VESIGARD Tablets (Darifenacin hydrobromide)

**Composition**

**VESIGARD 7.5** Extended Release Tablets

Each tablet contains:

Darifenacin (as a hydrobromide) ..... 7.5 mg

**Dosage Form**

Tablets

**Pharmacology**

**Mechanism of Action**

Darifenacin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.

*In vitro* studies using human recombinant muscarinic receptor subtypes show that darifenacin has greater affinity for the M3 receptor than for the other known muscarinic receptors (9- and 12-fold greater affinity for M3 compared to M1 and M5, respectively, and 59-fold greater affinity for M3 compared to both M2 and M4). M3 receptors are involved in contraction of human bladder and gastrointestinal smooth muscle, saliva production, and iris sphincter function. Adverse drug effects such as dry mouth, constipation and abnormal vision may be mediated through effects on M3 receptors in these organs.

In three cystometric studies performed in patients with involuntary detrusor contractions, increased bladder capacity was demonstrated by an increased volume threshold for unstable contractions and diminished frequency of unstable detrusor contractions after darifenacin extended-release treatment. These findings are consistent with an antimuscarinic action on the urinary bladder.

**Electrophysiology**

The effect of six-day treatment of 15-mg and 75-mg darifenacin on QT/QTc interval was evaluated in a multiple-dose, double-blind, randomized, placebo- and active-controlled (moxifloxacin 400 mg) parallel-arm design study in 179 healthy adults (44% male, 56% female) aged 18 to 65. Subjects included 18% poor metabolizer (PMs) and 82% extensive metabolizer (EMs). The QT interval was measured over a 24-hour period both predosing and at steady state. The 75-mg darifenacin extended-release dose was chosen because this achieves exposure similar to that observed in CYP2D6 poor metabolizers administered the highest recommended dose (15 mg) of darifenacin in the presence of a potent CYP3A4 inhibitor. At the doses studied, darifenacin did not result in QT/QTc interval prolongation at any time during the steady state, while moxifloxacin treatment resulted in a mean increase from baseline QTcF of about 7.0 msec when compared to placebo. In this study, darifenacin 15-mg and 75-mg doses demonstrated a mean heart rate change of 3.1 and 1.3
bpm, respectively, when compared to placebo. However, in the clinical efficacy and safety studies, the change in median HR following treatment with darifenacin was no different from placebo.

**Pharmacokinetics**

**Absorption**

After oral administration of darifenacin extended-release tablet to healthy volunteers, peak plasma concentrations of darifenacin are reached approximately 7 hours after multiple dosing and steady-state plasma concentrations are achieved by the sixth day of dosing.

A summary of mean (standard deviation, SD) steady-state pharmacokinetic parameters of darifenacin 7.5 mg and 15 mg extended-release tablets in EMs and PMs of CYP2D6 is provided in Table 1.

### Table 1: Mean (SD) Steady-State Pharmacokinetic Parameters from Darifenacin 7.5 mg and 15 mg Extended-Release Tablets Based on Pooled Data by Predicted CYP2D6 Phenotype

<table>
<thead>
<tr>
<th>Darifenacin Hydrobromide 7.5 mg (N = 68 EM, 5 PM)</th>
<th>Darifenacin Hydrobromide 15 mg (N = 102 EM, 17 PM)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AUC&lt;sub&gt;24&lt;/sub&gt;</strong> (ng•h/mL)</td>
<td><strong>AUC&lt;sub&gt;24&lt;/sub&gt;</strong> (ng•h/mL)</td>
</tr>
<tr>
<td>29.24 (15.47)</td>
<td>88.90 (67.87)</td>
</tr>
<tr>
<td><strong>C&lt;sub&gt;max&lt;/sub&gt;</strong> (ng/mL)</td>
<td><strong>C&lt;sub&gt;max&lt;/sub&gt;</strong> (ng/mL)</td>
</tr>
<tr>
<td>2.01 (1.04)</td>
<td>5.76 (4.24)</td>
</tr>
<tr>
<td><strong>C&lt;sub&gt;avg&lt;/sub&gt;</strong> (ng/mL)</td>
<td><strong>C&lt;sub&gt;avg&lt;/sub&gt;</strong> (ng/mL)</td>
</tr>
<tr>
<td>1.22 (0.64)</td>
<td>3.70 (2.83)</td>
</tr>
<tr>
<td><strong>T&lt;sub&gt;max&lt;/sub&gt;</strong> (h)</td>
<td><strong>T&lt;sub&gt;max&lt;/sub&gt;</strong> (h)</td>
</tr>
<tr>
<td>6.49 (4.19)</td>
<td>7.61 (5.06)</td>
</tr>
<tr>
<td><strong>t&lt;sub&gt;1/2&lt;/sub&gt;</strong> (h)</td>
<td><strong>t&lt;sub&gt;1/2&lt;/sub&gt;</strong> (h)</td>
</tr>
<tr>
<td>12.43 (5.64)</td>
<td>12.05 (12.37)</td>
</tr>
</tbody>
</table>

