**Package leaflet: Information for the user**

**Bivalirudin 250 mg powder for concentrate for solution for injection or infusion**
Bivalirudin

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**

1. What Bivalirudin is and what it is used for
2. What you need to know before you use Bivalirudin
3. How to use Bivalirudin
4. Possible side effects
5. How to store Bivalirudin
6. Contents of the pack and other information


## 1. What Bivalirudin is and what it is used for

Bivalirudin contains a substance called bivalirudin which is an antithrombotic medicine. Antithrombotics are medicines which prevent the formation of blood clots (thrombosis).

Bivalirudin is used to treat patients:
- with chest pain due to heart disease (acute coronary syndrome - ACS)
- who are having surgery to treat blockages in their blood vessels (angioplasty and/or percutaneous coronary intervention - PCI).

## 2. What you need to know before you use Bivalirudin

**Do not use Bivalirudin**

- if you are allergic to bivalirudin or any of the other ingredients of this medicine (listed in section 6) or hirudins (other blood thinning medicines).
- if you have, or have recently had, any bleeding from your stomach, intestines, bladder or other organs, for example, if you have noticed abnormal blood in your stools or urine (except from menstrual bleeding).
- if you have, or have had, difficulty with your blood clotting (a low platelet count).
- if you have severe high blood pressure.
- if you have an infection of the heart tissue.
- if you have severe kidney problems or if you need kidney dialysis.

Check with the doctor if you are unsure.

**Warnings and precautions**

Talk to your doctor before using Bivalirudin.

- if bleeding occurs (if this happens, treatment with Bivalirudin will be stopped). Throughout your treatment, the doctor will check you for any signs of bleeding.
- if you have been treated before with medicines similar to Bivalirudin (e.g. lepirudin).
- before the start of the injection or infusion, the doctor will tell you about the signs of allergic reaction. Such a reaction is uncommon (affects 1 to 10 users in 1,000).
- if you are having radiation treatment in the vessels that supply blood to the heart (treatment called beta or gamma brachytherapy).

After being treated with Bivalirudin for a cardiac event, you should stay in the hospital for at least 24 hours and you should be monitored for any symptoms or signs similar to the ones that remind you of your cardiac event and resulted in your hospitalization.

**Children and adolescents**

- if you are a child (less than 18 years of age), this medicine is not appropriate for you.

**Other medicines and Bivalirudin**

Tell your doctor
- if you are taking, have recently taken, or might take any other medicines.
- if you are taking blood thinners or medicines to prevent blood clots (anticoagulants or antithrombotics, e.g. warfarin, dabigatran, apixaban, rivaroxaban, acetylsalicylic acid, clopidogrel, prasugrel, ticagrelor).

These medicines may increase the risk of side effects such as bleeding when given at the same time as Bivalirudin. Your warfarin blood test result (INR test) may be affected by Bivalirudin.

**Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Bivalirudin should not be used during pregnancy, unless clearly necessary. Your doctor will decide whether or not this treatment is appropriate for you. If you are breast-feeding, the doctor will decide whether Bivalirudin should be used.

**Driving and using machines**

The effects of this medicine are known to be short-term. Bivalirudin is only given when a patient is in hospital. It is, therefore, unlikely to affect your ability to drive or to use machines.

**Bivalirudin contains sodium**
This medicine contains less than 23 mg of sodium per vial, which means that it is essentially "sodium free".

## 3. How to use Bivalirudin

Your treatment with Bivalirudin will be supervised by a doctor. The doctor will decide how much Bivalirudin you receive, and will prepare the medicine.

The dose given depends on your weight and on the kind of treatment you are being given.

**Dosage**

**For patients with acute coronary syndrome (ACS) who are treated medically** the recommended **starting dose** is:

- 0.1 mg/kg body weight as an intravenous injection, followed by an infusion (drip) into vein of 0.25 mg/kg body weight per hour for up to 72 hours.

If, after this, **you** then need percutaneous coronary intervention (PCI) treatment, the dosage will be increased to:

- 0.5 mg/kg body weight for the intravenous injection, followed by an infusion into vein of 1.75 mg/kg body weight, per hour for at least the duration of the PCI. This intravenous infusion may continue for up to 4 hours.

- When this treatment is finished, the infusion may go back to **0.25 mg/kg** body weight per hour.

