RIVASTIGMINE:

Class: Acetylcholinesterase Inhibitor

Indications: **Dementia associated with Alzheimer's or Parkinson's disease:**
Treatment of dementia with Lewy bodies

Available dosage form in the hospital: TAB (1.5MD,3MG, 4.5MG)

Dosage:

-Alzheimer's dementia, mild-to-moderate:

-*Oral:* Initial: 1.5 mg twice daily; may increase by 3 mg daily (1.5 mg/dose) every 2 weeks based on tolerability (maximum recommended dose: 6 mg twice daily)

Note: If GI adverse events occur, discontinue treatment for several doses then restart at the same or next lower dosage level; antiemetics have been used to control GI symptoms. If treatment is interrupted for longer than several days, restart the treatment at the lowest dose and titrate as previously described.

-*Transdermal patch:*

-*U.S. labeling:* Initial: Apply 4.6 mg/24 hours patch once daily; if well tolerated, may titrate (no sooner than every 4 weeks) to 9.5 mg/24 hours (continue as long as therapeutically beneficial), and then to 13.3 mg/24 hours (maximum dose); doses >13.3 mg/24 hours have not been shown to be more effective and are associated with significant increases in adverse events. Remove old patch and replace with a new patch every 24 hours. Recommended effective dose: Apply 9.5 mg/24 hours or 13.3 mg/24 hours patch once daily; remove old patch and replace with a new patch every 24 hours

-*Canadian labeling:* Initial: Apply 4.6 mg/24 hours patch once daily; if well tolerated, may titrate (no sooner than after 4 weeks) to 9.5 mg/24 hours (maximum recommended dose); continue as long as therapeutically beneficial.

Note: If intolerance is noted (nausea, vomiting), patch should be removed and treatment interrupted for several days and restarted at the same or lower dosage. If interrupted for more than 3 days, reinitiate at 4.6 mg/24 hours and titrate (no sooner than every 4 weeks) to lowest effective maintenance dose.

**Conversion from oral therapy: If oral daily dose <6 mg, switch to 4.6 mg/24 hours patch; if oral daily dose 6-12 mg, switch to 9.5 mg/24 hours patch. Apply patch on the next day following last oral dose.

-Alzheimer's dementia, severe: *Transdermal patch:* Initial: Apply 4.6 mg/24 hours patch once daily. Titrate dose as recommended for transdermal dosing for mild-to-moderate Alzheimer's dementia. Recommended effective dose: Apply 13.3 mg/24 hours patch once daily; remove old patch and replace with a new patch every 24 hours

-Parkinson's-related dementia, mild-to-moderate:

-*Oral:* Initial: 1.5 mg twice daily; may increase by 3 mg daily (1.5 mg per dose) every 4 weeks based on tolerability (maximum recommended dose: 6 mg twice daily)

-*Transdermal patch:* Initial: If well tolerated, may titrate (no sooner than every 4 weeks) to 9.5 mg/24 hours (continue as long as therapeutically beneficial), and then to 13.3 mg/24 hours (maximum dose); doses >13.3 mg/24 hours have not been shown to be more effective and are associated with significant increases in adverse events. Recommended effective dose: Apply 9.5 mg/24 hours or 13.3 mg/24 hours patch once daily; remove old patch and replace with a new patch every 24 hours

-Dementia with Lewy bodies (unlabeled use): *Oral:* Initial: 1.5 mg twice daily; may increase by 3 mg daily (1.5 mg per dose) every 2 weeks based on tolerability up to a maximum of 6 mg twice daily (titration lasted up to 8 weeks); study duration was 23 weeks (McKeith, 2000). An extension study was conducted in a limited number of patients (at the same dose) for up to 96 weeks (Grace 2001).

Geriatric

Following oral administration, clearance is significantly lower in patients >60 years of age, but dosage adjustments are not recommended. Age was not associated with exposure in patients treated transdermally. Titrate dose to individual's tolerance. Refer to adult dosing. **Note:** Canadian labeling recommends an initial oral dose of 1.5 mg once daily in patients >85 years of age with low body weight (<50 kg) or serious comorbidities, with a slower titration rate than used for adults.

Renal Impairment:

-U.S. labeling:

-Oral: No dosage adjustment necessary.

-Transdermal: No dosage adjustment necessary.

-Canadian labeling:

-Oral: Initial dose: 1.5 mg once daily; titrate dose at a rate slower than recommended for healthy adults

-Transdermal: No dosage adjustment provided in manufacturer's labeling (has not been studied); titrate dose cautiously

Hepatic Impairment:

-U.S. labeling:

-Oral: No dosage adjustment necessary.

-Transdermal:

-Mild-to-moderate impairment (Child Pugh score 5-9): Initial and maximum dose: 4.6 mg/24 hours

-Severe impairment: No dosage adjustment provided in manufacturer’s labeling (has not been studied).

-Canadian labeling:

-Oral:

-Mild-to-moderate impairment: Initial dose: 1.5 mg once daily; titrate dose at a rate slower than recommended for healthy adults

-Severe impairment: Use is contraindicated.

-Transdermal:

-Mild-to-moderate impairment: No dosage adjustment provided in manufacturer's labeling; titrate dose cautiously

-Severe impairment: Use is contraindicated.

Adjustment for Toxicity:

Transdermal patch: Patients <50 kg: Reduce maintenance dose to 4.6 mg/24 hours if toxicities develop.

Common side effect:

Central nervous system: Dizziness (1% to 21%), headache (3% to 17%)

Gastrointestinal: Nausea (5% to 47%), vomiting (5% to 31%), diarrhea (<1% to 19%), anorexia (3% to 17%), abdominal pain (1% to 13%)

Pregnancy Risk Factor: B