

MEDICATION GUIDE
SIMTRIYO® (Sim-TREE-YO)
(centanafadine)

extended-release capsules, for oral use, [controlled substance schedule pending]

What is the most important information I should know about SIMTRIYO?

SIMTRIYO may cause serious side effects, including:

- **Suicidal thoughts and actions in children 6 years of age and older.** Suicidal thoughts and actions can happen in children 6 years of age and older with attention deficit hyperactivity disorder (ADHD), **especially within the first few months of treatment.**

How can I watch for and try to prevent suicidal thoughts and actions?

- Pay close attention to and tell your healthcare provider right away about any changes, especially sudden changes in mood, behavior, actions, thoughts or feelings, or suicidal thoughts or actions. This is very important when SIMTRIYO treatment is started.
- Keep all follow-up visits with your healthcare provider as scheduled. Tell your healthcare provider about symptoms between visits as needed, especially if you have concerns.

Tell a healthcare provider right away if any of the following symptoms develop during treatment, especially if they are new, worse, or worry you:

- | | |
|-------------------------------------|---|
| ○ thoughts about suicide or dying | ○ trouble sleeping (insomnia) |
| ○ suicide attempts | ○ new or worsening irritability |
| ○ new or worsening depression | ○ acting aggressive, being angry, or violent |
| ○ new or worsening anxiety | ○ acting on dangerous impulses |
| ○ feeling very agitated or restless | ○ an extreme increase in activity and talking (mania) |
| ○ panic attacks | ○ other unusual changes in behavior or mood |
- **Abuse, misuse, and addiction.** SIMTRIYO has a chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of SIMTRIYO can lead to overdose and death. The risk of overdose and death is increased with higher doses of SIMTRIYO or when it is used in ways that are not approved, such as snorting or injection.
 - Your healthcare provider should check you or your child's risk for abuse, misuse, and addiction before starting treatment with SIMTRIYO and will monitor you or your child during treatment.
 - Do not give SIMTRIYO to anyone else because it may cause death or harm them.
 - Keep SIMTRIYO in a safe place and properly dispose of any unused medicine. See **"How should I store SIMTRIYO?"** for more information.
 - Tell your healthcare provider if you or your child have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

See **"What are the possible side effects of SIMTRIYO?"** for more information about side effects.

What is SIMTRIYO?

SIMTRIYO is a prescription medicine used to treat attention deficit hyperactivity disorder (ADHD) in adults and children 6 years of age and older weighing at least 44 pounds (20 kg).

SIMTRIYO is not recommended for use in children under 6 years of age or weighing less than 44 pounds (20 kg).

SIMTRIYO is a federally controlled substance (insert controlled substance schedule) because it contains centanafadine that can be a target for people who abuse prescription medicines or street drugs.

Who should not take SIMTRIYO?

Do not take SIMTRIYO if you or your child:

- are allergic to centanafadine or any of the ingredients in SIMTRIYO. See the end of this Medication Guide for a complete list of ingredients in SIMTRIYO.
- are taking, or have stopped taking within the past 14 days, a medicine called a monoamine oxidase inhibitor (MAOI).
- have a condition called pheochromocytoma (a rare tumor that usually grows in the adrenal glands which are above your kidneys).

Before taking SIMTRIYO, tell your healthcare provider about all your or your child's medical conditions, including if you or your child:

- have heart problems, heart disease, heart defects, or have a family history of sudden death, or high blood pressure
- have mental problems including psychosis, mania, bipolar illness, or depression, or have a family history of suicide, bipolar illness, or depression
- have circulation problems in fingers and toes
- have or had uncontrolled movements or sounds (tics) or Tourette's syndrome, or have a family history of tics or Tourette's syndrome
- have an allergy or sensitivity to FD&C Yellow No. 5 (tartrazine)
- have liver problems
- are pregnant or plan to become pregnant. It is not known if SIMTRIYO will harm the unborn baby. Talk to your healthcare provider about the risk to the unborn baby if you or your child take SIMTRIYO during pregnancy.
 - There is a pregnancy exposure registry for women who are exposed to SIMTRIYO during pregnancy. If you or your child become pregnant during treatment with SIMTRIYO, talk to your healthcare provider about registering with the National Pregnancy Registry for ADHD Medications at 1-866-961-2388 or visiting online at <https://womensmentalhealth.org/research/pregnancyregistry/adhd-medications/>.
- are breastfeeding or plan to breastfeed. It is not known if SIMTRIYO passes into the breast milk. Talk to your healthcare provider about the best way to feed the baby during treatment with SIMTRIYO.

Tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

SIMTRIYO and certain other medicines may affect each other causing possible serious side effects.

Especially tell your healthcare provider if you or your child take:

- a MAOI, including linezolid or intravenous methylene blue
- medicines used to treat mood, anxiety, psychotic or thought disorders, including selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants
- medicines used to treat migraine headaches called triptans
- tramadol, fentanyl, meperidine, methadone, or other opioids
- tryptophan
- St. John's Wort
- other central nervous system (CNS) stimulants including other ADHD medicines

Ask your healthcare provider if you are not sure if you or your child take any of these medicines. Your healthcare provider can tell you if it is safe to take SIMTRIYO with other medicines.

Do not start any new medicine during treatment with SIMTRIYO without first talking to your healthcare provider.

Know the medicines you or your child takes. Keep a list of them and show it to your healthcare provider and pharmacist when you or your child get a new medicine.

How should I take SIMTRIYO?

- Take SIMTRIYO exactly as your healthcare provider tells you to take it.
- Take SIMTRIYO 1 time each day in the morning at about the same time each day.
- Take SIMTRIYO with or without food.
- **Swallow SIMTRIYO capsules whole. Do not** cut, crush, or chew the capsules.
- **If SIMTRIYO cannot be swallowed whole:**
 - Open the capsule and sprinkle the entire contents over 1 tablespoon (15 mL) of applesauce or yogurt, **or** in 1 tablespoon (15 mL) of orange juice.
 - Swallow all of the mixture right away.
 - Drink water right after swallowing the mixture.
 - **Do not** chew the granules.
 - **Do not** save the mixture for later use.
- If you or your child miss a dose of SIMTRIYO, take it as soon as you remember but no later than 4 hours after the normal dosing time. **Do not** take more than 1 dose of SIMTRIYO in the same day.
- If you or your child take too much SIMTRIYO, call your healthcare provider or Poison Help Line at 1-800-222-1222, or go to the nearest hospital emergency room right away.

What should I avoid while taking SIMTRIYO?

Do not drink alcohol at the same time or within 2 hours of taking SIMTRIYO. This may cause a faster release of the SIMTRIYO medicine and can affect the way SIMTRIYO works and increase your risk for side effects.

What are the possible side effects of SIMTRIYO?

- See **“What is the most important information I should know about SIMTRIYO?”**

- **Risks in people with serious heart disease.** Sudden death has happened in people who have heart defects or other serious heart disease. Your healthcare provider should check you or your child carefully for heart problems before starting treatment with SIMTRIYO. Tell your healthcare provider or go to the nearest emergency room right away if any signs of heart problems develop such as chest pain, shortness of breath, or fainting.
- **Increased blood pressure and heart rate.** Your healthcare provider should check you or your child’s blood pressure and heart rate before starting treatment, if the dose is increased, and as needed during treatment with SIMTRIYO.

- **Mental problems (psychiatric reactions), including:**

- worsening behavior or thought problems in people with thought or psychotic disorders
- manic episodes in people with bipolar disorder
- new psychotic or manic symptoms in people without bipolar or psychotic disorders

Tell your healthcare provider right away if any mental symptoms or problems develop or worsen during treatment with SIMTRIYO, including:

- greatly increased energy
- racing thoughts
- unusually grand ideas
- talking more or faster than usual
- severe trouble sleeping
- reckless behavior
- excessive happiness or irritability
- seeing or hearing things that are not real (hallucinations).

- **Allergic reactions, including serious allergic reactions (anaphylaxis).** Serious allergic reactions can happen during treatment with SIMTRIYO and can lead to hospitalization. Your healthcare provider may stop treatment with SIMTRIYO if you develop allergic reactions. Tell your healthcare provider right away if you get any signs or symptoms including:

- raised, red areas on your skin (hives)
- skin redness or rash, itching, flaking or peeling
- dizziness or fainting
- swelling of face, eyes, lips, throat, or other areas
- difficulty in breathing or swallowing

- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with SIMTRIYO. SIMTRIYO treatment may be stopped if your child is not growing or gaining weight as expected.

- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud’s phenomenon).** Tell your healthcare provider if any of the following signs and symptoms of circulation problems develop during treatment:

- fingers or toes feel numb, cool, painful
- fingers or toes change color from pale, to blue, to red
- sensitivity to temperature in fingers or toes

Call your healthcare provider right away if any unexplained wounds appear on the fingers or toes during treatment with SIMTRIYO.

- **Serotonin Syndrome.** A potentially life-threatening problem called serotonin syndrome can happen when you take SIMTRIYO with certain other medicines. See **“Who should not take SIMTRIYO?”** and **“Especially tell your healthcare provider if you or your child take:”** Stop taking SIMTRIYO and tell your healthcare provider or go to the nearest hospital emergency room right away if any of the following signs and symptoms develop during treatment:

- agitation
- confusion
- fast heartbeat
- dizziness
- flushing
- tremors, stiff muscles, or muscle twitching
- seizures
- coma
- changes in blood pressure
- sweating
- high body temperature (hyperthermia)
- loss of coordination
- nausea, vomiting, diarrhea
- seeing or hearing things that are not real (hallucinations)

- **New or worsening tics or worsening Tourette’s syndrome.** Tell your healthcare provider if any new or worsening tics or worsening Tourette’s syndrome symptoms develop during treatment with SIMTRIYO.

- **Allergic reactions to FD&C Yellow No. 5.** SIMTRIYO 210 mg capsules contain a yellow food dye called tartrazine (FD&C No. 5) which may cause allergic-type reactions (including bronchial asthma) in certain people. If you are allergic to aspirin, you may be more likely to react to tartrazine. Tell your healthcare provider if any symptoms of allergic reactions develop during treatment, including hives, rash, swelling, or trouble breathing.

The most common side effects of SIMTRIYO in children 6 to 12 years of age include:

- rash
- decreased appetite

The most common side effects of SIMTRIYO in children 13 to 17 years or age include:

- decreased appetite
- headache
- nausea
- stomach area (abdominal) pain
- rash

The most common side effects of SIMTRIYO in adults include:

- headache
- decreased appetite
- trouble sleeping (insomnia)
- nausea
- dry mouth
- diarrhea

These are not all the possible side effects of SIMTRIYO.

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

How should I store SIMTRIYO?

- Store SIMTRIYO at room temperature, between 68°F to 77°F (20°C to 25°C).
- Store SIMTRIYO in a safe place, like a locked cabinet.
- Dispose of remaining, unused, or expired SIMTRIYO by a medicine take-back program at a U.S. Drug Enforcement Administration (DEA) authorized collection site. If no take-back program or DEA authorized collector is available, mix SIMTRIYO with an undesirable, nontoxic substance such as dirt, cat litter, or used coffee grounds to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and throw away SIMTRIYO in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.

Keep SIMTRIYO and all medicines out of the reach of children.

General information about the safe and effective use of SIMTRIYO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SIMTRIYO for a condition for which it was not prescribed. Do not give SIMTRIYO to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about SIMTRIYO that is written for health professionals.

What are the ingredients in SIMTRIYO?

Active ingredient: centanafadine

Inactive ingredients: The capsule beads contain colloidal silicon dioxide, ethyl acrylate and methyl methacrylate copolymer, hypromellose, mannitol, microcrystalline cellulose, plasacryl, poly (methyl acrylate-CO-methyl methacrylate-CO-methacrylic acid), polysorbate 80, and talc. The capsule shells contain hypromellose, titanium dioxide, FD&C Blue 1 (280 mg), FD&C Yellow 5 (210 mg), and FD&C Yellow 6 (140 mg). The capsules are imprinted with edible black ink.

Manufactured for Otsuka America Pharmaceutical, Inc., Rockville, MD 20850 USA

© 2026, Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan

For more information about SIMTRIYO go to www.simtriyo.com or call 1-833-468-7852.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Issued: 07/2026

26US26IBR0007