# **Rivaroxaban Viatris**
# Prescriber Guide

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to The Health Products Regulatory Authority: Website: www.hpra.ie.
Adverse reactions/events should also be reported to MAH at e-mail address pv.ireland@viatris.com.

# Contents

## Prescriber Guide

The Prescriber Guide provides recommendations for the use of rivaroxaban in order to minimise the risk of bleeding during treatment with Rivaroxaban Viatris.
The Prescriber Guide does not substitute the Rivaroxaban Viatris Summary of Product Characteristics (SmPC).

## Rivaroxaban Viatris patient alert card

A patient alert card must be provided to each patient who is prescribed Rivaroxaban Viatris 2.5 mg, 10 mg, 15 mg or 20 mg. Please explain the implications of anticoagulant treatment to patients and/or caregiver, in particular highlighting the need for:

- Treatment compliance
- Taking medication with food (for 15 mg and 20 mg only)
- Recognising signs or symptoms of bleeding
- When to seek medical attention

The patient alert card will inform treating physicians and dentists about the patient's anticoagulation treatment and will contain emergency contact information.

*Please instruct patients or caregiver to carry the patient alert card with them at all times and present it to every healthcare provider. Please also instruct the patient to tick the appropriate box on the patient alert card corresponding to the dose that they are taking.*

## 1. STROKE PREVENTION IN NON-VALVULAR AF

Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischaemic attack.

### 1.1 Dosing Recommendations

The recommended dose for prevention of stroke and systemic embolism in patients with non-valvular AF is 20 mg once daily.

In patients with moderate or severe renal impairment, the recommended dose is 15 mg once daily.

**Patients with renal impairment:**
In patients with moderate (creatinine clearance 30-49 ml/min) or severe (15-29 ml/ min) renal impairment the recommended dose is 15 mg once daily. Rivaroxaban Viatris is to be used with caution in patients with severe renal impairment, as limited clinical data indicates a significantly increased plasma concentration. Use is not recommended in patients with creatinine clearance < 15 ml/min.



Rivaroxaban Viatris should be used with caution in patients with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations.

**Duration of therapy:**
Rivaroxaban Viatris should be continued long term provided the benefit of stroke prevention therapy outweighs the potential risk of bleeding. Clinical surveillance in line with anticoagulation practice is recommended throughout the treatment period.

**Missed dose:**
If a dose is missed the patient should take Rivaroxaban Viatris immediately and continue on the following day with the once daily intake as recommended. The dose should not be doubled within the same day to make up for a missed dose.

**Patients with non-valvular atrial fibrillation undergoing PCI with stent placement:**
There is limited experience of a reduced dose of 15 mg Rivaroxaban Viatris once daily (or 10 mg Rivaroxaban Viatris once daily for patients with moderate renal impairment [creatinine clearance 30-49 ml/min]) in addition to a P2Y12 inhibitor for a maximum of 12 months in patients with non-valvular atrial fibrillation who require oral anticoagulation and undergo PCI with stent placement.

**Patients undergoing cardioversion:**
Rivaroxaban Viatris can be initiated or continued in patients who may require cardioversion. For transoesophageal echocardiogram (TEE) guided cardioversion in patients not previously treated with anticoagulants, Rivaroxaban Viatris treatment should be started at least 4 hours before cardioversion to ensure adequate anticoagulation.

## 2. ADULT AND CHILDREN: TREATMENT OF DVT AND PE AND PREVENTION OF RECURRENT DVT AND PE

Treatment of DVT and PE and prevention of recurrent DVT and PE in adults and children (not recommended for use in haemodynamically unstable PE patients).

### 2.1 Dosing Recommendations

**Adults**
Adult patients are initially treated with 15 mg **twice daily** for the first three weeks. This initial treatment is followed by 20 mg **once daily** for the continued treatment period. Patients with DVT/PE and renal impairment may be considered for dose reduction.

When extended prevention of recurrent DVT and PE is indicated (following completion of at least 6 months therapy for DVT or PE), the recommended dose is 10 mg **once daily**. In patients in whom the risk of recurrent DVT or

PE is considered high, such as those with complicated comorbidities, or who have developed recurrent DVT or PE on extended prevention with Rivaroxaban Viatris 10 mg **once daily**, a dose of Rivaroxaban Viatris 20 mg **once daily** should be considered.

Rivaroxaban Viatris 10 mg is not recommended for the initial 6 months treatment of DVT or PE.

