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

JUBLIA® (efinaconazole) topical solution, 10%
For topical use
Initial U.S. Approval: 2014

INDICATIONS AND USAGE
JUBLIA is an azole antifungal indicated for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum and Trichophyton mentagrophytes. (1)

DOSAGE AND ADMINISTRATION
• Apply JUBLIA to affected toenails once daily for 48 weeks using the integrated flow-through brush applicator. (2)
• When applying JUBLIA, ensure the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate, are completely covered. (2)
• For topical use only. (2)
• Not for oral, ophthalmic, or intravaginal use. (2)

ADVERSE REACTIONS
Table 1: Adverse Reactions Reported by at Least 1% of Subjects Treated for up to 48 Weeks

<table>
<thead>
<tr>
<th>Adverse Event, n (%)</th>
<th>JUBLIA N = 1227</th>
<th>Vehicle N = 413</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingrown toenail</td>
<td>28 (2.3%)</td>
<td>3 (0.7%)</td>
</tr>
<tr>
<td>Application site dermatitis</td>
<td>27 (2.2%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Application site vesicles</td>
<td>20 (1.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Application site pain</td>
<td>13 (1.1%)</td>
<td>1 (0.2%)</td>
</tr>
</tbody>
</table>

DRUG INTERACTIONS
In vitro studies have shown that JUBLIA, at therapeutic concentrations, neither inhibits nor induces cytochrome P450 (CYP450) enzymes.

FULL PRESCRIBING INFORMATION: CONTENTS*
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 ADVERSE REACTIONS
6 DRUG INTERACTIONS
7 USE IN SPECIFIC POPULATIONS
8 USE IN SPECIFIC POPULATIONS
9 CLINICAL PHARMACOLOGY
10 NONCLINICAL TOXICOLOGY
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
13 NONCLINICAL TOXICOLOGY
14 CLINICAL STUDIES
15 HOW SUPPLIED/STORAGE AND HANDLING
16 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
11 DESCRIPTION

JUBLIA (efinaconazole) topical solution, 10% is a clear colorless to pale yellow solution for topical use. Each gram of JUBLIA contains 100 mg of efinaconazole. Efinaconazole is an azole antifungal with a chemical name of ((2R,3R)-2-(2,4-difluorophenyl)-3-(4-methylenepiperidin-1-yl)-1-(1H-1,2,4-triazol-1-yl)butan-2-ol). The structural formula for efinaconazole is represented below:

Molecular Formula: C_{14}H_{14}F_{2}N_{3}O
Molecular Weight: 348.39

JUBLIA contains the following inactive ingredients: alcohol, anhydrous citric acid, butylated hydroxytoluene, C12-15 alkyl lactate, cyclomethicone, diisopropyl adipate, disodium edetate, and purified water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

JUBLIA topical solution is an azole antifungal [see Clinical Pharmacology (12.4)].

12.2 Pharmacodynamics

The pharmacodynamics of JUBLIA is unknown.

12.3 Pharmacokinetics

Systemic absorption of efinaconazole in 18 adult subjects with severe onychomycosis was determined after application of JUBLIA once daily for 28 days to patients’ 10 toenails and 0.5 cm adjacent skin. The concentration of efinaconazole in plasma was determined at multiple time points over the course of 24-hour periods on days 1, 14, and 28. Efinaconazole mean ± SD plasma Cmax on Day 28 was 0.67 ± 0.37 ng/mL and the mean ± SD AUC was 13.15 ± 9.91 ng·h/mL. The plasma concentration versus time profile at steady state was generally flat over a 24-hour dosing interval. In a separate study of healthy volunteers, the plasma half-life of efinaconazole following daily applications when applied to all 10 toenails for 7 days was 29.9 hours.

12.4 Microbiology

Mechanism of Action

Efinaconazole is an azole antifungal. Efinaconazole inhibits fungal lanosterol 14α-demethylase involved in the biosynthesis of ergosterol, a constituent of fungal cell membranes.

