WINREVAIR™
(sotatercept-csrk) for injection
45 mg, 60 mg

DOSAGE AND ADMINISTRATION GUIDE

Indication

WINREVAIR is an activin signaling inhibitor indicated for the treatment of adults with pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class (FC), and reduce the risk of clinical worsening events.

Selected Safety Information

Erythrocytosis: WINREVAIR may cause increases in hemoglobin (Hgb). Severe erythrocytosis may increase the risk of thromboembolic events or hyperviscosity syndrome. In clinical studies, moderate elevations in Hgb (>2 g/dL above upper limit of normal [ULN]) occurred in 15% of patients taking WINREVAIR while no elevations ≥4 g/dL above ULN were observed. Monitor Hgb before each dose for the first 5 doses, or longer if values are unstable, and periodically thereafter, to determine if dose adjustments are required.

Before prescribing WINREVAIR, please read the accompanying Prescribing Information. The Patient Information and Instructions for Use (1-vial kit, 2-vial kit) also are available.

WINREVAIR is administered once every 3 weeks by subcutaneous injection, according to patient body weight

WINREVAIR™ (sotatercept-csrk) for injection 45 mg, 60 mg

The recommended STARTING DOSE is 0.3 mg/kg

- **Obtain hemoglobin (Hgb) and platelet count prior to the first dose of WINREVAIR.**
- **Do not initiate treatment if platelet count is <50,000/mm^3 (<50 x 10^9/L).**

Injection volume for starting dose is calculated based on patient weight as follows:

$$\text{Injection volume (mL)} = \frac{\text{Weight (kg) x 0.3 mg/kg}}{\text{50 mg/mL}}$$

Injection volume should be rounded to the nearest 0.1 mL.

For example: (70 kg x 0.3 mg/kg) ÷ 50 mg/mL = 0.42 mL, rounds to 0.4 mL.

See the table below for selecting the appropriate kit based on calculated injection volume for starting dose.

Kit type based on injection volume for dose of 0.3 mg/kg

Injection Volume (mL)	Kit Type[a]
0.2 to 0.9	45 mg kit (containing 1 x 45 mg vial)
1 to 1.1	60 mg kit (containing 1 x 60 mg vial)

[a]For more information on selecting the appropriate product kit, see page 6.

Selected Safety Information *(continued)*

Severe Thrombocytopenia: WINREVAIR may decrease platelet count. Severe thrombocytopenia may increase the risk of bleeding. In clinical studies, severe thrombocytopenia (platelet count <50,000/mm^3 [<50 x 10^9/L]) occurred in 3% of patients taking WINREVAIR. Thrombocytopenia occurred more frequently in patients also receiving prostacyclin infusion. Do not initiate treatment if platelet count is <50,000/mm^3. Monitor platelets before each dose for the first 5 doses, or longer if values are unstable, and periodically thereafter to determine whether dose adjustments are required.

Serious Bleeding: In clinical studies, serious bleeding (eg, gastrointestinal, intracranial hemorrhage) was reported in 4% of patients taking WINREVAIR and 1% of patients taking placebo. Patients with serious bleeding were more likely to be on prostacyclin background therapy and/or antithrombotic agents, or have low platelet counts. Advise patients about signs and symptoms of blood loss. Evaluate and treat bleeding accordingly. Do not administer WINREVAIR if the patient is experiencing serious bleeding.

WINREVAIR is administered once every 3 weeks by subcutaneous injection, according to patient body weight

WINREVAIR™ (sotatercept-csrk) for injection 45 mg, 60 mg

The recommended TARGET DOSE is 0.7 mg/kg

- **After verifying acceptable Hgb and platelet count, increase to the target dose of 0.7 mg/kg.**
- **Continue treatment at 0.7 mg/kg every 3 weeks unless dosage adjustments are required.**

Injection volume for target dose is calculated based on patient weight as follows:

$$\text{Injection volume (mL)} = \frac{\text{Weight (kg)} \times 0.7 \text{ mg/kg}}{50 \text{ mg/mL}}$$

Injection volume should be rounded to the nearest 0.1 mL.
For example: (70 kg x 0.7 mg/kg) ÷ 50 mg/mL = 0.98 mL, rounds to 1 mL.
See the table below for selecting the appropriate kit based on calculated injection volume for target dose.

