Darifenacin hydrobromide extended-release tablets should not exceed 7.5 mg (base). Darifenacin hydrobromide extended-release tablets are not recommended for use in patients with moderate hepatic impairment (Child-Pugh C). Darifenacin hydrobromide extended-release tablets may be taken with or without food, and should be swallowed whole and not chewed, divided or crushed.

### CONTRAINDICATIONS

Darifenacin hydrobromide extended-release tablets are contraindicated in patients with, or at risk for, the following conditions (4):

- Urinary retention
- Incontinence, caused by sphincter underactivity
- Recent or uncontrolled intracranial pressure
- Hypersensitivity to any component of darifenacin hydrobromide extended-release tablets

### ADVERSE REACTIONS

#### In SPECIFIC POPULATIONS

In Studies 1, 2 and 3 combined, the safety and effectiveness of darifenacin hydrobromide extended-release tablets were evaluated in patients with moderate hepatic impairment (Child-Pugh B) treated at 7.5 mg (base) daily. The most frequently reported adverse reactions in patients with moderate hepatic impairment (7.5 mg base) were constipation (16.4%), dry mouth (14.6%), nausea (5.6%), and nasopharyngitis (4.5%). The safety and effectiveness of darifenacin hydrobromide extended-release tablets were also evaluated in pediatric patients (7.5 mg and 15 mg base) who were 5 to 17 years of age and had an underlying chronic disease which may increase the risk of dry mouth. The most frequently reported adverse reactions in pediatric patients treated with darifenacin hydrobromide extended-release tablets were constipation (21.3%) and nasopharyngitis (19.5%). The safety and effectiveness of darifenacin hydrobromide extended-release tablets were also evaluated in patients with severe hepatic impairment (Child-Pugh C). Darifenacin hydrobromide extended-release tablets may be taken with or without food. The tablet should be swallowed whole with water and not chewed, divided or crushed.

### PHARMACOKINETICS

#### Extended-release tablets 7.5 mg and 15 mg (base) (5)

After oral administration of darifenacin hydrobromide extended-release tablets to healthy volunteers, peak plasma concentrations of darifenacin are reached approximately seven hours after multiple dosing and steady-state plasma concentrations are achieved within approximately 24 hours. Steady-state plasma concentrations of darifenacin are maintained for at least 28 days after once-daily administration. Steady-state plasma concentrations of darifenacin are approximately proportional to dose over the dosage range of 7.5 mg (base) and 15 mg (base) daily.

In Studies 1, 2 and 3 combined, the serious adverse reactions to darifenacin hydrobromide extended-release tablets were urinary incontinence and constipation.
Darifenacin extended-release tablets contain the active ingredient darifenacin hydrobromide, which is a medication used to treat overactive bladder. The overactive bladder symptoms may include:

- Urge to urinate more often than normal
- Frequent urination
- Urinating at night
- Incontinence
- Urine leakage
- Urgency: a strong need to urinate right away
- Urgency incontinence episodes
- Frequency incontinence episodes
- Frequency

Darifenacin extended-release tablets come in two strengths:

- 7.5 mg tablets
- 15 mg tablets

Each tablet may also contain the following inactive ingredients:

- Magnesium stearate, polyglylic glycol, polyethylene glycol, sac, titanium dioxide, D&C Yellow No. 10, aluminum lake and FD&C yellow No. 5 aluminum lake.

Darifenacin extended-release tablets may contain the following inactive ingredients:

- Carbomer, colorants, croscarmellose sodium, dextrin, elongated white particles, gelatin, HPMC, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, propyl gallate, sac, sodium alginate, titanium dioxide, triethyl citrate, white particles, yellow lacquer coat, yellow lacquer coat.

Important information about darifenacin extended-release tablets:

- Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature (CRT)]. Protect from light.

These are not all the possible side effects of darifenacin extended-release tablets. For more information about darifenacin extended-release tablets, talk to your doctor or pharmacist.

The mean Cmax and exposure (AUC) values for darifenacin after oral administration of darifenacin extended-release tablets are:

- 7.5 mg tablets: Cmax = 3.64 ng/mL, AUC = 19.9 ng·h/mL
- 15 mg tablets: Cmax = 6.40 ng/mL, AUC = 51.2 ng·h/mL

Darifenacin tablets are formulated to provide sustained release of drug over a 12-hour period. The mean plasma concentration-time course for darifenacin following oral administration of darifenacin extended-release tablets is shown in the figure below.

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The clinical effectiveness of darifenacin was evaluated in several randomized, double-blind, placebo-controlled studies (Studies 1, 2, and 3). In these studies, darifenacin was given orally to patients with overactive bladder symptoms for 12 weeks. The primary efficacy outcome was the reduction in the number of urinary urgency incontinence episodes per week, as compared to baseline.

The mean reduction in the number of urinary urgency incontinence episodes per week for darifenacin extended-release tablets compared to placebo is shown in the table below.

In the table above, the mean reduction in the number of urinary urgency incontinence episodes per week for darifenacin extended-release tablets compared to placebo is shown for Studies 1, 2, and 3.

Here is the table with the mean reduction in the number of urinary urgency incontinence episodes per week for darifenacin extended-release tablets compared to placebo for Studies 1, 2, and 3:

<table>
<thead>
<tr>
<th>Study</th>
<th>Placebo</th>
<th>Darifenacin 7.5 mg</th>
<th>Darifenacin 15 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26.0</td>
<td>36.7</td>
<td>30.7</td>
</tr>
<tr>
<td>2</td>
<td>22.0</td>
<td>31.3</td>
<td>27.0</td>
</tr>
<tr>
<td>3</td>
<td>17.0</td>
<td>22.5</td>
<td>19.8</td>
</tr>
</tbody>
</table>

These data show that darifenacin extended-release tablets were statistically superior to placebo for reduction in the number of urinary urgency incontinence episodes per week. Darifenacin extended-release tablets were also statistically superior to placebo for reduction in the number of urgency incontinence episodes per week in Study 3.

Darifenacin extended-release tablets were statistically superior to placebo for reduction in the number of urgency incontinence episodes per week in all three studies (Studies 1, 2, and 3). The difference between darifenacin extended-release tablets and placebo was statistically significant for all three study periods.

In Study 1, the mean reduction in the number of urinary urgency incontinence episodes per week for darifenacin extended-release tablets compared to placebo was 36.7 episodes per week (p < 0.05, Wilcoxon rank-sum test). In Study 2, the mean reduction was 31.3 episodes per week (p < 0.05, Wilcoxon rank-sum test). In Study 3, the mean reduction was 22.5 episodes per week (p < 0.05, Wilcoxon rank-sum test).

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