### Children

Rivaroxaban Viatris is not recommended for use in children less than 6 months of age who:

- at birth had <37 weeks gestation, or
- have a body weight of less than 2.6 kg, or
- who have had less than 10 days of oral feeding.

The dose of Rivaroxaban Viatris cannot be reliably determined in these children and has not been studied.

For all other children, Rivaroxaban Viatris treatment should be initiated following ≥5 days of initial anticoagulation treatment with parenteral heparins.

Dosing is based on body weight. To ensure that a therapeutic dose is maintained, the weight of the child should be monitored, and the dose reviewed regularly, especially for children below 12 kg. Dose adjustments should be made based on changes in body weight only.

Rivaroxaban Viatris 15 mg Tablets, Rivaroxaban Viatris 20 mg Tablets or granules for oral suspension can be used to achieve the appropriate weight-based dose.

For patients who are unable to swallow whole tablets, other pharmaceutical forms such as granules for oral suspension should be used. Rivaroxaban Viatris is not available as granules for oral suspension.

- For children weighing >2.6kg and <30kg, use the granules for oral suspension.
- For children and adolescents weighing ≥30 and <50kg, use the 15 mg tablet or granules for oral suspension.
- For children and adolescents weighing ≥50kg, use the 20 mg tablet or granules for oral suspension.



**Body-weight-adjusted Rivaroxaban Viatris dosing schedule for children from birth to less than 18 years of age in ml of suspension and mg of tablets.**

| Pharmaceutical form | Body weight [kg] | | Regimen [mg] (1mg=1ml suspension) | | | Total daily dose [mg] (1mg=1ml suspension) |
|---|---|---|---|---|---|---|
| | Min | Max | OD once a day | BID 2 times a day | TID 3 times a day | |
| Oral suspension | 2.6 | <3 | | | 0.8 | 2.4mg |
| | 3 | <4 | | | 0.9mg | 2.7m |
| | 4 | <5 | | | 1,4mg | 4.2mg |
| | 5 | <7 | | | 1.6mg | 4.8mg |
| | 7 | <8 | | | 1.8mg | 5.4mg |
| | 8 | <9 | | | 2.4mg | 7.2mg |
| | 9 | <10 | | | 2.8mg | 8.4mg |
| | 10 | <12 | | | 3.0mg | 9.0mg |
| | 12 | <30 | | 5mg | | 10mg |
| Tablets or oral suspension | 30 | <50 | 15mg | | | 15mg |
| | ≤50 | | 20mg | | | 20mg |

### Measures to reduce dosing errors with the granules for oral suspension

- The prescriber and dispensing pharmacist should clearly explain to the patient or caregiver the individual weight-adjusted dose volume and frequency.
- The dispensing pharmacist should clearly write the prescribed dosage on the outer carton and advise the patient or caregiver which blue syringe (Liquid Dosing Device) to use to ensure that the correct volume is administered.

### Patients with renal impairment:

### Adults

Rivaroxaban Viatris is to be used with caution in patients with severe renal impairment and is not recommended in patients with creatinine clearance <15 ml/min. Limited clinical data for patients with severe renal impairment (creatinine clearance 15-29 ml/min) indicate that rivaroxaban plasma concentrations are significantly increased. Therefore, Rivaroxaban Viatris is to be used with caution in these patients.

Patients with moderate (creatinine clearance 30-49 ml/min) or severe (15-29 ml/min) renal impairment treated for acute DVT, acute PE and prevention of recurrent DVT and PE do not require a dose reduction.

However, during the continued treatment phase, a reduction of the dose from 20 mg once daily to 15 mg once daily should be considered if the patient's assessed risk for bleeding outweighs the risk for recurrent DVT and PE. The recommendation for the use of 15 mg is based on PK modelling and has not been studied in this clinical setting. When the recommended dose is 10 mg once daily, no dose adjustment from the recommended dose is necessary.

Rivaroxaban Viatris should be used with caution in patients with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations.

### Children

No dose adjustment is required for children aged ≥1 year with mild renal impairment (glomerular filtration rate: 50ml ≤ 80ml/min/1.73m2), based on data in adults and limited data in paediatric patients.

Rivaroxaban Viatris is not recommended in children aged ≥1 year with moderate or severe renal impairment (glomerular filtration rate <50ml/min/1.73m2), as no clinical data is available.