Kit type based on injection volume for dose of 0.7 mg/kg

Injection Volume (mL)	Kit Type[a]
0.4 to 0.9	45 mg kit (containing 1 x 45 mg vial)
1 to 1.2	60 mg kit (containing 1 x 60 mg vial)
1.3 to 1.8	90 mg kit (containing 2 x 45 mg vials)
1.9 to 2.4	120 mg kit (containing 2 x 60 mg vials)

[a]For more information on selecting the appropriate product kit, see page 6.

Selected Safety Information *(continued)*

Embryo-Fetal Toxicity: Based on findings in animal reproduction studies, WINREVAIR may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use an effective method of contraception during treatment with WINREVAIR and for at least 4 months after the final dose. Pregnancy testing is recommended for females of reproductive potential before starting WINREVAIR treatment.

Impaired Fertility: Based on findings in animals, WINREVAIR may impair female and male fertility. Advise patients on the potential effects on fertility.

Missed dose, overdose, and underdose

- If a dose of WINREVAIR is missed, administer as soon as possible.
  - If the missed dose of WINREVAIR is not administered within 3 days of the scheduled date, adjust the schedule to maintain 3-week dosing intervals.
- In case of an overdose, monitor for erythrocytosis.

Dosage modifications due to Hgb increase or platelet count decrease

Check Hgb and platelet count before each dose for the first 5 doses, or longer if values are unstable. Thereafter, monitor Hgb and platelet count periodically.

Delay treatment for at least 3 weeks if any of the following occur:

- Hgb increases >2.0 g/dL from the previous dose and is above ULN.
- Hgb increases >4.0 g/dL from baseline.
- Hgb increases >2.0 g/dL above ULN.
- Platelet count decreases to <50,000/mm^3 (<50.0 x 10^9/L).

Recheck Hgb and platelet count before reinitiating treatment. For treatment delays lasting >9 weeks, restart treatment at 0.3 mg/kg, and escalate to 0.7 mg/kg after verifying acceptable Hgb and platelet count.

Selected Safety Information *(continued)*

Adverse Reactions: The most common adverse reactions occurring in the Phase 3 clinical trial (≥10% for WINREVAIR and at least 5% more than placebo) were as follows: headache (24.5% vs 17.5%), epistaxis (22.1% vs 1.9%), rash (20.2% vs 8.1%), telangiectasia (16.6% vs 4.4%), diarrhea (15.3% vs 10.0%), dizziness (14.7% vs 6.2%), and erythema (13.5% vs 3.1%).

Lactation: Because of the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with WINREVAIR, and for 4 months after the last dose.

Preparation and administration

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Administration is subject to monitoring of Hgb and platelet count.

WINREVAIR is intended for use under the guidance of a healthcare professional. Patients and caregivers may administer WINREVAIR when considered appropriate and when they receive training and follow-up from the healthcare provider on how to reconstitute, prepare, measure, and inject WINREVAIR.

Confirm at subsequent visits that the patient and/or caregiver can correctly prepare and administer WINREVAIR, particularly if the dose changes or the patient requires a different kit.

Refer to the Instructions for Use (IFU) for detailed instructions on the proper preparation and administration of WINREVAIR.

Selected Safety Information *(continued)*

Pediatric Use: The safety and effectiveness of WINREVAIR have not been established in patients less than 18 years of age.

Geriatric Use: A total of 81 patients ≥65 years of age participated in clinical studies for PAH, of which 52 (16%) were treated with WINREVAIR. Bleeding events occurred more commonly in the older WINREVAIR subgroup, but with no imbalance between age subgroups for any specific bleeding event.

