ULCERATIVE COLITIS (UC) TREATMENT OPTIONS

In-office Discussion Guide

INDICATION

ZEPOSIA® (ozanimod) is a prescription medicine used to treat moderately to severely active ulcerative colitis (UC) in adults. It is not known if ZEPOSIA is safe and effective in children.

SELECTED IMPORTANT SAFETY INFORMATION

Do not take ZEPOSIA if you:

- have had a heart attack, chest pain (unstable angina), stroke or mini-stroke (transient ischemic attack or TIA), or certain types of heart failure in the last 6 months
- have or have had a history of certain types of an irregular or abnormal heartbeat (arrhythmia) that is not corrected by a pacemaker
- have untreated, severe breathing problems during your sleep (sleep apnea)
- take certain medicines called monoamine oxidase (MAO) inhibitors (such as selegiline, phenelzine, linezolid)

Talk to your healthcare provider before taking ZEPOSIA if you have any of these conditions or do not know if you have any of these conditions.

ZEPOSIA may cause serious side effects, including:

- **Infections.** ZEPOSIA can increase your risk of serious infections that can be life-threatening and cause death. ZEPOSIA lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 3 months of stopping treatment. Your healthcare provider may do a blood test of your white blood cells before you start taking ZEPOSIA.

  Call your healthcare provider right away if you have any of these symptoms of an infection during treatment with ZEPOSIA and for 3 months after your last dose of ZEPOSIA:
  - fever
  - feeling very tired
  - flu-like symptoms
  - cough
  - painful and frequent urination (signs of a urinary tract infection)
  - rash
  - headache with fever, neck stiffness, sensitivity to light, nausea, or confusion (these may be symptoms of meningitis, an infection of the lining around your brain and spine)

  Your healthcare provider may delay starting or may stop your ZEPOSIA treatment if you have an infection.
- **Progressive multifocal leukoencephalopathy (PML).** ZEPOSIA can increase your risk for PML, which is a rare brain infection that usually leads to death or severe disability. If PML happens, it usually happens in people with weakened immune systems but has happened in people who do not have weakened immune systems. Symptoms of PML get worse over days to weeks. Call your doctor right away if you have any new or worsening symptoms of PML that have lasted several days, including: weakness on one (1) side of your body, changes in your vision, changes in your thinking or memory, confusion, changes in your personality, loss of coordination in your arms or legs, decreased strength, and/or problems with balance.

Please see additional Important Safety Information throughout and Prescribing Information and Medication Guide.

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TREATMENT OPTIONS FOR ULCERATIVE COLITIS (UC) IN ADULTS[a]

This informational overview is not intended to compare the safety, efficacy, or uses of these treatments.