Activity In Vitro and In Vivo

Efinaconazole has been shown to be active against isolates of the following microorganisms, both in vitro and in clinical infections. Efinaconazole exhibits in vitro minimum inhibitory concentrations (MICs) of 0.06 mcg/mL or less against most (≥90%) isolates of the following microorganisms:

- Trichophyton rubrum
- Trichophyton mentagrophytes

Mechanism of Resistance

Efinaconazole drug resistance development was studied in vitro against T. mentagrophytes, T. rubrum and C. albicans. Serial passage of fungal cultures in the presence of sub-growth inhibitory concentrations of efinaconazole increased the MIC by up to 4-fold. The clinical significance of these in vitro results is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons).

Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay).

No effects on fertility were observed in male and female rats that were administered subcutaneous doses up to 25 mg/kg/day efinaconazole (279 times the MRHD based on AUC comparisons) prior to and during early pregnancy. Efinaconazole delayed the estrous cycle in females at 25 mg/kg/day but not at 5 mg/kg/day (56 times MRHD based on AUC comparisons).

14 CLINICAL STUDIES

The safety and efficacy of once daily use of JUBLIA for the treatment of onychomycosis of the toenail were assessed in two 52-week prospective, multi-center, randomized, double-blind clinical trials in patients 18 years and older (18 to 70 years of age) with 20% to 50% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement. The trials compared 48 weeks of treatment with JUBLIA to the vehicle solution. The Complete Cure rate was assessed at Week 52 (4 weeks after completion of therapy). Complete cure was defined as 0% involvement of the target toenail (no clinical evidence of onychomycosis of the target toenail) in addition to Mycologic Cure, defined as both negative fungal culture and negative KOH. Table 2 lists the efficacy results for trials 1 and 2.

<table>
<thead>
<tr>
<th>Table 2: Efficacy Endpoints</th>
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<tbody>
<tr>
<td>Trial 1</td>
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<tr>
<td></td>
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<tr>
<td>Complete Curea</td>
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<tr>
<td>Complete or Almost Complete Curea</td>
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<tr>
<td>Mycologic Curea</td>
</tr>
</tbody>
</table>

Note: a Complete cure defined as 0% clinical involvement of the target toenail plus negative KOH and negative culture.

16 HOW SUPPLIED/STORAGE AND HANDLING

JUBLIA (efinaconazole) topical solution, 10% is a clear, colorless to pale yellow solution supplied in a white plastic bottle with an integrated flow-through brush applicator as follows:

- 4 mL (NDC 0187-5400-04)
- 8 mL (NDC 0187-5400-08)

Storage and Handling Conditions: Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

- Solution is flammable; keep away from heat or flame
- Protect from freezing
- Keep out of the reach of children
- Keep bottle tightly closed
- Store in upright position

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

- JUBLIA is for external use only and is not for ophthalmic, oral, or intravaginal use. It is for use on toenails and immediately adjacent skin only.
- Apply JUBLIA once daily to clean dry toenails. Wait for at least 10 minutes after showering, bathing, or washing before applying.
- Use JUBLIA only on the affected toenails, as directed by your healthcare provider.
- Inform a healthcare professional if the area of application shows signs of persistent irritation (for example, redness, itching, swelling).
- The impact of nail polish or other cosmetic nail products on the efficacy of JUBLIA has not been evaluated.
- Flammable, avoid use near heat or open flame.

Manufactured by:
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

by:
Valeant Pharmaceuticals International, Inc.
Laval, Quebec H7L 4A8, Canada

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U.S. Patents 7,214,506; 8,039,494; 8,486,976; and 9,302,009
Rev. 09/2016 9462903
Important information: JUBLIA is for use on toenails and surrounding skin only. Do not use JUBLIA in your mouth, eyes, or vagina.

What is JUBLIA?
JUBLIA is a prescription medicine used to treat fungal infections of the toenails. It is not known if JUBLIA is safe and effective in children.

What should I tell my healthcare provider before using JUBLIA?
Before you use JUBLIA, tell your healthcare provider about all your medical conditions, including if you:
• are pregnant or plan to become pregnant. It is not known if JUBLIA can harm your unborn baby.
• are breastfeeding or plan to breastfeed. It is not known if JUBLIA passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use JUBLIA?
See the “Instructions for Use” at the end of this Patient Information leaflet for detailed information about the right way to use JUBLIA.
• Use JUBLIA exactly as your healthcare provider tells you to use it. Apply JUBLIA to your affected toenails 1 time each day. Wait for at least 10 minutes after showering, bathing, or washing before applying JUBLIA. JUBLIA is used for 48 weeks.
• It is not known if the use of nail polish or other cosmetic nail products (such as gel nails or acrylic nails) will affect how JUBLIA works.