Preparation and administration *(continued)*

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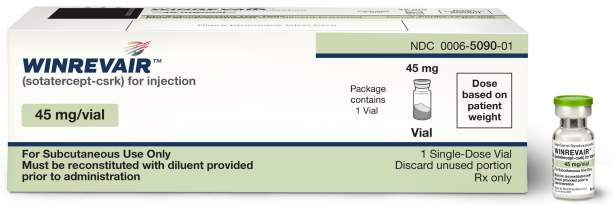
Selecting the appropriate product kit

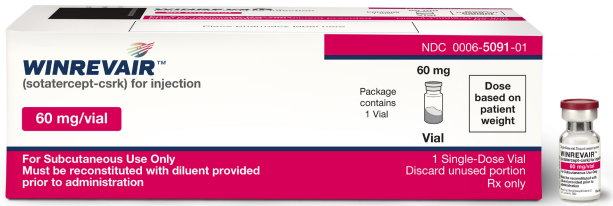
If a patient's body weight requires the use of two 45 mg vials or two 60 mg vials of lyophilized product, use a 2-vial kit instead of two individual 1-vial kits. A 2-vial kit includes instructions to combine the contents of two vials, which aids in measuring the proper dosage and eliminates the need for multiple injections.

1-vial kits

45 mg kit

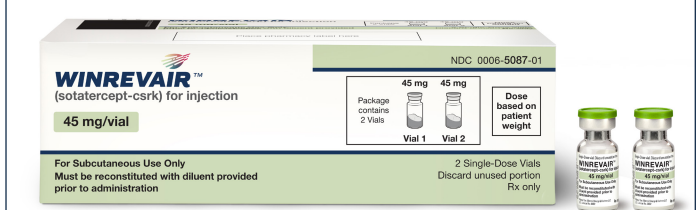


60 mg kit

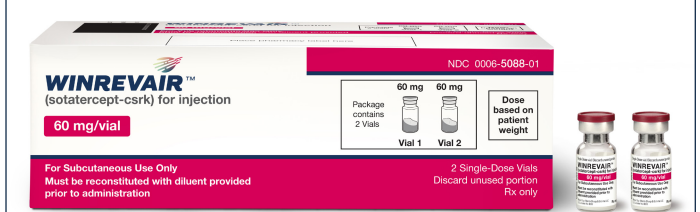


2-vial kits

2 x 45 mg kit



2x 60 mg kit



Not actual size.

Selected Safety Information

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Preparation and administration *(continued)*

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Reconstitution instructions

1. Remove the injection kit from the refrigerator and wait 15 minutes to allow the prefilled syringe(s) and drug product to come to room temperature prior to preparation.
2. Attach the vial adapter to the vial.
3. Visually inspect the pre-filled syringe for any damage or leaks and the Sterile Water for Injection inside to ensure there are no visible particles.
4. Snap off the cap of the pre-filled syringe and attach the syringe to the vial adapter.
5. Inject all of the Sterile Water for Injection from the attached syringe into the vial containing the lyophilized powder. This will provide a final concentration of 50 mg/mL.
6. Gently swirl the vial to reconstitute the drug product. DO NOT shake or vigorously agitate.
7. Allow the vial to stand for up to 3 minutes to allow bubbles to disappear.
8. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
9. When properly mixed, WINREVAIR should be clear to opalescent and colorless to slightly brownish-yellow and does not have clumps or powder.
10. If prescribed a 2-vial presentation, repeat the steps within this section to prepare the second vial.
11. Use the reconstituted solution as soon as possible, but no later than 4 hours after reconstitution. Discard unused reconstituted solution.

Selected Safety Information *(continued)*

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Preparation and administration *(continued)*

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Syringe preparation

1. Turn the syringe and vial upside-down and withdraw the appropriate volume for injection, based on the patient's weight.
   - If the dose amount requires the use of two vials, withdraw the entire contents of the first vial and slowly transfer full contents into the second vial.
   - Turn the syringe and vial upside-down and withdraw the required amount of drug product.
   - If necessary, remove excess drug product.
2. If necessary, remove excess air from the syringe.

Selected Safety Information *(continued)*

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Preparation and administration *(continued)*

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Administration instructions

WINREVAIR is for subcutaneous injection.

1. Select the injection site on the abdomen (at least 2 inches away from navel), upper thigh, or upper arm, and swab with an alcohol wipe. Select a new site for each injection that is not scarred, tender, or bruised.
   - For administration by the patient or caregiver, use only the abdomen and upper thigh (see IFU).
2. Perform subcutaneous injection.

Dosage forms and strengths

- For injection: 45 mg white to off-white lyophilized cake or powder appearance in a single-dose vial.
- For injection: 60 mg white to off-white lyophilized cake or powder appearance in a single-dose vial.

Selected Safety Information *(continued)*

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