LUMATEPERONE (Caplyta) Fact Sheet

Bottom Line:
Lumateperone is the newest second-generation antipsychotic, approved to treat adults with schizophrenia or bipolar disorder. It appears to have a good tolerability profile and the convenience of once-daily dosing and no titration. But for now, cost relegates it to second-line use.

FDA Indications:
Schizophrenia; bipolar I or II depression.

Off-Label Uses:
Unipolar depression.

Dosage Forms:
Capsules: 10.5 mg, 21 mg, 42 mg.

Dosage Guidance:
Start, target, and max dose of 42 mg QD with food; no titration needed.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $$$$$

Side Effects:
- Most common: Somnolence, sedation, dry mouth, nausea, dizziness.
- Serious but rare: See class warnings in chapter introduction.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Dopamine D2 and serotonin 5-HT2A receptor antagonist.
- Metabolized primarily by UGT1A1, 1A4, 2B15 and CYP3A4, CYP2C8, CYP1A2; t ½: 18 hours.
- Avoid use with potent inhibitors and inducers of CYP3A4.

Clinical Pearls:
- Lumateperone may be better tolerated if taken at dinner due to sedating effects.
- Lower affinity at D2 receptors means relatively lower risk for EPS.
- In studies to date, lumateperone appears to have low levels of akathisia, weight gain, metabolic side effects, and prolactin elevation.
- New lower-dose capsules to be used for patients with moderate or severe hepatic impairment or those taking potent CYP3A4 inhibitors.
- Indication for depression associated with bipolar I and bipolar II followed original schizophrenia indication.
- Promising antidepressant effects were seen in Study 403, which trialed lumateperone monotherapy in patients with major depression with mixed features and bipolar depression with mixed features. An indication is pending FDA review.
- A long-acting injectable of lumateperone is currently in development.

Fun Fact:
This antipsychotic was expected to be approved a couple of years earlier, but a Phase 3 study in 2016 in nearly 700 patients showed no difference from placebo at both 20 mg and 60 mg. This may have been a "failed trial" with a high placebo response rate, and risperidone also failed to separate from placebo in this study.