**Effect of food**

Following single dose administration of darifenacin extended-release tablet with food, the AUC of darifenacin was not affected, while the **C<sub>max</sub>** was increased by 22% and **T<sub>max</sub>** was shortened by 3.3 hours. There is no effect of food on multiple-dose pharmacokinetics from darifenacin extended-release tablet.

**Distribution**

Darifenacin is approximately 98% bound to plasma proteins (primarily to alpha-1-acid-glycoprotein). The steady-state volume of distribution (Vss) is estimated to be 163 L.

**Metabolism**

Darifenacin is extensively metabolized by the liver following oral dosing. Metabolism is mediated by cytochrome P450 enzymes CYP2D6 and CYP3A4.

The three main metabolic routes are as follows:

(i) Monoxygenation in the dihydrobenzofuran ring
(ii) Dihydrobenzofuran ring opening
(iii) N-dealkylation of the pyrrolidine nitrogen

The initial products of the hydroxylation and N-dealkylation pathways are the major circulating metabolites but they are unlikely to contribute significantly to the overall clinical effect of darifenacin.

**Variability in Metabolism**

“N = 25; “N = 8; “N = 2; “N = 1; AUC<sub>24</sub> = Area under the plasma concentration versus time curve for 24h; C<sub>max</sub> = Maximum observed plasma concentration; C<sub>avg</sub> = Average plasma concentration at steady-state; T<sub>max</sub> = Time of occurrence of C<sub>max</sub>; t<sub>1/2</sub> = Terminal elimination half-life. Regarding EM and PM

The mean oral bioavailability of darifenacin hydrobromide in EMs at steady state is estimated to be 15% and 19% for 7.5-mg and 15-mg tablets, respectively.
A subset of individuals (approximately 7% Caucasians and 2% African Americans) are poor metabolizer (PM) of CYP2D6-metabolized drugs. Individuals with normal CYP2D6 activity are referred to as extensive metabolizers (EMs). The metabolism of darifenacin in PMs will be principally mediated via CYP3A4. The darifenacin ratios (PM:EM) for Cmax and AUC following darifenacin 15 mg once-daily at steady state were 1.9 and 1.7, respectively.

**Excretion**

Following administration of an oral dose of $^{14}$C-darifenacin solution to healthy volunteers, approximately 60% of the radioactivity was recovered in the urine and 40% in the faeces. Only a small percentage of the excreted dose was unchanged darifenacin (3%). Estimated darifenacin clearance is 40 litres/hour for EMs and 32 litres/hour for PMs. The elimination half-life of darifenacin following chronic dosing is approximately 13-19 hours.

**Pharmacokinetics in Special Populations**

**Age:** A population pharmacokinetic analysis of patient data indicated a trend for clearance of darifenacin to decrease with age (6 percent per decade relative to a median age of 44). Following administration of darifenacin extended-release 15 mg once daily, darifenacin exposure at steady-state was approximately 12 percent to 19 percent higher in volunteers between 45 and 65 years of age compared to younger volunteers aged 18 to 44 years.

