

XARELTO® GRANULES FOR ORAL SUSPENSION

Consumer Medication Information Leaflet (RiMUP)

Rivaroxaban (1mg/ml)

What is in this leaflet

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What *Xarelto* is used for

Xarelto is used in full-term newborn babies, infants and toddlers, children and adolescents below 18 years to: treat blood clots and prevent re-occurrence of blood clots in the veins or in the blood vessels of the lungs, following an initial treatment of at least 5 days with injectable medicines used to treat blood clots.

How *Xarelto* works

Xarelto works by blocking a blood clotting factor (factor Xa) and thus reducing the tendency of the blood to form clots.

Before you use *Xarelto*

- When you must not use it

Do not take *Xarelto*

- if you are allergic to rivaroxaban or any of the other ingredients of this medicine listed at the end of the leaflet;
- if you are bleeding excessively
- have a disease or condition in an organ of the body that increases the risk of serious bleeding (e.g. stomach ulcer, injury or bleeding in the brain, recent surgery of the brain or eyes)
- are taking medicines to prevent blood clotting (e.g. warfarin, dabigatran, apixaban or heparin), except

- when changing medicines to prevent blood clotting or
- while getting heparin through a venous or arterial line to keep it open.

- have a liver disease associated with an increased risk of bleeding

- are pregnant or breast-feeding

- Before you start to use it

Inform your doctor if you

- you or the child have an increased risk of bleeding. This could be the case in situations such as:

- moderate or severe kidney disease; as the kidney function may affect the amount of medicine that works in the body

- if you or the child are taking other medicines to prevent blood clotting (e.g. warfarin, dabigatran, apixaban or heparin), if these are absolutely necessary

- bleeding disorders

- very high blood pressure, not controlled by medical treatment

- diseases of stomach or bowel that might result in bleeding, e.g. inflammation of the bowels or stomach, or inflammation of the food pipe due to a disease where stomach acid goes upwards into the food pipe or tumours located in the stomach or bowels or genital tract or urinary tract

- a problem with the blood vessels in the back of the eyes (retinopathy)

- a lung disease where the bronchi are widened and filled with pus (bronchiectasis), or previous bleeding from the lung

- you or the child have a prosthetic heart valve

- you or the child have a disease called antiphospholipid syndrome (a disorder of the immune system that causes an increased risk of blood clots)

- your or the child's blood pressure is unstable

- another treatment or surgical procedure is planned to remove the blood clot from the lungs

If any of the above apply to you or to the child, tell your doctor before you take or give *Xarelto*. The doctor will decide, if you or the child should be treated with this medicine and should be kept under closer observation.

If you or the child need to have an operation

- It is very important to take or give *Xarelto* before and after the operation exactly at the times your doctor has told you.

- If the operation involves a catheter or injection into the spinal column (e.g. for epidural or spinal anaesthesia or pain reduction):

- it is very important to take or give *Xarelto* before and after the injection or removal of the catheter exactly at the times your doctor has told you

- tell your doctor immediately if you or the child get numbness or weakness of the legs or problems with the bowel or bladder after the end of anaesthesia. In this case, urgent care is necessary.

Children and adolescents

Do not give *Xarelto* to children under 6 months of age who

- were born before 37 weeks of pregnancy, or

- weigh less than 2.6 kg, or
- had less than 10 days of breast or formula feeding

In these cases, dosing of Xarelto cannot be reliably determined and has not been studied in these children.

Xarelto oral suspension is to be used for patients below 18 years to treat blood clots and prevent re-occurrence of blood clots in the veins or in the blood vessels of the lungs. There is not enough information on its use in children and adolescents in other indications.