If you need to have a coronary artery bypass graft operation, treatment with bivalirudin will either be stopped one hour before the operation or an additional dose of 0.5 mg/kg body weight will be given by injection followed by an infusion of 1.75 mg/kg body weight per hour.

**For patients starting with percutaneous coronary intervention (PCI)** the recommended dose is:

- **0.75 mg/kg** body weight as an injection, followed immediately by an infusion of **1.75 mg/kg** body weight, per hour (the intravenous infusion may continue for up to 4 hours).

If you have kidney problems, the dose of Bivalirudin Reig Jofre may need to be reduced.

In older people, if their kidney function is decreased, the dose may need to be reduced.

The doctor will decide for how long you should be treated.

Bivalirudin Reig Jofre is for injection, followed by infusion (drip), into a vein (never into a muscle). This is administered and supervised by a doctor experienced in caring for patients with heart disease.

**If you receive more of this medicine than you should**
Your doctor will decide how to treat you, including stopping the drug and monitoring for signs of ill effects.
If you have any further questions on the use of this medicine, ask your doctor.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
If you get any of the following, potentially serious, side effects:

- **while you are in hospital: tell the doctor or nurse immediately**
- **after you've left hospital: contact your doctor directly or go immediately to the Emergency Department of your nearest hospital**

The most common, (may affect up to 1 in 10 people) serious side effect of treatment with Bivalirudin is major bleeding, which could occur anywhere inside the body (e.g. stomach, digestive system (including vomiting blood or passing blood with the stools), abdomen, lungs, groin, bladder, heart, eye, ear, nose or brain)**.** This may, **rarely**, result in a stroke or be fatal. Swelling or pain in the groin or the arm, back pain, bruising, headache, coughing blood, pink or red urine, sweating, feeling faint or sick or dizzy due to low blood pressure may be signs of

internal bleeding. Bleeding is more likely to occur when Bivalirudin is used in combination with other anticoagulant or antithrombotic medicines (see section 2 'Taking other medicines').

- Bleeding and bruising at the puncture site (after PCI treatment) may be painful. Rarely this may require surgery to repair the blood vessel in the groin (fistula, pseudoaneurysm) (may affect up to 1 in 1,000 people). Uncommonly (may affect up to 1 in 100 people) the number of blood platelets may be low which can worsen any bleeding. Gum bleeding (uncommon, may affect up to 1 in 100 people) is usually not serious.
- Allergic reactions, are uncommon (may affect up to 1 in 100 people) and usually not serious, but can become severe under some circumstances, and in rare cases may be fatal due to low blood pressure (shock). They may begin with limited symptoms such as itching, redness of the skin, rash or small bumps on the skin. Occasionally, reactions can be more severe with throat itching, throat tightening, swelling of the eyes, face, tongue or lips, high pitched whistling during inhaling (stridor), difficulty breathing or exhaling (wheezes).
- Thrombosis (blood clot) is an uncommon side effect (may affect up to 1 in 100 people) which may result in serious or fatal complications such as heart attack. Thrombosis includes coronary artery thrombosis (blood clot in the heart arteries or within a stent being felt as a heart attack which can also be fatal) and/or thrombosis in the catheter, both of which are rare (may affect up to 1 in 1,000 people).

If you get any of the following, (potentially less serious), side effects:

- **while you are in hospital: tell the doctor or nurse**
- **after you've left hospital: first seek advice from your doctor. If you cannot get access to your doctor, go immediately to the Emergency Department of your nearest hospital**

Very common side effects (may affect more than 1 in 10 people):
- Minor bleeding

Common side effects (may affect up to 1 in 10 people):
- Anaemia (a low blood cell count)
- Haematoma (bruising)

Uncommon side effects (may affect up to 1 in 100 people):
- Nausea (feeling sick) and/or vomiting (being sick)

Rare side effects (may affect up to 1 in 1000 people):
- INR test (warfarin blood test result) increased (see Section 2, Other medicines and Bivalirudin Reig Jofre)
- Angina or chest pain
- Slow heartbeat
- Rapid heartbeat
- Shortness of breath
- Reperfusion injury (no or slow reflow): impaired flow in the heart arteries after they have been reopened

**Reporting of side effects**
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard
By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Bivalirudin

As Bivalirudin is a hospital only medicine, storage of Bivalirudin is the responsibility of healthcare professionals.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after 'EXP'. The expiry date refers to the last day of that month.