**Pediatric:** The pharmacokinetics of darifenacin has not been studied in the pediatric population.

**Gender:** PK parameters were calculated for 22 male and 25 female healthy volunteers. Darifenacin C_{max} and AUC at steady-state were approximately 57 percent to 79 percent and 61 percent to 73 percent higher in females than in males, respectively.

**Renal Impairment:** A study of subjects with varying degrees of renal impairment (creatinine clearance between 10 and 136 mL/min) given darifenacin 15 mg once daily to steady-state demonstrated no clear relationship between renal function and darifenacin clearance.

**Hepatic Impairment:** Darifenacin pharmacokinetics were investigated in subjects with mild (Child-Pugh A) or moderate (Child-Pugh B) impairment of hepatic function given darifenacin 15 mg once daily to steady-state. Mild hepatic impairment had no effect on the pharmacokinetics of darifenacin. However, protein binding of darifenacin was affected by moderate hepatic impairment. After adjusting for plasma protein binding, unbound darifenacin exposure was estimated to be 4.7-fold higher in subjects with moderate hepatic impairment than subjects with normal hepatic function. Subjects with severe hepatic impairment (Child-Pugh C) have not been studied.

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**Indications**

**VESIGARD** extended-release tablets are indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency.

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**Dosage And Administration**

The recommended starting dose of **VESIGARD** extended-release tablets is 7.5 mg once daily. Based upon individual response, the dose may be increased to 15 mg once daily, as early as two weeks after starting therapy. **VESIGARD** extended release tablets should be taken once daily along with water. They may be taken with or without food, and should be swallowed whole and not chewed, divided or crushed.

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**Hepatic Impairment**

For patients with moderate hepatic impairment (Child-Pugh B) or when co-administered with potent CYP3A4 inhibitors (for example, ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin and nefazadone), the daily dose of **VESIGARD** extended-release tablets should not exceed 7.5 mg. **VESIGARD** is not recommended for use in patients with...
Severe hepatic impairment (Child-Pugh C).

### Contraindications

**VESIGARD** extended-release tablets are contraindicated in patients with, or at risk for, the following conditions:
- Urinary retention,
- Gastric retention or
- Uncontrolled narrow-angle glaucoma.

### Warnings And Precautions

#### General

**Risk of Urinary Retention**

**VESIGARD** should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention.

**Decreased Gastrointestinal Motility**

**VESIGARD** should be administered with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention. **VESIGARD**, like other anticholinergic drugs, may decrease gastrointestinal motility and should be used with caution in patients with conditions such as severe constipation, ulcerative colitis, and myasthenia gravis.

**Controlled Narrow-Angle Glaucoma**

**VESIGARD** should be used with caution in patients being treated for narrow-angle glaucoma and only where the potential benefits outweigh the risks.

**Angio-oedema**

Angioedema of the face, lips, tongue, and/or larynx have been reported with darifenacin. In some cases angio-oedema occurred after the first dose. Angio-oedema associated with upper airway swelling may be life threatening. If involvement of the tongue, hypopharynx, or larynx occurs, darifenacin should be promptly discontinued and appropriate therapy and/or measures necessary to ensure a patent airway should be promptly provided.

**Central Nervous System Effects**

Darifenacin is associated with anticholinergic central nervous system (CNS) effects. A variety of CNS anticholinergic effects have been reported, including headache, confusion, hallucinations and somnolence. Patients should be monitored for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing the dose. Advise patients not to drive or operate heavy machinery until they know how darifenacin affects them. If a patient experiences anticholinergic CNS effects, dose reduction or drug discontinuation should be considered.

#### Drug Interactions

**Other Anticholinergic Agents**

The concomitant use of **VESIGARD** extended-release tablets with other anticholinergic agents may increase the frequency and/or severity of dry mouth, constipation, blurred vision and other anticholinergic pharmacological effects. Anticholinergic agents may potentially alter the absorption of some concomitantly administered drugs due to the effects on gastrointestinal motility.

**Effects of Other Drugs on Darifenacin**

Darifenacin metabolism is primarily mediated by the cytochrome P450 enzymes CYP2D6 and CYP3A4. Therefore, inducers of CYP3A4 or inhibitors of either of these enzymes may alter darifenacin pharmacokinetics.

