Cross Titration with Caplyta

In response to your inquiry regarding cross titration when initiating a patient on Caplyta (lumateperone) the following information is available.

Caplyta (lumateperone) is indicated for the treatment of schizophrenia in adults.[1]

Summary

Titration is a method used for by clinicians during treatment initiation, discontinuation, or both depending on specific requirements associated with the medication. Many antipsychotic medications used for schizophrenia require titration both when initiating and discontinuing treatment. During treatment discontinuation, this method is generally employed to avoid withdrawal side effects.

- Abrupt discontinuation of antipsychotics is associated with symptom relapse.[2]
- Caplyta (lumateperone) does not require dose titration.[1]

Caplyta (lumateperone) does not require dose titration; however, clinicians should use their clinical judgement in titrating other medications prior to their discontinuation as appropriate.

Supporting Data

- In a randomized, placebo-controlled study of Caplyta (lumateperone) versus placebo, 435 patients were not allowed to continue other antipsychotic medication from screening through study day 1, although, tapering could be considered on a case-by-case basis, but the medication had to be stopped by study day 3.[3]
- In an open-label crossover study of Caplyta (lumateperone), 301 patients were required to discontinue other antipsychotics prior to beginning the 6-week treatment period with tapering allowed as appropriate.[4]
- A meta-analysis which included patients with schizophrenia, broken down into 795 inpatients and 211 outpatients, noted that the risk of relapse in the first 6 months after abrupt treatment discontinuation was higher in inpatients than outpatients (49.6% ± 1.8% vs. 31.4% ± 3.2%). Overall, the risk of relapse reached 50% 30 weeks after abrupt discontinuation (30.3 ± 15.4 weeks).[5]
- The most commonly reported adverse effects from clinical trails are somnolence/sedation and dry mouth.[1]
- Caplyta (lumateperone) has a half-life of elimination of ~18 hours.[1]
- It is recommended that coadministration of CYP3A4 inducers or moderate-to-strong CYP3A4 inhibitors be avoided with Caplyta (lumateperone).[1]

Caplyta (lumateperone) does not require dose titration, but clinical judgement should be applied by clinicians prior to discontinuation of other antipsychotic medications as appropriate. Individual medication and patient specific factors should be considering prior to discontinuation of any medications. Caplyta (lumateperone) has a half-life of roughly 18 hours leading to daily dosing, and patients will reach steady state roughly 90 hours after initiation.

References

1. Caplyta. Package insert. Intra-Cellular Therapies Inc.; 2019.
2. Horowitz MA, Murray RM, Taylor D. Tapering Antipsychotic Treatment. *JAMA Psychiatry*. 2021;78(2):125-126. doi:10.1001/jamapsychiatry.2020.2166
3. Correll CU, Davis RE, Weingart M, et al. Efficacy and Safety of Lumateperone for Treatment of Schizophrenia: A Randomized Clinical Trial [published correction appears in JAMA Psychiatry. 2020 Feb 19;:]. *JAMA Psychiatry*. 2020;77(4):349-358. doi:10.1001/jamapsychiatry.2019.4379
4. Correll CU, Vanover KE, Davis RE, Chen R, Satlin A, Mates S. Safety and tolerability of lumateperone 42 mg: An open-label antipsychotic switch study in outpatients with stable schizophrenia. *Schizophr Res*. 2021;228:198-205. doi:10.1016/j.schres.2020.12.006
5. Viguera AC, Baldessarini RJ, Hegarty JD, van Kammen DP, Tohen M. Clinical risk following abrupt and gradual withdrawal of maintenance neuroleptic treatment. *Arch Gen Psychiatry*. 1997;54(1):49-55. doi:10.1001/archpsyc.1997.01830130055011