In children aged <1 year, estimation of serum creatinine instead of GFR is applied. Rivaroxaban Viatris is not recommended in children aged <1 year with serum creatinine results above 97.5th percentile, as no clinical data is available (see SmPC granules for oral suspension for reference values).

### Duration of therapy:

### Adults

The duration of therapy should be individualised after assessment of the treatment benefit against the risk for bleeding. Clinical surveillance in line with anticoagulation practice is recommended throughout the treatment period.

### Children

**All children, except those aged <2 years with catheter-related thrombosis**

Therapy with Rivaroxaban Viatris should be continued for at least 3 months. Treatment can be extended up to 12 months when clinically necessary. The benefit-risk of continued therapy after 3 months should be assessed on an individual basis taking into account the risk for recurrent thrombosis versus the potential bleeding risk.

**Children aged <2 years with catheter-related thrombosis**

Therapy with Rivaroxaban Viatris should be continued for at least 1 month. Treatment can be extended up to 3 months when clinically necessary. The benefit-risk of continued therapy after 1 month should be assessed on an individual basis taking into account the risk for recurrent thrombosis versus the potential bleeding risk.



### Missed dose:

### Adults

**Twice daily treatment period** (15 mg bid for the first three weeks): If a dose is missed, the patient should take Rivaroxaban Viatris immediately to ensure intake of 30 mg Rivaroxaban Viatris per day. In this case two 15 mg tablets may be taken at once. Continue with the regular 15 mg twice daily intake on the following day

**Once daily treatment period** (beyond three weeks): If a dose is missed, the patient should take Rivaroxaban Viatris immediately and continue on the following day with the once daily intake as recommended. The dose should not be doubled within the same day to make up for a missed dose

### Children

- Once daily regimen: A missed dose should be taken as soon as possible after it is noticed, but only on the same day. If this is not possible, the patient should skip the dose and continue with the next dose as prescribed. The patient should not take two doses to make up for a missed dose
- Two times daily regimen: A missed morning dose should be taken immediately when it is noticed, and it may be taken together with the evening dose. A missed evening dose can only be taken in the same evening
- Three times daily regimen: The three times daily administration schedule with approximately 8-hour intervals should be resumed at the next scheduled dose without compensating for the missed dose

**On the following day**, the child should continue with the regular once, twice, or three times daily regimen.

## 3. ADULT: PREVENTION OF VTE IN ADULT PATIENTS UNDERGOING ELECTIVE HIP OR KNEE REPLACEMENT SURGERY

### 3.1 Dosing Recommendations

The recommended dose is 10 mg Rivaroxaban Viatris taken orally **once daily.** The initial dose should be taken 6 to 10 hours after surgery, provided that haemostasis has been established.

### Patients with renal impairment:

Rivaroxaban Viatris is to be used with caution in patients with severe (creatinine clearance 15 - 29 ml/min) renal impairment. Use is not recommended in patients with creatinine clearance < 15 ml/min (see SmPC sections 4.2 and 5.2). Patients with mild (creatinine clearance 50-80 ml/min) or moderate (creatinine clearance 30-49 ml/min) renal impairment treated for prevention of VTE in adult patients undergoing elective hip or knee replacement surgery do not require a dose reduction.

In patients with moderate renal impairment (creatinine clearance 30 - 49 ml/min) concomitantly receiving other medicinal products which increase

rivaroxaban plasma concentrations Rivaroxaban Viatris is to be used with caution.

**Duration of therapy:**
The duration of treatment depends on the individual risk of the patient for venous thromboembolism which is determined by the type of orthopaedic surgery.

- For patients undergoing major hip surgery, a treatment duration of 5 weeks is recommended
- For patients undergoing major knee surgery, a treatment duration of 2 weeks is recommended

**Missed dose:**
If a dose is missed the patient should take Rivaroxaban Viatris immediately and then continue the following day with once daily intake as before. The dose should not be doubled within the same day to make up for a missed dose.

## 4. ADULT: USE IN CORONARY ARTERY DISEASE AND PERIPHERAL ARTERY DISEASE

Prevention of atherthrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events.

### 4.1 Dosing Recommendations

**Patients taking Rivaroxaban Viatris 2.5 mg twice daily should also take a daily dose of 75-100 mg acetylsalicylic acid (ASA).**

Safety and efficacy of Rivaroxaban Viatris2.5 mg twice daily in combination with ASA plus clopidogrel/ticlopidine has only been studied in patients with recent ACS (see below).