Freeze-dried powder: This medicinal product does not require any special storage conditions

Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 2-8ºC. Store in a refrigerator (2ºC-8ºC). Do not freeze.

Diluted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 25ºC. Do not store above 25ºC. Do not freeze.

'From a microbiological point of view, unless the method of opening/ reconstitution/ dilution precludes the risk of microbial contamination, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of user.'

The solution should be a clear to slightly opalescent, colourless to slightly yellow solution.
The doctor will check the solution and will discard it, if it contains particles or is discoloured.

## 6. Contents of the pack and other information

### What Bivalirudin contains

- The active substance is bivalirudin.
- Each vial contains 250 mg bivalirudin.
- After reconstitution (addition of 5 ml water for injections to the vial to dissolve the powder), 1 ml contains 50 mg bivalirudin.
- After dilution (mixing 5 ml of the reconstituted solution into an infusion bag [total volume of 50 ml] of glucose solution or sodium chloride solution), 1 ml contains 5 mg bivalirudin. The other ingredients are mannitol and sodium hydroxide (for pH adjustment).

### What Bivalirudin looks like and contents of the pack

Bivalirudin is a powder for concentrate for solution for injection or infusion (powder for concentrate).
Bivalirudin is a white to off-white powder in a glass vial.
Bivalirudin is available in cartons containing 2 and 10 vials.

### Marketing Authorisation Holder and Manufacturer

### Marketing Authorisation Holder

Reig Jofre UK Limited
Follaton House, Plymouth Road,
Totnes, Devon, TQ9 5NE, UK

### Manufacturer

Laboratorio Reig Jofré S.A.

Gran Capitán, 10
08970 Sant Joan Despí (Barcelona)
Spain

**This medicinal product is authorized in the Member States of the EEA under the following names:**

Denmark: Bivalirudin Reig Jofre 250 mg pulver til koncentrat til injektionsvæske eller infusionsvæske, opløsning
Spain: Bivalirudina Sala 250mg polvo para concentrado para solución inyectable o perfusión
Finland: Bivalirudin Reig Jofre 250 mg, kuiva-aine välikonsentraatiksi injektio-/infuusionestettä varten, liuos
Island: Bivalirudin Reig Jofre 250 mg stofn fyrir innrennslis- eða stungulyfsþykkni, lausn Norway: Bivalirudin Reig Jofre 250 mg pulver til konsentrat til injeksjons- eller infusjonsvæske, oppløsning
Sweden: Bivalirudin Reig Jofre 250 mg pulver till koncentrat till injektions-/infusionsvätska, lösning
United Kingdom: Bivalirudin 250 mg powder for concentrate for solution for injection or infusion

This leaflet was approved in 08/2025

Detailed information on this medicinal product is available on the website of United Kingdom/MHRA

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The following information is intended for healthcare professionals only:

Healthcare professionals should refer to the Summary of Product Characteristics for full prescribing information.

Bivalirudin is indicated as an anticoagulant in adult patients undergoing percutaneous coronary intervention (PCI), including patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI.

Bivalirudin is also indicated for the treatment of adult patients with unstable angina/non-ST segment elevation myocardial infarction (UA/NSTEMI) planned for urgent or early intervention.

Bivalirudin should be administered with acetylsalicylic acid and clopidogrel.

**Instructions for preparation**

Aseptic procedures should be used for the preparation and administration of Bivalirudin.

Add 5 ml sterile water for injections to one vial of Bivalirudin and swirl gently until completely dissolved and the solution is clear.

Withdraw 5 ml from the vial, and further dilute in a total volume of 5% 50 ml of glucose solution for injection, or sodium chloride 9 mg/ml (0.9%) solution for injection to give a final bivalirudin concentration of 5 mg/ml.

The reconstituted/diluted solution should be inspected visually for particulate matter and discolouration. Solutions containing particulate matter should not be used.

The reconstituted/diluted solution will be a clear to slightly opalescent, colourless to slightly yellow solution.

Any unused product or waste material should be disposed of in accordance with local requirements.

**Incompatibilities**

The following medicinal products should not be administered in the same intravenous line as bivalirudin since they result in haze formation, micro-particulate formation or gross precipitation; alteplase, amiodarone HCl, amphotericin B, chlorpromazine hydrochloride (HCl), diazepam, prochlorperazine edisylate, reteplase, streptokinase and vancomycin HCl.

