Mandell Center Medication Protocol: Zeposia (Ozanimod)

Indications and Usage:

- Indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Prior to initiating ZEPOSIA, the following are required:

Labwork: within 6 months or after discontinuation of previous MS therapy

- CBC with differential
- Liver Profile
- VZV Antibody (IgG) unless confirmed case of vaccination or history of chicken pox

Cardiologic Assessment:

- ECG to determine whether pre-existing conduction abnormalities are present.
- Patients with the following need cardiology clearance:
  - With significant QT prolongation (QTcF > 450 msec in males, > 470 msec in females).
  - With arrhythmias requiring treatment with Class 1a or Class III anti-arrhythmic drugs.
  - With ischemic heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension.
  - With a history of with second-degree Mobitz type II or higher AV block, sick-sinus syndrome, or sinoatrial heart block.

Current or prior medications:

- If patients are taking anti-neoplastic, immunosuppressive, immune-modulating therapies, or if there is a history of prior use of these drugs, consider possible unintended additive immunosuppressive.
- Determine if patients are taking drugs that could slow heart rate or atrioventricular conduction. MAO inhibitors contraindicated.

Ophthalmic Assessment:

- In patients with a history of uveitis, macular edema, or diabetes obtain an evaluation of the fundus, including the macula.

Respiratory effects:

- Spirometric evaluation of respiratory function should be performed during therapy if clinically indicated (history of COPD, severe asthma).
Imaging:
- Baseline MRI Brain (with or without contrast per provider) within 3 months prior to first treatment course (may also be performed at provider discretion).
*For patients transitioning from Tysabri, MRI brain with and without contrast to be performed for JCV positive patients upon discontinuing Tysabri and at 6 months after discontinuing Tysabri.
- MRI Brain (with or without contrast) to be performed at provider discretion for patients with progressive forms of MS.

Vaccinations:
- If live attenuated vaccine immunizations are required, administer at least 1 month prior to initiation. Avoid the use of live attenuated vaccines during and for 3 months after treatment with ZEPOSIA.

Contraception:
- Women of childbearing potential should be counseled on the potential for a serious risk to the fetus and the need for contraception during treatment and for 3 months after stopping ZEPOSIA.

Dosing and Administration:

*Initiate ZEPOSIA with a 7-day titration, as shown below:
- Days 1-4 0.23 mg once daily
- Days 5-7 0.46 mg once daily
- Day 8 and thereafter 0.92 mg once daily

Delayed or Missed Dosing:
- Delay initiation of ZEPOSIA in patients with an active infection until the infection is resolved.
- Do not skip a dose.

Reinitiating ZEPOSIA After Treatment Interruption:
- If a dose of ZEPOSIA is missed during the first 2 weeks of treatment, reinitiate treatment using the titration regimen.
- If a dose of ZEPOSIA is missed after the first 2 weeks of treatment, continue with the treatment as planned.

Management of Medication Reaction:
- Call your healthcare provider if you feel you are experiencing any medication related side effects.
Patient Counseling Information:

Diet:

- Avoid certain foods that are high (over 150 mg) in tyramine such as aged, fermented, cured, smoked and pickled foods. Eating these foods while taking ZEOSIA may increase blood pressure.

Infection:

- Consider interruption of treatment with ZEOSIA if a patient develops a serious infection.
- Because the elimination of ZEOSIA after discontinuation may take up to 3 months, continue monitoring for infections throughout this period.

Disease Rebound:

- Severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of a S1P receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping ZEOSIA treatment.

Follow up monitoring:

- Initial follow-up with provider every 3 months for the first year, then every 6 months.
- Labwork: every 3 months year one, then every 6 months thereafter if stable
  - CBC with differential
  - Liver Profile
- ALC <= 0.3 and or WBC <= 2.0 change to QOD dosing and repeat CBC w diff in 1 month
- Prompt Ophthalmic evaluation with vision change.
- Imaging:
  - MRI Brain with and without contrast 6 months after initiation of Zeposia.
  - Annual MRI Brain and C-Spine without contrast (or per provider discretion).

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Reference: Zeposia PI revision 9/2020

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