Dual antiplatelet therapy has not been studied in combination with Rivaroxaban Viatris 2.5 mg twice daily in patients with CAD and/or PAD.

**Patients with renal impairment:**
No dose adjustment is required in patients with mild renal impairment (creatinine clearance 50 - 80 ml/min) or moderate renal impairment (creatinine clearance 30 - 49 ml/min). Rivaroxaban Viatris is to be used with caution in patients with severe renal impairment (CrCl 15–29 ml/min) and is not recommended in patients with CrCl <15 ml/min.

In patients with moderate renal impairment (CrCl 30–49 ml/min) concomitantly receiving other medicinal products that increase rivaroxaban plasma concentrations, Rivaroxaban Viatris is to be used with caution.

**Duration of therapy:**
Duration of treatment should be determined for each individual patient based on regular evaluations and should consider the risk for thrombotic events versus the bleeding risks.



**Missed dose:**
If a dose is missed, the patient should continue with the regular 2.5 mg Rivaroxaban Viatris dose as recommended at the next scheduled time. The dose should not be doubled to make up for a missed dose.

## 5. USE IN ACSsp (ACUTE CORONARY SYNDROME SECONDARY PREVENTION)

Prevention of atherothrombotic events in adult patients after an ACS with elevated cardiac biomarkers, co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine.

### 5.1 Dosing Recommendations

Treatment should be regularly evaluated in the individual patient weighing the risk for the ischaemic events against the bleeding risks. Extension of treatment beyond 12 months should be done on an individual patient basis as experience up to 24 months is limited.

The recommended dose of Rivaroxaban Viatris is 2.5 mg **twice daily**, starting as soon as possible after stabilisation of the index ACS event but at the earliest 24 hours after hospital admission and at the time when parenteral anticoagulation therapy would normally be discontinued.

**In addition to Rivaroxaban Viatris 2.5 mg, patients should also take a daily dose of 75-100 mg ASA or a daily dose of 75-100 mg ASA in addition to either a daily dose of 75 mg clopidogrel or a standard daily dose of ticlopidine.**

Treatment in combination with other antiplatelet agents, e.g. prasugrel or ticagrelor, has not been studied and is not recommended.

**Patients with renal impairment:**
Rivaroxaban Viatris is to be used with caution in patients with severe renal impairment (creatinine clearance 15-29 ml/min), as limited clinical data indicates a significantly increased plasma concentration, consequently increasing bleeding risk. Use is not recommended in patients with creatinine clearance <15 ml/min. No dose adjustment is necessary in patients with mild renal impairment (creatinine clearance 50-80 ml/min) or moderate renal impairment (creatinine clearance 30-49 ml/min).

In patients with moderate renal impairment (creatinine clearance 30-49 ml/min) concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations. Rivaroxaban Viatris is to be used with caution.

**Duration of therapy:**
Treatment should be regularly evaluated in the individual patient weighing the risk for ischaemic events against the bleeding risks. Extension of treatment beyond 12 months should be done on an individual patient basis as experience up to 24 months is limited.

**Missed dose:**
If a dose is missed the patient should continue with the regular 2.5 mg Rivaroxaban Viatris dose as recommended at the next scheduled time. The dose should not be doubled to make up for a missed dose.

## 6 ORAL INTAKE

Rivaroxaban Viatris 2.5 and 10 mg can be taken with or without food.

**Rivaroxaban Viatris 15 mg and 20 mg and 1 mg/ml granules for oral suspension must be taken with food.** The intake of these doses with food at the same time supports the required absorption of the drug, thus ensuring a high oral bioavailability.

### Adults

For patients who are unable to swallow whole tablets, a Rivaroxaban Viatris tablet may be crushed and mixed with water or apple puree immediately prior to use and then administered orally. After the administration of crushed Rivaroxaban Viatris 15 mg or 20 mg film-coated tablets, the dose should be immediately followed by food.

The crushed Rivaroxaban Viatris tablet may also be given through gastric tubes after confirmation of the correct gastric placement of the tube. The crushed tablet should be administered in a small amount of water via a gastric tube after which it should be flushed with water. After the administration of crushed Rivaroxaban Viatris 15 mg or 20 mg film-coated tablets, the dose should then be immediately followed by enteral feeding.