Taking other medicines

Tell your doctor or pharmacist if you or the child are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Enhanced effects ranging up to an increased risk of side effects:

- some medicines for fungal infections (e.g. fluconazole, itraconazole, voriconazole, posaconazole), unless they are only applied to the skin
- ketoconazole tablets (used to treat Cushing's syndrome - when the body produces an excess of cortisol)
- some medicines for bacterial infections (e.g. clarithromycin, erythromycin)
- some medicines for HIV/AIDS (e.g. ritonavir)
- other medicines to reduce blood clotting (e.g. enoxaparin, clopidogrel or vitamin K antagonists such as warfarin and acenocoumarol)
- medicines to relieve inflammation and pain (e.g. naproxen or acetylsalicylic acid)
- dronedarone, a medicine to treat abnormal heart beat
- some medicines to treat depression (selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs))

If any of the above apply to you or the child, tell your doctor before taking or

giving Xarelto, because the effect of Xarelto may be increased. Your doctor will decide, if you or the child should be treated with this medicine and should be kept under closer observation.

If the doctor thinks that you or the child are at increased risk of developing stomach or bowel ulcers, a preventive ulcer treatment might be necessary.

- If you or the child are taking:
 - some medicines to treat epilepsy (phenytoin, carbamazepine, phenobarbital)
 - St John's Wort (*Hypericum perforatum*), a herbal product used for depression
 - rifampicin, an antibiotic

If any of the above apply to you or the child, tell your doctor before taking or giving Xarelto, because the effect of Xarelto may be reduced. The doctor will decide, if you or the child should be treated with Xarelto and should be kept under closer observation.

Pregnancy and breast-feeding

- If you or the adolescent are pregnant or breast-feeding **do not take or give Xarelto**.
- If there is a **chance** that you or the adolescent could **become pregnant**, a reliable **contraceptive** should be used while taking Xarelto.
- If you or the adolescent become pregnant while taking this medicine, tell your doctor immediately, who will decide how the treatment should be continued.

How to use Xarelto

- How much to use

Always take this medicine or give this medicine to the child exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Make sure that the correct information on how much and how often to take or give Xarelto is written on the designated area of the carton. If not, ask your pharmacist or doctor to provide the relevant information.

-How much to take

Instructions for Use

For how to prepare and take or give the Xarelto oral suspension:

- See the Instructions for Use booklet included in the carton and

How much to take or give

The dose of Xarelto depends on the patient's body weight. It will be calculated by the doctor as an amount (volume) in millilitres (mL) of the oral suspension. This should be measured out using the blue syringe (either 1 mL or 5 mL or 10 mL syringe, see table 1) supplied with this medicine. Your doctor will prescribe the volume required including the particular syringe you should use.

Your doctor will tell you how much of the oral suspension you or the child must take.

Do not adjust the dose yourself.

All materials to prepare and administer the oral suspension are provided with the medicine (except for drinking water.) Only use non-carbonated water to avoid bubbles. Only use the syringe provided to administer Xarelto to ensure accurate dosing. Do not use any other method to administer the solution, e.g. alternative syringe, spoon etc.

As the Xarelto dose is based on body weight it is important to keep scheduled doctor's visits because the dose may need to be adjusted as the weight changes, especially for children below 12 kg. This ensures that the child receives the correct dose of Xarelto.

Your doctor may also prescribe tablets if you or the child are able to swallow the tablet and are weighing at least 30 kg.

- When to use it

Take or give Xarelto oral suspension with feeding (breast milk or formula feeding) or with a meal. Each Xarelto dose has to be swallowed along with one typical serving of liquid (for example 20 mL in children aged 6 months up to 240 mL in adolescents). This typical serving may include usual amount of drink used for feeding (e.g. breast milk, infant formula, nutrition drink).

Your doctor may give the oral suspension also via a stomach tube.

Take or give the oral suspension as directed every day until the doctor tells you to stop.

Take or give the oral suspension at the same time every day to help you to remember it. Consider setting an alarm to remind you.

Please observe the child to ensure the full dose is taken.

If the doctor has told you to take or give Xarelto:

- once a day, do this approximately 24 hours apart
- twice a day, do this approximately 12 hours apart
- three times a day, do this approximately 8 hours apart

- How long to use it

Your doctor will decide how long you or the child must continue treatment.

If you or the child spits up the dose or vomits

- less than 30 minutes after the intake of Xarelto, take or give a new dose.
- more than 30 minutes after the intake of Xarelto, do not take or give a new dose. Continue to take or give the next Xarelto dose at the next scheduled time.

