Pimavanserin

Practice Based Recommendations

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Pimavanserin (Nuplazid) is the only medication approved by the Food and Drug Administration for the treatment of hallucinations and delusions associated with Parkinson’s disease psychosis. Pimavanserin is a selective serotonin inverse agonist with a half-life of 57 hours. It takes approximately 12 days to reach steady state plasma levels and may take up to 6 weeks to see maximum benefit. Pimavanserin was approved for use in 2016, therefore, there is limited experience in using the drug. Based on our experience with over 130 Parkinson’s disease psychosis patients started on pimavanserin, we present recommendations on the initiation of pimavanserin, particularly when switching from another antipsychotic with suboptimal benefit or that is causing side effects. It should be noted that this information is provided only to inform other clinicians about the approach we have found to be most effective and should not be considered a guideline on how you should use this medication. The package insert should be reviewed, paying particular attention to issues related to QTC, CYP3A4 inducers and antagonists.

Initiation of pimavanserin in patients not taking another antipsychotic

- Pimavanserin should be started at 34 mg once daily at any time during the day (2 17mg tablets taken together once daily)
- Pimavanserin is typically not titrated at initiation or discontinuation

Initiation of pimavanserin in patients taking quetiapine (Seroquel) or clozapine (Clozaril)

- Pimavanserin should be started at 34mg once daily (2 17 mg tablets taken together once daily)

- Concomitant quetiapine ≤ 100 mg daily
  - Continue quetiapine at current dose for 4 weeks with pimavanserin 34mg daily
  - At 4 weeks reduce quetiapine by 50%
  - Reduce quetiapine by 50% weekly until on 12.5 mg and then discontinue
    - If efficacy is reduced at any time during the down titration of quetiapine return to the previous dose level. Reduction can be attempted again after 1 week or the patient may need to continue both medications. A clinical decision needs to be made whether the response and side effects are better using both antipsychotics or if the patient should return to the previous antipsychotic.

- Concomitant quetiapine >100 mg daily
  - Continue quetiapine at current dose for 6 weeks with pimavanserin 34mg daily
  - At 6 weeks reduce quetiapine by 25%
  - Reduce quetiapine by 25% weekly until on 12.5mg and then discontinue
- If efficacy is reduced at any time during the down titration of quetiapine return to the previous dose level. Reduction can be attempted again after 1 week or the patient may need to continue both medications. A clinical decision needs to be made whether the response and side effects are better using both antipsychotics or if the patient should return to the previous antipsychotic.

- Concomitant clozapine
  - Continue clozapine at current dose for 6 weeks with pimavanserin 34mg daily
  - At 6 weeks, reduce clozapine by 6.25mg weekly until discontinued
  - If efficacy is reduced at any time during the down titration of clozapine return to the previous dose level. Reduction can be attempted again after 1 week or the patient may need to continue both medications. A clinical decision needs to be made whether the response and side effects are better using both antipsychotics or if the patient should return to the previous antipsychotic.
  - Do not remove from clozapine registry for a couple of months so that patient will not have to be re-enrolled if clozapine restarted.

**See diagram on the next page**

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* If efficacy is reduced at any time during the down titration return to the previous dose level. Reduction can be attempted again after 1 week or the patient may need to continue both medications. A clinical decision needs to be made whether the response and side effects are better using both antipsychotics or if the patient should return to the previous antipsychotic.