved from baseline levels by Week 12. The percentage of subjects that had symptoms present before treatment (at baseline), during treatment, and the percent with symptoms present at Week 12 are shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Local Skin Reactions - Percent of Subjects with Symptoms Present. Results from the Phase 3 Trial of ONEXTON Gel 1.2%/3.75% (N = 243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>before Treatment</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Erythema</td>
</tr>
<tr>
<td>Scaling</td>
</tr>
<tr>
<td>Itching</td>
</tr>
<tr>
<td>Burning</td>
</tr>
<tr>
<td>Stinging</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 vivo antagonism is not known.

7.2 Concomitant Topical Medications

Concomitant topical acne therapy should be used with caution since a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents. If irritancy or dermatitis occurs, reduce frequency of application or temporarily interrupt treatment and resume once the irritation subsides. Treatment should be discontinued if the irritation persists.

7.3 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

Pregnancy Category C.

There are no adequate and well-controlled studies in pregnant women treated with ONEXTON Gel. ONEXTON Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal reproductive/developmental toxicity studies have not been conducted with ONEXTON Gel or benzoyl peroxide. Developmental toxicity studies of clindamycin performed in rats and mice using oral doses of up to 600 mg/kg/day (240 and 120 times amount of clindamycin in the highest recommended adult human dose based on mg/m², respectively) or subcutaneous doses of up to 200 mg/kg/day (80 and 40 times the amount of clindamycin in the highest recommended adult human dose based on mg/m², respectively) revealed no evidence of teratogenicity.

8.3 Nursing Mothers

It is not known whether clindamycin is excreted in human milk after topical application of ONEXTON Gel. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to use ONEXTON Gel while nursing, taking into account the importance of the drug to the mother.

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, aqueous gel formulation intended for topical use. Clindamycin phosphate is a water-soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxy group of the parent antibiotic lincocin.
increase in the incidence of keratoacanthoma at the treated skin site of male rats in a 2-year dermal carcinogenicity study in rats. In an oral (gavage) carcinogenicity study in rats, treatment with the gel formulation at doses of 300, 900, and 3000 mg/kg/day (1.2, 3.6, and 12 times amount of clindamycin and 1.6, 4.8, and 16 times amount of benzoyl peroxide in the highest recommended adult human dose of 2.5 g ONEXTON Gel based on mg/m², respectively) for up to 97 weeks did not cause any increase in tumors. In a 12-week dermal photocarcinogenicity study in hairless mice (40 weeks of treatment followed by 12 weeks of observation), the median time to onset of skin tumor formation decreased and the number of tumors per mouse increased relative to controls following chronic concurrent topical administration of the higher concentration benzoyl peroxide formulation (5000 and 10,000 mg/kg/day, 5 days/week) and exposure to ultraviolet radiation.

Clindamycin phosphate was not genotoxic in the human lymphocyte chromosome aberration assay. Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types, to be mutagenic in *S. typhimurium* tests by some but not all investigators, and to cause sister chromatid exchanges in Chinese hamster ovary cells.

Fertility studies have not been performed with ONEXTON Gel or benzoyl peroxide, but fertility and mating ability have been studied with clindamycin. Fertility studies in rats treated orally with up to 300 mg/kg/day of clindamycin (approximately 120 times the amount of clindamycin in the highest recommended adult human dose of 2.5 g ONEXTON Gel, based on mg/m²) revealed no effects on fertility or mating ability.

### 14 CLINICAL STUDIES

The safety and efficacy of once-daily use of ONEXTON Gel was assessed in a 12-week multi-center, randomized, blinded trial in subjects 12 years and older with moderate to severe acne vulgaris. This trial evaluated ONEXTON Gel compared to vehicle gel.