Contact the doctor if you or the child repeatedly spit up the dose or vomit after taking Xarelto.

- If you forget to use it

If you are taking or giving Xarelto once a day, take or give the missed Xarelto dose as soon as you remember on the same day. If this is not possible, skip this dose. Then take or give the next Xarelto dose on the following day. Do not take or give more than one dose per day.

If you are taking or giving Xarelto twice a day:

- Missed morning dose: Take or give the missed dose as soon as

you remember. You may take or give it together with the evening dose.

- Missed evening dose: You may take or give the missed dose only in the same evening. Do not take or give two doses the next morning.

If you are taking or giving Xarelto three times a day, do not make up for the missed dose. Continue with the next scheduled dose (given every 8 hours).

On the day following a missed dose, continue as prescribed by the doctor once, twice or three times a day.

- If you use too much (overdose)

Contact your doctor immediately if you have taken or given too much Xarelto oral suspension. Taking or giving too much Xarelto increases the risk of bleeding.

While you are using it

- Things you must do

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

- Things you must not do

Do not stop Xarelto without talking to your doctor first, because Xarelto treats and prevents serious conditions.

- Things to be careful of

Driving and using machines

Xarelto may cause dizziness or fainting. You or the child should not drive, ride a bicycle or use any tools or machines if affected by these symptoms

Xarelto contains sodium benzoate and sodium

This medicine contains 1.8 mg sodium benzoate (E 211) in each mL oral suspension. Sodium benzoate (E 211) may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

This medicine contains less than 1 mmol sodium (23 mg) per millilitre, that is to say essentially "sodium-free".

Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Like other similar medicines to reduce the formation of blood clots, Xarelto may cause bleeding which may potentially be life threatening. Excessive bleeding may lead to a sudden drop in blood pressure (shock). In some cases the bleeding may not be obvious.

Tell your doctor immediately if you or the child experience any of the following side effects:

- Signs of bleeding

- bleeding into the brain or inside the skull (symptoms can include headache, one-sided weakness, vomiting, seizures, decreased level of consciousness, and neck stiffness.
A serious medical emergency. Seek medical attention immediately!)
- long or excessive bleeding
- exceptional weakness, tiredness, paleness, dizziness, headache, unexplained swelling, breathlessness, chest pain or angina pectoris
- Your doctor may decide to keep you or the child under closer observation or change the treatment.

- Signs of severe skin reactions

- spreading intense skin rash, blisters or mucosal lesions, e.g. in the mouth or eyes (Stevens-Johnson syndrome/toxic epidermal necrolysis)
- a drug reaction that causes rash, fever, inflammation of internal organs, blood abnormalities and systemic illness (DRESS syndrome)
- The frequency of these side effects is very rare (up to 1 in 10,000 people).

- **Signs of severe allergic reactions**
 - swelling of the face, lips, mouth, tongue or throat; difficulty swallowing; hives and breathing difficulties; sudden drop in blood pressure

- The frequencies of severe allergic reactions are very rare (anaphylactic reactions, including anaphylactic shock; may affect up to 1 in 10,000 people) and uncommon (angioedema and allergic oedema; may affect up to 1 in 100 people).

Overall list of possible side effects found in adults and children and adolescents:

Common (may affect up to 1 in 10 people)

- reduction in red blood cells which can make the skin pale and cause weakness or breathlessness
- bleeding in the stomach or bowel, urogenital bleeding (including blood in the urine and heavy menstrual bleeding), nose bleed, bleeding in the gum
- bleeding into the eye (including bleeding from the whites of the eyes)
- bleeding into tissue or a cavity of the body (haematoma, bruising)
- coughing up blood
- bleeding from the skin or under the skin
- bleeding following an operation
- oozing of blood or fluid from surgical wound
- swelling in the limbs
- pain in the limbs
- impaired function of the kidneys (may be seen in tests performed by your doctor)
- fever
- stomach ache, indigestion, feeling or being sick, constipation, diarrhoea
- low blood pressure (symptoms may be feeling dizzy or fainting when standing up)
- decreased general strength and energy (weakness, tiredness), headache, dizziness
- rash, itchy skin