**CYP2D6 Inhibitors:** No dosing adjustments are recommended in the presence of CYP2D6 inhibitors (e.g. paroxetine,
fluoxetine, quinidine and duloxetine). Darifenacin exposure following 30 mg once daily at steady state was 33% higher in the presence of the potent CYP2D6 inhibitor, paroxetine 20 mg.

**CYP3A4 Inhibitors:** The systemic exposure of darifenacin is increased in the presence of CYP3A4 inhibitors. The daily dose of darifenacin should not exceed 7.5 mg when co-administered with potent CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin and nefazodone). In a drug interaction study, when a 7.5 mg once-daily dose of darifenacin extended-release tablets was given to steady state and co-administered with the potent CYP3A4 inhibitor, ketoconazole 400 mg, mean darifenacin Cmax increased to 11.2 ng/mL for EMs (n=10) and 55.4 ng/mL for one PM subject (n=1). Mean AUC increased to 143 and 939 ng.h/mL for EMs and for one PM subject, respectively. When a 15 mg daily dose of darifenacin was given with ketoconazole, mean darifenacin Cmax increased to 67.6 ng/mL and 58.9 ng/mL for EMs (n=3) and one PM subject (n=1), respectively. Mean AUC increased to 1,110 ng.h/mL and 931 ng.h/mL for EMs and for one PM subject, respectively.

No dosing adjustments are recommended in the presence of moderate CYP3A4 inhibitors (e.g., erythromycin, fluconazole, diltiazem and verapamil). The mean Cmax and AUC of darifenacin following 30 mg once-daily dosing at steady state were 128% and 95% higher, respectively, in the presence of erythromycin. Coadministration of fluconazole and darifenacin 30 mg once daily at steady state increased darifenacin Cmax and AUC by 88% and 84%, respectively. The mean Cmax and AUC of darifenacin following 30 mg once daily at steady state were 42% and 34% higher, respectively, in the presence of cimetidine, a mixed CYP P450 enzyme inhibitor.

**Effects of Darifenacin on Other Drugs**

**In Vitro Studies:** Based on in vitro human microsomal studies, darifenacin extended-release tablets are not expected to inhibit CYP1A2 or CYP2C9 at clinically relevant concentrations.

**In Vivo Studies:** The potential for clinical doses of darifenacin extended-release to act as inhibitors of CYP2D6 or CYP3A4 substrates was investigated in specific drug interaction studies.

**CYP2D6 Substrates:** Caution should be taken when darifenacin extended-release tablet is used concomitantly with medications that are predominantly metabolized by CYP2D6 and which have a narrow therapeutic window, such as flecainide, thioridazine and tricyclic antidepressants.

The mean Cmax and AUC of imipramine, a CYP2D6 substrate, were increased 57% and 70%, respectively, in the presence of erythromycin. Coadministration of fluconazole and darifenacin 30 mg once daily at steady state increased darifenacin Cmax and AUC by 88% and 84%, respectively. The mean Cmax and AUC of darifenacin following 30 mg once daily at steady state were 42% and 34% higher, respectively, in the presence of cimetidine, a mixed CYP P450 enzyme inhibitor.

**CYP3A4 Substrates:** Darifenacin (30 mg daily) co-administered with a single oral dose of midazolam 7.5 mg resulted in a 17% increase in midazolam exposure.

**Combination Oral Contraceptives:** Darifenacin (10 mg t.i.d) had no effect on the pharmacokinetics of combination oral contraceptives containing levonorgestrel (0.15 mg) and ethinylestradiol (0.03 mg).

**Warfarin:** Darifenacin had no significant effect on prothrombin time when a single dose of warfarin 30 mg was co-administered with darifenacin (30 mg daily) at steady state. Standard therapeutic prothrombin time monitoring for warfarin should be continued.

**Digoxin:** Darifenacin (30 mg daily) did not have a clinically relevant effect on the pharmacokinetics of digoxin (0.25 mg) at steady-state. Routine therapeutic drug monitoring for digoxin should be continued. Darifenacin (30 mg daily) co-administered with digoxin (0.25 mg) at steady state resulted in a 16% increase in digoxin exposure.