What should I avoid while using JUBLIA?
• JUBLIA is flammable. Avoid heat and flame while applying JUBLIA to your toenail.

What are the possible side effects of JUBLIA?
JUBLIA may cause irritation at the treated site. The most common side effects include: ingrown toenail, redness, itching, swelling, burning or stinging, blisters, and pain. Tell your healthcare provider if you have any side effects that bother you or that do not go away. These are not all the possible side effects of JUBLIA. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

How should I store JUBLIA?
• Store JUBLIA at room temperature, between 68°F to 77°F (20°C to 25°C). Do not freeze JUBLIA.
• Keep the bottle tightly closed and store in an upright position.
• JUBLIA is flammable. Keep away from heat and flame.

Keep JUBLIA and all medicines out of the reach of children.

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

What are the ingredients in JUBLIA?
Active ingredients: efinaconazole
Inactive ingredients: alcohol, anhydrous citric acid, butylated hydroxytoluene, C12-15 alkyl lactate, cyclomethicone, diisopropyl adipate, disodium edetate, and purified water.

Manufactured for:
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Laval, Quebec H7L 4A8, Canada
For more information, call 1-800-321-4576.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Rev. 09/2016
**Important information:** JUBLIA is for use on toenails and surrounding skin only. Do not use JUBLIA in your mouth, eyes or vagina.

Read this Instructions for Use that comes with JUBLIA before you start using it. Talk to your healthcare provider if you have any questions.

**How to apply JUBLIA:**

Your toenails should be clean and dry before you apply JUBLIA.

<table>
<thead>
<tr>
<th>Step 1: Remove the cap from the JUBLIA bottle.</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="Remove the cap" /></td>
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</tbody>
</table>

| Step 2: Hold the bottle upside down directly over the affected toenail. By turning the bottle upside down, the entire brush will become moistened with the solution.  
Apply one drop of JUBLIA onto the toenail.  
**Do not squeeze** the bottle, or press or rub the brush firmly against the toenail while applying JUBLIA. |
<table>
<thead>
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<tbody>
<tr>
<td><img src="image2.png" alt="Hold the bottle" /></td>
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| Step 3: For the big toenail, also apply a second drop to the end of the toenail using the tip of the brush.  
If needed, repeat Step 2 to re-wet the brush. |
<table>
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<tbody>
<tr>
<td><img src="image3.png" alt="Apply second drop" /></td>
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</table>

| Step 4: Use the brush to gently spread JUBLIA around the entire toenail, including the cuticle, folds of the skin next to the sides of the toenail, and underneath the nail.  
**Do not** squeeze the bottle, or press or rub the brush firmly against the toenail while spreading JUBLIA with the brush. |
<table>
<thead>
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<tbody>
<tr>
<td><img src="image4.png" alt="Spread JUBLIA" /></td>
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<table>
<thead>
<tr>
<th>Step 5: Repeat Steps 2 to 4 to apply JUBLIA to each affected toenail.</th>
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<tbody>
<tr>
<td><img src="image5.png" alt="Repeat Steps" /></td>
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<table>
<thead>
<tr>
<th>Step 6: Let JUBLIA dry completely.</th>
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<tbody>
<tr>
<td><img src="image6.png" alt="Let JUBLIA dry" /></td>
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</table>

<table>
<thead>
<tr>
<th>Step 7: After applying JUBLIA to your affected toenails, place the cap on the bottle and screw it on tightly.</th>
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<tbody>
<tr>
<td><img src="image7.png" alt="After applying JUBLIA" /></td>
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</table>

<table>
<thead>
<tr>
<th>Step 8: Wash your hands with soap and water after applying JUBLIA.</th>
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<tbody>
<tr>
<td><img src="image8.png" alt="Wash hands" /></td>
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</tbody>
</table>

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