Treatment Option for Those Patients With Mild-to-Moderate UC: 5-aminosalicylate (5-ASA)	Approved Treatment Options for Those Patients With Moderate-to-Severe UC								Treatment Option for Those Patients With Severe, Uncontrolled UC: Surgery
Classes of Treatment	**Sphingosine 1-Phosphate (S1P) Receptor Modulator**	**Anti-Integrin**	**Anti-Interleukin (IL)**	**Anti-Tumor Necrosis Factor (TNF)**			**Janus Kinase (JAK) Inhibitor**		
							Post TNF (Treatments for use after TNF therapy fails)		
How It's Thought to Work	Acts on S1P receptors on immune cells, helping to keep these cells from moving out of the lymph nodes and into the colon	Prevents certain white blood cells from entering into the gastrointestinal tract	Targets specific ILs (ILs are naturally occurring proteins)	Blocks a protein called TNF-α			Blocks JAK enzymes		
Approved Treatments	**ZEPOSIA® (ozanimod)[1]**	**Entyvio® (vedolizumab) (A type of biologic)[2]**	**Stelara® (ustekinumab) (A type of biologic)[3]**	**Humira® (adalimumab) (A type of biologic)[4]**	**Remicade® (infliximab) (A type of biologic)[5]**	**Simponi® (golimumab) (A type of biologic)[6]**	**Xeljanz/Xeljanz XR® (tofacitinib)[7]**	**Rinvoq® (upadacitinib)[8]**	
Who It's For	For adults with moderately to severely active UC	For adults with moderately to severely active UC	For adults with moderately to severely active UC	For adults with moderately to severely active UC. It is not known if Humira is effective in people who stopped responding to or could not tolerate anti-TNF medicines	For adults with moderately to severely active UC who have not responded well to other therapies - To reduce signs and symptoms - To induce and maintain clinical remission - To promote intestinal healing - To reduce or stop the need for steroids	For adults with moderately to severely active UC when certain other medicines have not worked well enough or cannot be tolerated, or if it is necessary to continue taking steroid medicines - To begin helping some of the symptoms - In people who respond to Simponi, to get their UC under control (induce remission) and keep UC under control (sustain remission) - To begin to improve the way the lining of the large intestine looks to a doctor during colonoscopy	For adults with moderately to severely active UC when 1 or more TNF blocker medicines have been used, and did not work well or cannot be tolerated	For adults with moderately to severely active UC when 1 or more TNF blocker medicines have been used, and did not work well or cannot be tolerated	
How to Take	**Start:** A once-daily pill, using the 7-day starter pack to increase dosage gradually **Continue:** A once-daily pill Take as directed by your doctor if certain liver problems exist.	**Start:** An intravenous (IV) infusion dose at Weeks 0, 2, and 6 **Continue:** An IV infusion dose every 8 weeks	**Start:** An IV infusion dose at Week 0 **Continue:** A dose given by injection under the skin (subcutaneous) every 8 weeks	**Start:** A dose given by injection under the skin (subcutaneous) at 1st and 15th days **Continue:** A dose given by injection under the skin (subcutaneous) every 2 weeks	**Start:** An IV infusion dose at Weeks 0, 2, and 6 **Continue:** An IV infusion dose every 8 weeks	**Start:** A dose given by injection under the skin (subcutaneous) at Weeks 0 and 2 **Continue:** A dose given by injection under the skin (subcutaneous) every 4 weeks	**Start:** A once- or twice-daily pill for at least 8 weeks **Continue:** A once-or twice-daily pill	**Start:** A once-daily pill for at least 8 weeks **Continue:** A once-daily pill, using the lowest dosage possible	

[a]This is not an all-inclusive list of treatment options for UC.
Please refer to the individual drug's full prescribing information for complete indication, dosing, and treatment information.

There are additional considerations for selecting a treatment. Please talk to your doctor about treatment options and what might be right for you.

SELECTED IMPORTANT SAFETY INFORMATION (cont'd)

- **Slow heart rate (also known as bradyarrhythmia) when you start taking ZEPOSIA.** ZEPOSIA may cause your heart rate to temporarily slow down, especially during the first 8 days. You will have a test to check the electrical activity of your heart called an electrocardiogram (ECG) before you take your first dose of ZEPOSIA.

SELECTED IMPORTANT SAFETY INFORMATION (cont'd)

Call your healthcare provider if you experience the following symptoms of slow heart rate:

- dizziness
- lightheadedness
- feeling like your heart is beating slowly or skipping beats
- shortness of breath
- confusion
- chest pain
- tiredness

Please see additional Important Safety Information throughout and Prescribing Information and Medication Guide.

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SELECTED IMPORTANT SAFETY INFORMATION (cont'd)

Follow directions from your healthcare provider when starting ZEPOSIA and when you miss a dose.

Continue reading for additional possible serious side effects of ZEPOSIA.

Before taking ZEPOSIA, tell your healthcare provider about all of your medical conditions, including if you:

- have a fever or infection, or are unable to fight infections due to a disease, or take or have taken medicines that lower your immune system
- received a vaccine in the past 30 days or are scheduled to receive a vaccine. ZEPOSIA may cause vaccines to be less effective
- before you start ZEPOSIA, your healthcare provider may give you a chickenpox (Varicella Zoster Virus) vaccine if you have not had one before
- have had chickenpox or have received the vaccine for chickenpox. Your healthcare provider may do a blood test for the chickenpox virus. You may need to get the full course of the vaccine and wait 1 month before taking ZEPOSIA
- have a slow heart rate
- have an irregular or abnormal heartbeat (arrhythmia)
- have a history of stroke
- have or have had heart problems, including a heart attack or chest pain
- have high blood pressure
- have liver problems
- have breathing problems, including during your sleep
- have eye problems, especially an inflammation of the eye called uveitis
- have diabetes
- are or plan to become pregnant or if you become pregnant within 3 months after you stop taking ZEPOSIA. ZEPOSIA may harm your unborn baby. If you are a female who can become pregnant, talk to your healthcare provider about what birth control method is right for you during your treatment with ZEPOSIA and for 3 months after you stop taking ZEPOSIA
- are breastfeeding or plan to breastfeed. It is not known if ZEPOSIA passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take ZEPOSIA