Patients should be informed that anticholinergic agents, such as **VESIGARD**, might produce clinically significant adverse effects related to anticholinergic pharmacological activity, including constipation, urinary retention and blurred vision. Heat prostration (due to decreased sweating) can occur when anticholinergics such as **VESIGARD** is used in a hot environment. Because anticholinergics, such as **VESIGARD**, may produce dizziness or blurred vision, patients should be
advised to exercise caution in decisions to engage in potentially dangerous activities until the drug's effects have been determined.

Patients should be informed that darifenacin may produce clinically significant angio-oedema that may result in airway obstruction. Patients should be advised to promptly discontinue darifenacin therapy and seek immediate medical attention if they experience oedema of the tongue or laryngopharynx, or difficulty breathing.

**VESIGARD** extended-release tablets should be taken once daily along with water. They may also be taken with or without food. The tablet should be swallowed whole and not chewed, divided or crushed.

### Renal Impairment

No dose adjustment is recommended for patients with renal impairment. A study of subjects with varying degrees of renal impairment (creatinine clearance between 10 and 136 mL/min) given darifenacin extended-release tablet 15 mg once daily to steady state demonstrated no clear relationship between renal function and darifenacin clearance.

### Hepatic Impairment

The daily dose of **VESIGARD** extended-release tablets should not exceed 7.5 mg for patients with moderate hepatic impairment (Child-Pugh B). **VESIGARD** has not been studied in patients with severe hepatic impairment (Child-Pugh C) and therefore is not recommended for use in this patient population.

### Pregnancy

**Pregnancy Category C**

There are no studies of darifenacin in pregnant women. **VESIGARD** extended-release tablets should be used during pregnancy only if the benefit to the mother outweighs the potential risk to the fetus.

### Lactation

Darifenacin is excreted into the milk of rats. It is not known whether darifenacin is excreted into human milk and, therefore, caution should be exercised before **VESIGARD** extended-release tablets are administered to a nursing woman.

### Paediatric Use

The safety and effectiveness of **VESIGARD** extended-release tablets in pediatric patients have not been established.

### Geriatric Use

In the fixed-dose, placebo-controlled, clinical studies, 30% of patients treated with darifenacin extended-release tablets were over 65 years of age. No overall differences in safety or efficacy were observed between these patients (n=207) and younger patients aged below 65 years (n=464). No dose adjustment is recommended for elderly patients.

### Undesirable Effects

#### Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of darifenacin was evaluated in controlled clinical trials in a total of 8,830 patients, 6,001 of whom were treated with darifenacin. Of this total, 1,069 patients participated in three, 12-week, randomized, placebo-controlled, fixed-dose efficacy and safety studies (Studies 1, 2 and 3). Of this total, 337 and 334 patients received darifenacin 7.5
mg daily and 15 mg daily, respectively. In all long-term trials combined, 1,216 and 672 patients received treatment with darifenacin for at least 24 and 52 weeks, respectively.

In Studies 1, 2 and 3 combined, the serious adverse reactions to darifenacin were urinary retention and constipation. In Studies 1, 2 and 3 combined, dry mouth leading to study discontinuation occurred in 0%, 0.9%, and 0% of patients treated with darifenacin 7.5 mg daily, darifenacin 15 mg daily and placebo, respectively. Constipation leading to study discontinuation occurred in 0.6%, 1.2%, and 0.3% of patients treated with darifenacin 7.5 mg daily, darifenacin 15 mg daily and placebo, respectively.

Table 2 lists the rates of identified adverse reactions, derived from all reported adverse events in 2 percent or more of patients treated with 7.5 mg or 15 mg darifenacin, and greater than placebo in Studies 1, 2 and 3. In these studies, the most frequently reported adverse reactions were dry mouth and constipation. The majority of the adverse reactions were mild or moderate in severity and most occurred during the first two weeks of treatment.