### Children

For children weighing ≥ 30kg who are unable to swallow whole tablets, Rivaroxaban Viatris granules for oral suspension should be used. If the oral suspension is not immediately available, when doses of Rivaroxaban Viatris 15mg of 20mg are prescribed, these could be provided by crushing the 15mg or 20mg tablet and mixing it with water or soft foods such as apple puree immediately prior to use and administered orally.

The oral suspension and the crushed Rivaroxaban Viatris tablet may be given through nasogastric or gastric feeding tube. Gastric placement of the tube should be confirmed before administering Rivaroxaban Viatris. Avoid administration of Rivaroxaban Viatris distal to the stomach.

## 7 PERIOPERATIVE MANAGEMENT

If an invasive procedure or surgical intervention is required, if possible, and based on the clinical judgement of the physician:

- Rivaroxaban Viatris 2.5mg should be stopped at least 12 hours before the intervention
- Rivaroxaban Viatris 10/15/20 mg should be stopped at least 24 hours before the intervention



If the procedure cannot be delayed, the increased risk of bleeding due to Rivaroxaban Viatris should be assessed against the urgency of the intervention. Rivaroxaban Viatris should be restarted as soon as possible after the invasive procedure or surgical intervention provided the clinical situation allows and adequate haemostasis has been established as determined by the treating physician.

## 8. SPINAL/EPIDURAL ANAESTHESIA OR PUNCTURE

When neuraxial (spinal/epidural) anaesthesia or puncture is employed, patients treated with antithrombotic agents are at risk of developing an epidural or spinal haematoma which can result in long-term or permanent paralysis. The risk may be increased by:

- post-operative use of indwelling epidural catheters;
- concomitant use of medicinal products affecting haemostasis;
- traumatic or repeated epidural or spinal puncture

Patients must be frequently monitored for signs and symptoms of neurological impairment (e.g. numbness or weakness of the legs, bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary. Prior to neuraxial intervention the physician should consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis.

**Indication-specific recommendations:**

- Stroke prevention in non-valvular AF in adults
- Treatment of DVT and PE and prevention of recurrent DVT and PE in adults and children

There is no clinical experience with the use of 15 mg or 20 mg Rivaroxaban Viatris in these situations.

To reduce the potential risk of bleeding associated with the concurrent use of Rivaroxaban Viatris and neuraxial (epidural/spinal) anaesthesia or spinal puncture, consider the pharmacokinetic profile of Rivaroxaban Viatris.

Placement or removal of an epidural catheter or lumbar puncture is best performed when the anticoagulant effect of Rivaroxaban Viatris is estimated to be low. However, the exact timing to reach a sufficiently low anticoagulant effect in each patient is not known. For the placement/removal of an epidural catheter and based on the general PK characteristics at least 2x half-life, i.e. at least 18 hours in young patients and 26 hours in elderly patients should elapse after the last administration of Rivaroxaban Viatris (see section 5.2 of the SmPC). Following removal of the catheter, at least 6 hours should elapse before the next Rivaroxaban Viatris dose is administered.

If traumatic puncture occurs, the administration of Rivaroxaban Viatris is to be delayed for 24 hours.

No data is available on the placement or removal of a neuraxial catheter in children while on Rivaroxaban Viatris. Discontinue Rivaroxaban Viatris and consider a short acting parenteral anticoagulant.

- Prevention of VTE in adult patients undergoing elective hip or knee replacement surgery

To reduce the potential risk of bleeding associated with the concurrent use of Rivaroxaban Viatris and neuraxial (epidural/spinal) anaesthesia or spinal puncture, consider the pharmacokinetic profile of Rivaroxaban Viatris. Placement or removal of an epidural catheter or lumbar puncture is best performed when the anticoagulant effect of Rivaroxaban Viatris is estimated to be low. However, the exact timing to reach a sufficiently low anticoagulant effect in each patient is not known.

For the placement or removal of an epidural catheter and based on the general PK characteristics at least 2x half-life, i.e. at least 18 hours should elapse after the last administration of rivaroxaban before removal of an epidural catheter (see section 5.2 of the SmPC). Following removal of the catheter, at least 6 hours should elapse before the next Rivaroxaban Viatris dose is administered. If traumatic puncture occurs the administration of Rivaroxaban Viatris is to be delayed for 24 hours.