Tell your healthcare provider about all the medicines you take or have recently taken, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using ZEPOSIA with other medicines can cause serious side effects. Especially tell your healthcare provider if you take or have taken:

- medicines that affect your immune system, such as alemtuzumab
- medicines to control your heart rhythm (antiarrhythmics), or heartbeat
- CYP2C8 inducers such as rifampin
- CYP2C8 inhibitors such as gemfibrozil (medicine to treat high fat in your blood)
- opioids (pain medicine), medicines to treat depression, and medicines to treat Parkinson's disease
- medicines to control your heart rate and blood pressure (beta blocker medicines and calcium channel blocker medicines)

You should not receive **live** vaccines during treatment with ZEPOSIA, for at least 1 month before taking ZEPOSIA and for 3 months after you stop taking ZEPOSIA. Vaccines may not work as well when given during treatment with ZEPOSIA.

ZEPOSIA can cause serious side effects, including:

- **liver problems.** Your healthcare provider will do blood tests to check your liver before you start taking ZEPOSIA. Call your healthcare provider right away if you have any of the following symptoms:
  - unexplained nausea
  - vomiting
  - stomach area (abdominal) pain
  - tiredness
  - loss of appetite
  - yellowing of the whites of your eyes or skin
  - dark colored urine
- **increased blood pressure.** Your healthcare provider should check your blood pressure during treatment with ZEPOSIA. A sudden, severe increase in blood pressure (hypertensive crisis) can happen when you eat certain foods that contain high levels of tyramine.
- **breathing problems.** Some people who take ZEPOSIA have shortness of breath. Call your healthcare provider right away if you have new or worsening breathing problems.
- **a problem with your vision called macular edema.** Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis. Your healthcare provider should test your vision before you start taking ZEPOSIA if you are at higher risk for macular edema or any time you notice vision changes during treatment with ZEPOSIA. Call your healthcare provider right away if you have any of the following symptoms:
  - blurriness or shadows in the center of your vision
  - sensitivity to light
  - a blind spot in the center of your vision
  - unusually colored vision
- **swelling and narrowing of the blood vessels in your brain.** Posterior Reversible Encephalopathy Syndrome (PRES) is a rare condition that has happened with ZEPOSIA and with drugs in the same class. Symptoms of PRES usually get better when you stop taking ZEPOSIA. If left untreated, it may lead to stroke. Your healthcare provider will do a test if you have any symptoms of PRES. Call your healthcare provider right away if you have any of the following symptoms:
  - sudden severe headache
  - sudden confusion
  - sudden loss of vision or other changes in your vision
  - seizure

The most common side effects of ZEPOSIA can include:

- upper respiratory tract infections
- elevated liver enzymes
- low blood pressure when you stand up (orthostatic hypotension)
- painful and frequent urination (signs of urinary tract infection)
- back pain
- high blood pressure
- headache

These are not all of the possible side effects of ZEPOSIA. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see additional Important Safety Information throughout and Prescribing Information and Medication Guide.

Please refer to the individual drug's full prescribing information for complete indication, dosing, and treatment information.

References: 1. ZEPOSIA. Prescribing Information. Bristol-Myers Squibb Company; 2022. **2.** Entyvio. Prescribing Information. Takeda Pharmaceuticals U.S.A., Inc; 2021. **3.** Stelara. Prescribing Information. Janssen Pharmaceutical Companies; 2020. **4.** Humira. Prescribing Information. AbbVie, Inc; 2021. **5.** Remicade. Prescribing Information. Janssen Pharmaceutical Companies; 2021. **6.** Simponi. Prescribing Information. Janssen Pharmaceutical Companies; 2019. **7.** Xeljanz. Prescribing Information. Pfizer, Inc; 2022. **8.** Rinvoq. Prescribing Information. AbbVie, Inc; 2022.

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Bristol Myers Squibb is committed to transparency. For information on the list price of ZEPOSIA as well as information regarding average out-of-pocket costs and assistance programs, please visit our pricing information page at ZEPOSIA.com/ulcerative-colitis/cost.

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