Table 2: Incidence of Identified Adverse Reactions, Derived from All Adverse Events Reported in ≥2% of Patients Treated with Darifenacin Extended-release Tablets and More Frequent with Darifenacin than with Placebo in Studies 1, 2, and 3

<table>
<thead>
<tr>
<th>Body System</th>
<th>Adverse Reaction</th>
<th>Percentage of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Darifenacin extended-release tablets 7.5 mg N=337</td>
<td>Darifenacin extended-release tablets 15 mg N=334</td>
</tr>
<tr>
<td>Digestive</td>
<td>Dry Mouth</td>
<td>20.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>Abdominal Pain</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td></td>
</tr>
<tr>
<td>Urogenital</td>
<td>Urinary Tract Infection</td>
<td>4.7</td>
</tr>
<tr>
<td>Nervous</td>
<td>Dizziness</td>
<td>0.9</td>
</tr>
<tr>
<td>Body as a Whole</td>
<td>Asthenia</td>
<td>1.5</td>
</tr>
<tr>
<td>Eye</td>
<td>Dry Eyes</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Other adverse reactions reported by 1% to 2% of darifenacin treated patients includes: abnormal vision, accidental injury, back pain, dry skin, flu syndrome, hypertension, vomiting, peripheral edema, weight gain, arthralgia, bronchitis, pharyngitis, rhinitis, sinusitis, rash, pruritus, urinary tract disorder and vaginitis.

Another randomized 12-week, placebo-controlled, dose-titration regimen study in which darifenacin extended-release tablet was administered in accordance with dosing recommendations. All patients initially received placebo or darifenacin extended-release tablet 7.5 mg daily, and after two weeks, patients and physicians were allowed to adjust upward to darifenacin extended-release 15 mg if needed. In this study, the most commonly reported adverse reactions were also constipation and dry mouth. Table 3 lists the identified adverse reactions, derived from all adverse events reported in >3% of patients treated with darifenacin extended-release tablet and greater than placebo.

Table 3: Number (%) of Adverse Reactions, Derived from All Adverse Events Reported in >3% of Patients Treated with Darifenacin Extended-Release Tablets, and More Frequent with Darifenacin Extended-Release
than Placebo, in the Placebo-Controlled, Dose-Titration, Phase III Study

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Darifenacin Extended-Release Tablets 7.5 mg/15 mg N=268</th>
<th>Placebo N=127</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>56 (20.9%)</td>
<td>10 (7.9%)</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>50 (18.7%)</td>
<td>11 (8.7%)</td>
</tr>
<tr>
<td>Headache</td>
<td>18 (6.7%)</td>
<td>7 (5.5%)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>12 (4.5%)</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (4.1%)</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>10 (3.7%)</td>
<td>4 (3.1%)</td>
</tr>
<tr>
<td>Accidental Injury</td>
<td>8 (3.0%)</td>
<td>3 (2.4%)</td>
</tr>
<tr>
<td>Flu Syndrome</td>
<td>8 (3.0%)</td>
<td>3 (2.4%)</td>
</tr>
</tbody>
</table>

Postmarketing Experience

The following adverse reactions have been reported during post approval use of darifenacin extended-release tablets. Because these spontaneously reported events are from the voluntarily from a population of uncertain size, it is not always possible to reliably estimate frequency or establish a causal relationship to drug exposure.

**Dermatologic:** erythema multiforme and interstitial granuloma annulare

**General:** hypersensitivity reactions, including angioedema with airway obstruction and anaphylactic reaction

**Central Nervous:** confusion, hallucinations and somnolence

**Cardiovascular:** palpitations and syncope

Overdosage

Overdosage with antimuscarinic agents, including VESIGARD extended-release tablets, can result in severe antimuscarinic effects. Treatment should be symptomatic and supportive. In the event of overdosage, ECG monitoring is recommended. Darifenacin extended-release tablets have been administered in clinical trials at doses up to 75 mg (five times the maximum therapeutic dose) and signs of overdose were limited to abnormal vision.

Shelf-Life

24 months

Storage And Handling Instructions

Store in a cool, dry place.

Packaging Information

VESIGARD: Strip of 10 tablets

Last Updated: Dec 2013
VESIGARD Tablets

Source URL: https://ciplamed.com/content/vesigard-tablets