The initial dose of QUDEXY XR is 25 mg/day nightly for the first week. Based upon tolerability, the dose may be increased at weekly intervals to a maximum daily dose of 200 mg/day. The maintenance dose is 25 to 200 mg/day, given as a single daily dose or in two divided doses. Patients should be started on the lowest effective dose and titrated up to the target dose as rapidly as possible, according to the judgment of the treating physician. Other measures, such as immediately discontinuing the use of an anticonvulsant, may be needed in patients with severe toxicity. Patients treated with QUDEXY XR should be monitored closely for evidence of decreased alertness and should be provided with simple, basic instructions to follow, especially during the titration period.

Patients 2 to 15 years of age receiving 5 mg to 9 mg/kg/day (recommended dose range) of immediate-release topiramate oral liquid or sprinkle formulations as an adjunct to other concomitant AEDs had adverse reactions including somnolence, difficulty with memory, difficulty with concentration/attention, and paresthesia (see Table 8). These reactions were observed frequently during the titration period than during the maintenance period. Among adverse reactions reported in pediatric patients less than 2 years old less than 3 years old receiving 5 mg to 9 mg/kg/day (recommended dose range) of immediate-release topiramate oral liquid or sprinkle formulations as an adjunct to other concomitant AEDs were paresthesia, anorexia, weight loss, taste perversion, diarrhea, and vomiting (see Table 8). The safety and effectiveness of topiramate in patients younger than 2 years have not been established.

The most common adverse reactions in the controlled trial (Study 1) that occurred in more than 2% of patients treated with topiramate and were more frequently reported than in the placebo group in pediatric patients were somnolence, anorexia, weight loss, and vomiting. The most common adverse reactions in the controlled trial (Study 1) that occurred in more than 2% of patients treated with topiramate and were more frequently reported than in the placebo group in adult patients were somnolence, anorexia, weight loss, and vomiting. The most common adverse reactions reported in patients treated with topiramate that occurred at a rate greater than 1% and at a frequency at least twice that of placebo were somnolence, anorexia, weight loss, vomiting, headache, and dizziness.

Topiramate, USP, is a sulfamate-substituted monosaccharide. QUDEXY XR (topiramate) extended-release capsules contain topiramate extended-release microspheres and are available in strengths of 25 mg, 50 mg, and 100 mg.

Topiramate extends the half-life of topiramate. Clinical laboratory results indicated decreases in serum potassium after topiramate dosing with increases in creatinine and urinalysis indicating proteinuria. Markedly abnormally low serum bicarbonate values indicative of metabolic acidosis were observed at the lowest dose tested, which was associated with an increased incidence of malformations, is less than the MRHD for epilepsy or migraine on a mg/m2 basis. Some patients may experience a large increase in amitriptyline concentration in the presence of topiramate.

Topiramate is eliminated by metabolism. Topiramate is metabolized by cytochrome P450 CYP2C9 isozymes and by non-enzymatic pathways. The metabolites of topiramate are not pharmacologically active. Clinical laboratory results indicated decreases in serum potassium after topiramate dosing with increases in creatinine and urinalysis indicating proteinuria. Markedly abnormally low serum bicarbonate values indicative of metabolic acidosis were observed at the lowest dose tested, which was associated with an increased incidence of malformations, is less than the MRHD for epilepsy or migraine on a mg/m2 basis. Some patients may experience a large increase in amitriptyline concentration in the presence of topiramate.

The effects of switching between QUDEXY XR and immediate-release topiramate were also frequently during the titration period than during the maintenance period. Comparison of the Kaplan-Meier survival curves of time to remission in the major depressive disorder (MDD) response domain indicated a significantly greater proportion of patients who were in remission at 16 weeks after initiating treatment with topiramate tablets or placebo. In Study 8, patients were stabilized on optimum dosages of immediate-release topiramate initial monotherapy and were randomized to receive topiramate treatment or no treatment. The primary efficacy outcome measure of effectiveness was the percent reduction in drop attacks and a parental global assessment.

The most common adverse reactions in the controlled trial (Study 1) that occurred in more than 2% of patients treated with topiramate and were more frequently reported than in the placebo group in pediatric patients were somnolence, difficulty with memory, hypoesthesia, and nausea (see Table 8). Some patients may experience a large increase in amitriptyline concentration in the presence of topiramate.

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Table 4 shows absolute and relative risk by indication for all evaluated AEDs. The most common adverse reactions in the controlled trial (Study 1) that occurred in more than 2% of patients treated with topiramate and were more frequently reported than in the placebo group in pediatric patients were somnolence, difficulty with memory, difficulty with concentration/attention) was dose-related and occurred more frequently in pediatric patients than in the placebo group.

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### Pharmacodynamics

The mean reduction from baseline to the last 12 weeks of the double-blind phase in average monthly migraine attack rate is shown in Table 15. The 100 mg immediate-release formulation of topiramate was significantly more effective than placebo or the 50 mg formulation in the reduction of the number of migraine days (not adjusted for multiple comparisons).

### Safety

#### Kidney Stones

Can develop with topiramate treatment alone or with topiramate treatment with concomitant use of other drugs (e.g., diuretics). Instruct patients, particularly those with predisposing factors, to maintain an adequate fluid intake to decrease the risk of kidney stones.

### Drug Interactions

Inform pregnant women and women of childbearing potential that use of QUDEXY XR during pregnancy may cause harm to the fetus. Inform women of childbearing potential who are not planning to become pregnant during treatment with QUDEXY XR that use of QUDEXY XR during pregnancy may cause harm to the fetus. Inform women of childbearing potential that use of QUDEXY XR during breastfeeding may cause harm to the infant.

### Usage

Inform patients about the possible development of hyperammonemia with or without symptoms, and to discontinue therapy if they experience signs of hyperammonemia (e.g., nausea, vomiting, change in mental status, confusion, or coma).

### Precautions

#### Breastfeeding

Avoid breastfeeding while taking QUDEXY XR.

### References

1. **Table 15. Change From Baseline to Double-Blind Phase in Average Monthly Migraine Attack Rate**

<table>
<thead>
<tr>
<th>Category</th>
<th>Median 100 mg immediate-release</th>
<th>Median 50 mg immediate-release</th>
<th>Median Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent Reduction (%)</td>
<td>40.0</td>
<td>26.0</td>
<td>13.0</td>
</tr>
</tbody>
</table>

**ANCOVA model on ranks that includes subject's stratified age at baseline, treatment group, and baseline average monthly migraine attack rate as covariates. *p<0.001***

### Acknowledgment

This information is up-to-date as of 2019. For the most recent information, please consult the package insert or contact the manufacturer.

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