The co-primary efficacy variables for this trial were:

1. **Mean absolute change from baseline at Week 12 in:**
   - Inflammatory lesion counts
   - Non-inflammatory lesion counts

2. **Percent of subjects who had a 2-grade reduction from baseline on an Evaluator’s Global Severity (EGS) score.**

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

<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, and 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 results of the trial at Week 12 are presented in Table 3:

<table>
<thead>
<tr>
<th></th>
<th>ONEXTON Gel N = 253</th>
<th>Vehicle Gel N = 245</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EGSS:</strong> Clear or Almost Clear 2-grade reduction from baseline</td>
<td>29%</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Inflammatory Lesions:</strong> 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> 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>

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**PATIENT INFORMATION**

**ONEXTON® (ON-EX-TUN)**

*(clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/3.75%*

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**Important information:** For use on skin only (topical use). Do not get ONEXTON Gel in your mouth, eyes, vagina, on your lips, or on cuts or open wounds.

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**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. ONEXTON Gel contains clindamycin phosphate and benzoyl peroxide.

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.

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**Who should not use ONEXTON Gel?**

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.

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**What should I tell my doctor before using ONEXTON Gel?**

Before using ONEXTON Gel, tell your doctor about all of your medical conditions, including if you:

- plan to have surgery with general anesthesia.
- 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. ONEXTON Gel contains the medicine clindamycin. Clindamycin when taken by mouth or by injection has been reported to appear in breast milk. You and your doctor should decide if you will use ONEXTON Gel while breastfeeding.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, herbal supplements, and skin products you use. Using other topical acne products may increase the irritation of your skin when used with ONEXTON Gel.

- Especially tell your doctor if you take a medicine that contains erythromycin. ONEXTON Gel should not be used with products that contain erythromycin.

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**How should I use ONEXTON Gel?**

- Use ONEXTON Gel exactly as your doctor tells you to use it.
- 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.
- To apply ONEXTON Gel to your face, use the pump to dispense 1 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 1 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**

- After applying the ONEXTON Gel this way, spread the gel over your face and gently rub it in. It is important to spread the gel over your whole face.
- Wash your hands with soap and water after applying ONEXTON Gel.
- 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.
- Do not use more ONEXTON Gel than prescribed.
What should I avoid while using ONEXTON Gel?
- Limit your time in sunlight. Avoid using tanning beds or sun lamps. If you have to be in sunlight, wear a wide-brimmed hat or other protective clothing, and a sunscreen with SPF 15 rating or higher.
- Avoid getting ONEXTON Gel in your hair or on colored fabric. ONEXTON Gel may bleach hair or colored fabric.

What are possible side effects with ONEXTON Gel?
ONEXTON Gel may cause serious side effects, including:
- Inflammation of the colon (colitis). Stop using ONEXTON Gel and call your doctor right away if you have severe watery diarrhea or bloody diarrhea.
- Allergic reactions. Stop using ONEXTON Gel, call your doctor and get help right away if you get severe itching, swelling of your face, eyes, lips, tongue, or throat, or trouble breathing.

The most common side effect with ONEXTON Gel is skin irritation. Stop using ONEXTON Gel and call your doctor if you have a skin rash or burning, 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 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. You may also report side effects to Valeant Pharmaceuticals North America LLC at 1-800-321-4576.

How should I store ONEXTON Gel?
- Store ONEXTON Gel at room temperature at or below 77°F (25°C). Do not freeze.
- Store pump upright.
- Keep the container tightly closed.
- The expiration date of ONEXTON Gel is 10 weeks from the date you fill your prescription. Safely throw away expired ONEXTON Gel.

Keep ONEXTON Gel and all medicines out of 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 symptoms you have. It may harm them. You can also ask your doctor or pharmacist for information about ONEXTON Gel that is written for health professionals.

What are the ingredients in ONEXTON Gel?
Active ingredients: clindamycin phosphate 1.2% and benzoyl peroxide 3.75%
Inactive ingredients: carbomer 980, potassium hydroxide, propylene glycol, and purified water

Manufactured for: Dow Pharmaceutical Sciences, a division of Valeant Pharmaceuticals North America LLC Bridgewater, NJ 08807 USA
By: Valeant Pharmaceuticals International, Inc., Laval, Quebec H7L 4A8, Canada
U.S. Patent Numbers: 8,288,434; 9,504,704 and 9,561,208
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For more information about ONEXTON Gel, call 1-800-321-4576.
This Patient Information has been approved by the U.S. Food and Drug Administration.

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