- Use in coronary artery disease and peripheral artery disease in adult patients
- Use in ACSsp (acute coronary syndrome secondary prevention) in adult patients

There is no clinical experience with the use of 2.5 mg Rivaroxaban Viatris with ASA alone or with ASA plus clopidogrel or ticlopidine in these situations. To reduce the potential risk of bleeding associated with the concurrent use of Rivaroxaban Viatris and neuraxial (epidural/ spinal) anaesthesia or spinal puncture, consider the pharmacokinetic profile of Rivaroxaban Viatris.

Placement or removal of an epidural catheter or lumbar puncture is best performed when the anticoagulant effect of Rivaroxaban Viatris is estimated to be low. However, the exact timing to reach a sufficiently low anticoagulant effect in each patient is not known. Platelet aggregation inhibitors should be discontinued as suggested by the manufacturer's prescribing information.

## 9. CONVERTING FROM VITAMIN K ANTAGONISTS (VKA) TO RIVAROXABAN VIATRIS

For patients treated for **prevention of stroke and systemic embolism,** treatment with VKA should be stopped and Rivaroxaban Viatris therapy should be initiated when the **INR is ≤ 3.0.**

For patients treated for **DVT, PE and prevention of recurrent DVT and PE,** treatment with VKA should be stopped and Rivaroxaban Viatris therapy should be initiated when the **INR is ≤ 2.5.**

**INR measurement is not appropriate to measure the anticoagulant activity of Rivaroxaban Viatris,** and therefore should not be used for this purpose. Treatment with Rivaroxaban only does not require routine coagulation monitoring.

## 10. CONVERTING FROM RIVAROXABAN VIATRIS TO VKA

It is important to ensure adequate anticoagulation while minimising the risk of bleeding during conversion of therapy.

### Adults:

When converting to VKA, Rivaroxaban Viatris and VKA should overlap until the INR is ≥ 2.0. For the first two days of the conversion period, standard initial dosing of VKA should be used followed by VKA dosing guided by INR testing. **INR measurement is not appropriate to measure the anticoagulant activity of Rivaroxaban Viatris. While patients are on both Rivaroxaban Viatris and VKA the INR should be tested the next day, just before the next dose of Rivaroxaban Viatris (but not within 24 hours of the previous dose; any sooner and Rivaroxaban Viatris will interfere with the INR result).** Once Rivaroxaban Viatris has been discontinued, after 24 hours, INR values reliably reflect VKA dosing.

### Children:

Children who convert from Rivaroxaban Viatris to VKA need to continue Rivaroxaban Viatris for 48 hours after the first dose of VKA. After 2 days of co-administration an INR should be obtained prior to the next scheduled dose of Rivaroxaban Viatris. Co-administration of Rivaroxaban Viatris and VKA is advised to continue until the INR is ≥2.0.

## 11. CONVERTING FROM PARENTERAL ANTICOAGULANTS TO RIVAROXABAN VIATRIS

- Patients with continuously administered parenteral drug such as intravenous unfractionated heparin: Rivaroxaban Viatris should be started at the time of discontinuation
- Patients with parenteral drug on a fixed dosing scheme such as Low Molecular Weight Heparin (LMWH): discontinue parenteral drug and start Rivaroxaban Viatris 0 to 2 hours before the time of the next scheduled administration of the parenteral drug

## 12. CONVERTING FROM RIVAROXABAN VIATRIS TO PARENTERAL ANTICOAGULANTS

Discontinue Rivaroxaban and give the first dose of the parenteral anticoagulant at the time the next Rivaroxaban dose would have been taken.

## 13. CONTRAINDICATIONS

Like all anticoagulants, Rivaroxaban Viatris may increase the risk of bleeding. Therefore, Rivaroxaban Viatris is contraindicated in patients

- With clinically significant active bleeding
- With a lesion or condition if considered to be a significant risk of major

bleeding. This may include current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities

- Receiving concomitant treatment with any other anticoagulants e.g. unfractionated heparin (UFH), LMWH (enoxaparin, dalteparin, etc.), heparin derivatives (fondaparinux, etc.), oral anticoagulants (warfarin, dabigatran etexilate, apixaban, etc.) except under the circumstances of switching therapy to or from Rivaroxaban Viatris or when UFH is given at doses necessary to maintain an open central venous or arterial catheter
- With hepatic disease associated with coagulopathy and clinically relevant bleeding risk including Child-Pugh class B and C cirrhotic patients
- Concomitant treatment of ACS with antiplatelet therapy is contraindicated in patients with a prior stroke or a transient ischaemic attack (TIA)
- Also concomitant treatment of CAD/PAD with Rivaroxaban Viatris 2.5mg and ASA is contraindicated in patients with previous haemorrhagic or lacunar stroke, or any stroke within a month.