- blood tests may show an increase in some liver enzymes

Uncommon (may affect up to 1 in 100 people)

- bleeding into the brain or inside the skull (see above, possible side effects which may be a sign of bleeding)
- bleeding into a joint causing pain and swelling
- thrombocytopenia (low number of platelets, which are cells that help blood to clot)
- allergic reactions, including allergic skin reactions
- impaired function of the liver (may be seen in tests performed by your doctor)
- blood tests may show an increase in bilirubin, some pancreatic or liver enzymes or in the number of platelets
- fainting
- feeling unwell
- faster heartbeat
- dry mouth
- hives

Rare (may affect up to 1 in 1,000 people)

- bleeding into a muscle
- cholestasis (decreased bile flow), hepatitis incl. hepatocellular injury (inflamed liver incl. liver injury)
- yellowing of the skin and eye (jaundice)
- localised swelling
- collection of blood (haematoma) in the groin as a complication of the cardiac procedure where a catheter is inserted in your leg artery (pseudoaneurysm)

Very rare (may affect up to 1 in 10,000 people)

- accumulation of eosinophils, a type of white granulocytic blood cells that cause inflammation in the lung (eosinophilic pneumonia)

Not known (frequency cannot be estimated from the available data)

- kidney failure after a severe bleeding
- increased pressure within muscles of the legs or arms after a bleeding, which leads to pain, swelling,

altered sensation, numbness or paralysis (compartment syndrome after a bleeding)

Side effects in children and adolescents

In general, the side effects observed in children and adolescents treated with Xarelto were similar in type to those observed in adults and were primarily mild to moderate in severity.

Side effects that were observed more often in children and adolescents:

Very common (may affect more than 1 in 10 people)

- Headache
- fever
- nose bleeding
- vomiting

Common (may affect up to 1 in 10 people)

- raised heartbeat
- blood tests may show an increase in bilirubin (bile pigment)
- thrombocytopenia (low number of platelets which are cells that help blood to clot)
- heavy menstrual bleeding

Uncommon (may affect up to 1 in 100 people)

- blood tests may show an increase in a subcategory of bilirubin (direct bilirubin, bile pigment)

Countermeasures

If you or the child get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my (Consumer → Reporting Side Effects to Medicines ((ConSERF) or Vaccines (AEFI)).

Storage and Disposal of Aspirin Cardio

- Storage

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 carton and on the bottle after EXP.

The expiry date refers to the last day of that month.

After preparation, the shelf life of the suspension is 14 days at room temperature.

Do not store above 30 °C.

Do not freeze. Store the prepared suspension upright.

- Disposal

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Product Description

- What it looks like

Xarelto granules for oral suspension are white granules in a glass bottle with child resistant screw cap.

- Ingredients

- Active ingredient

The active substance is rivaroxaban. One glass bottle contains 51.7 mg (for the 100 mL bottle) or 103.4 mg (for the 250 mL bottle) of rivaroxaban. After preparation, each mL of the suspension contains 1 mg of rivaroxaban.

- Inactive ingredients

Citric acid, anhydrous (E 330), hypromellose (2910), mannitol (E 421), microcrystalline cellulose, carboxymethylcellulose sodium, sodium benzoate (E 211) (see section 2 “Xarelto contains sodium benzoate and sodium”), sucralose (E 955), xanthan gum (E 415), flavour sweet and creamy (consist of flavouring substances, maltodextrin (maize), propylene glycol (E 1520) and acacia gum (E 414)).

Dosage form and content:

- For children weighing **less than 4 kg:**

Folding box with one brown glass bottle (100 mL) containing 2.625 g granules (corresponding to 51.7 mg rivaroxaban), two 1 mL blue syringes, one 50 mL water syringe and one adapter.

- For children weighing **4 kg or more:**

Folding box with one brown glass bottle (250 mL) containing 5.25 g granules (corresponding to 103.4 mg rivaroxaban), two 5 mL and two 10 mL blue syringes, one 100 mL water syringe and one adapter.

- MAL number(s):

MALXXXXXXXXXX

Manufacturer

Bayer AG
51368 Leverkusen
Germany

Product Registration Holder

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