The following six medicinal products show dose-concentration incompatibilities with bivalirudin. See section 6.2 for the summary of compatible and incompatible concentrations of these compounds. The medicinal products incompatible with bivalirudin at higher concentrations are: dobutamine hydrochloride, famotidine, haloperidol lactate, labetalol hydrochloride, lorazepam and promethazine HCl.

**Contraindications**

Bivalirudin is contraindicated in patients with:

- a known hypersensitivity to the active substance or to any of the excipients listed in section 6.1, or to hirudins
- active bleeding or increased risk of bleeding because of haemostasis disorders and/or irreversible coagulation disorders
- severe uncontrolled hypertension
- subacute bacterial endocarditis
- severe renal impairment (GFR<30 ml/min) and in dialysis-dependent patients. (See section 4.3 of SmPC).

**Posology**

*Patients undergoing PCI, including primary PCI*

The recommended dose of bivalirudin for patients undergoing PCI is an intravenous bolus of 0.75 mg/kg body weight followed immediately by an intravenous infusion at a rate of 1.75 mg/kg body weight/hour for at least the duration of the procedure. The infusion of 1.75 mg/kg body weight/hour may be continued for up to 4 hours post-PCI as clinically warranted and further continued at a reduced infusion dose of 0.25 mg/kg/h for 4-12 hours as clinically necessary.

Patients should be carefully monitored following primary PCI for signs and symptoms consistent with myocardial ischaemia.

*Patients with unstable angina/non-ST segment elevated myocardial infarction (UA/NSTEMI)*

The recommended starting dose of bivalirudin for patients with acute coronary syndrome (ACS) is an intravenous bolus of 0.1 mg/kg followed by an infusion of 0.25 mg/kg/h. Patients who are to be medically managed may continue the infusion of 0.25 mg/kg/h for up to 72 hours.

If the patient proceeds to PCI, an additional bolus of 0.5 mg/kg of bivalirudin should be administered before the procedure and the infusion increased to 1.75 mg/kg/h for the duration of the procedure.
Following PCI, the reduced infusion dose of 0.25 mg/kg/h may be resumed for 4 to 12 hours as

clinically necessary.

For patients who proceed to coronary artery bypass graft (CABG) surgery off pump, the intravenous infusion of bivalirudin should be continued until the time of surgery. Just prior to surgery, a 0.5 mg/kg bolus dose should be administered followed by a 1.75 mg/kg/h intravenous infusion for the duration of the surgery.

For patients who proceed to CABG surgery on pump, the intravenous infusion of bivalirudin should be continued until 1 hour prior to surgery after which the infusion should be discontinued and the patient treated with unfractionated heparin (UFH).

To ensure appropriate administration of bivalirudin, the completely dissolved, reconstituted and diluted product should be thoroughly mixed prior to administration (see section 6.6). The bolus dose should be administered by a rapid intravenous push to ensure that the entire bolus reaches the patient before the start of the procedure.

Intravenous infusion lines should be primed with bivalirudin to ensure continuity of drug infusion after delivery of the bolus.

The infusion dose should be initiated immediately after the bolus dose is administered, ensuring delivery to the patient prior to the procedure, and continued uninterrupted for the duration of the procedure. The safety and efficacy of a bolus dose of bivalirudin without the subsequent infusion has not been evaluated and is not recommended even if a short PCI procedure is planned.

An increase in the activated clotting time (ACT) may be used as an indication that a patient has received bivalirudin.

*Renal insufficiency*
Bivalirudin is contraindicated in patients with severe renal insufficiency (GFR<30 ml/min) and also in dialysis-dependent patients (see section 4.3).

In patients with mild or moderate renal insufficiency, the ACS dose (0.1 mg/kg bolus/0.25 mg/kg/h infusion) should not be adjusted.

Patients with moderate renal impairment (GFR 30-59 ml/min) undergoing PCI (whether being treated with bivalirudin for ACS or not) should receive a lower infusion rate of 1.4 mg/kg/h. The bolus dose should not be changed from the posology described under ACS or PCI above.

*Hepatic impairment*
No dose adjustment is needed.
(For full information on posology see section 4.2 of SmPC)

**Shelf life**

30 months
Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 2-8ºC. Store in a refrigerator (2ºC –8ºC). Do not freeze.
Diluted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 25ºC. Do not store above 25ºC. Do not freeze.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in use storage times and conditions are the responsibility of user.