***Rivaroxaban Viatris is also contraindicated in the following situations:***

- Hypersensitivity to the active substance or to any of the excipients
- During pregnancy. Women of child-bearing potential should avoid becoming pregnant during treatment with Rivaroxaban Viatris
- During breastfeeding. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from therapy

## 14. SPECIAL POPULATIONS

The risk of bleeding increases with increasing age. Several sub-groups of patients are at increased risk of bleeding and should be carefully monitored for signs and symptoms of bleeding complications.
Use in these patients should be balanced against the benefit in terms of prevention of atherothrombotic events. Any unexplained fall in haemoglobin or blood pressure should lead to a search for a bleeding site.

### Patients with renal impairment:

### Adults:

See dosing recommendations for patients with moderate (CrCl 30–49 mL/min) or severe (CrCl 15–29 mL/min) renal impairment. Rivaroxaban Viatris is to be used with caution in patients with severe renal impairment, as limited clinical data indicates a significantly increased plasma concentration. Use is not recommended in patients with creatinine clearance < 15 ml/min.

Rivaroxaban Viatris should be used with caution in patients with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations.



### Children:

In children aged ≥1 year no dose adjustment is required with mild renal impairment (glomerular filtration rate: 50-80ml/min/1.73m2). Rivaroxaban Viatris is not recommended in children aged ≥1 year with moderate or severe renal impairment (glomerular filtration rate <50 ml/min/1.73m2), as no clinical data is available.

Rivaroxaban Viatris is not recommended in children aged <1 year with serum creatinine results above 97.5th percentile, as no clinical data is available (see SmPC Granules for oral suspension for reference values)

- **Patients concomitantly receiving other medicinal products:**
  - Use of Rivaroxaban Viatris is not recommended with systemic azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g. ritonavir)
  - Care is to be taken in patients concomitantly receiving drugs affecting haemostasis such as NSAIDs, ASA, platelet aggregation inhibitors or selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs)
  - After an acute coronary syndrome, patients on treatment with Rivaroxaban Viatris and ASA or Rivaroxaban Viatris and ASA plus clopidogrel/ticlopidine should only receive concomitant treatment with NSAIDs if the benefit outweighs the bleeding risk
  - The interaction with erythromycin, clarithromycin or fluconazole is likely not clinically relevant in most patients but can be potentially significant in high-risk patients (For patients with renal impairment see further above).
  - Interaction studies have only been performed in adults. The extent of interactions in the paediatric population is not known. The warnings above should be taken into account also for the paediatric population

- **Patients with other haemorrhagic risk factors:**

As with other antithrombotics, Rivaroxaban Viatris is not recommended in patients with an increased bleeding risk such as:

  - congenital or acquired bleeding disorders
  - uncontrolled severe arterial hypertension
  - other gastrointestinal disease without active ulceration that can potentially lead to bleeding complications (e.g. inflammatory bowel disease, oesophagitis, gastritis and gastroesophageal reflux disease)
  - vascular retinopathy
  - bronchiectasis or history of pulmonary bleeding

- **Patients with prosthetic valves:**

Safety and efficacy of Rivaroxaban Viatris have not been studied in patients with prosthetic heart valves; therefore, there are no data to support that Rivaroxaban Viatris provides adequate anticoagulation in this patient population. Treatment with Rivaroxaban Viatris is not recommended for these patients

- **Patients with cancer:**

Patients with malignant disease may simultaneously be at higher risk of bleeding and thrombosis. The individual benefit of antithrombotic treatment should be weighed against risk for bleeding in patients with active cancer dependent on tumour location, antineoplastic therapy and stage of disease. Tumours located in the gastrointestinal or genitourinary tract have been associated with an increased risk of bleeding during Rivaroxaban Viatris therapy.
In patients with malignant neoplasms at high risk of bleeding, the use of Rivaroxaban Viatris is contraindicated

- **Rivaroxaban Viatris should be used with caution in ACS patients.**

Rivaroxaban Viatris, co-administered with ASA alone or with ASA plus clopidogrel or ticlopidine, should be used with caution in ACS patients:

- o ≥75 years of age. The benefit risk of the treatment should be individually assessed on a regular basis
- o with a lower weight (<60 kg)
- o Concomitant treatment of ACS with Rivaroxaban Viatris and antiplatelet therapy is contraindicated in patients with a prior stroke or a transient ischaemic attack (TIA).

## 15. OVERDOSE

Due to limited absorption a ceiling effect with no further increase in average plasma exposure is expected at supratherapeutic doses of 50 mg Rivaroxaban Viatris and above in adults, however, no data is available at supratherapeutic doses in children. A decrease in the relative bioavailability for increasing doses (in mg/kg bodyweight) was found, suggesting absorption limitations for higher doses, even when taken together with food in children. A specific reversal agent antagonising the pharmacodynamic effect of rivaroxaban is available (refer to the SmPC of andexanet alfa), however, it is not established in children. The use of activated charcoal to reduce absorption in case of overdose may be considered.

## 16. HOW TO MANAGE BLEEDING COMPLICATIONS

Should bleeding complications arise in a patient receiving Rivaroxaban Viatris, the next Rivaroxaban Viatris administration should be delayed or treatment discontinued as appropriate.
Individualised bleeding management may include:

- Symptomatic treatment, such as mechanical compression, surgical intervention, fluid replacement and haemodynamic support, blood product or component transfusion
- If bleeding cannot be controlled with the above measures, either the administration of a specific factor Xa inhibitor reversal agent (andexanet alfa) or a specific procoagulant reversal agent, such as prothrombin complex concentrate (PCC), activated prothrombin complex concentrate (APCC) or recombinant factor VIIa (r-FVIIa) should be considered. However, there is currently very limited clinical experience with the use of these medicinal products in adults and in children receiving Rivaroxaban Viatris. Due to the high plasma protein binding Rivaroxaban Viatris is not expected to be dialysable.

## 17. COAGULATION TESTING

Rivaroxaban Viatris does not require routine coagulation monitoring. However, measuring Rivaroxaban Viatris levels may be useful in exceptional situations where knowledge of Rivaroxaban Viatris exposure may help to make clinical decisions, e.g. overdose and emergency surgery.
Anti-FXa assays with Rivaroxaban Viatris (rivaroxaban) specific calibrators to measure rivaroxaban levels are now commercially available. If clinically indicated haemostatic status can also be assessed by PT using Neoplastin as described in the SmPC.

The following coagulation tests are increased: Prothrombin time (PT), activated partial thromboplastin time (aPTT) and calculated PT international normalised ratio (INR). Since the INR was developed to assess the effects of VKAs on the PT, it is therefore not appropriate to use the INR to measure activity of Rivaroxaban Viatris. Dosing or treatment decisions should not be based on results of INR except when converting from Rivaroxaban Viatris to VKA as described above.

## 18. DOSING OVERVIEW TABLE

Please consult SmPC for full product information

| **INDICATON**[1] | **DOSING**[1] | **SPECIAL PATIENT POPULATIONS**[1] |
|---|---|---|
| **Stroke prevention** in adult patients with non-valvular atrial fibrillation[a] | **Rivaroxaban Viatris 20 mg once daily** Impaired renal function with CrCl 15-49 ml/min[b]: **Rivaroxaban Viatris 15mg once daily** | **PCI with stent placement** (for max. 12 months): **Rivaroxaban Viatris 15mg once daily** plus a P2Y12 inhibitor (e.g. clopidogrel) **- Rivaroxaban Viatris10mg once daily** plus a P2Y12 inhibitor (e.g. clopidogrel) for patients with impaired renal function (CrCl 30-49 ml/min[b]) |
| Treatment of **DVT** and **PE**[c], and prevention of recurrent DVT and PE | | |

| | | |
|---|---|---|
| Adults | Treatment & prevention of recurrence:<br>**Day 1 - 21:** Rivaroxaban Viatris 15mg twice daily<br>Prevention of recurrence:<br>**Day 22 onwards:** Rivaroxaban Viatris 20mg once daily<br>***Impaired renal function with CrCl 15-49 ml/min:*** Rivaroxaban Viatris15mg once daily, **if patient's assessed risk for bleeding outweighs risk for recurrence**<br>Extended prevention of recurrence: **After at least 6 months treatment:** Rivaroxaban Viatris 10mg once daily | **Extended prevention of recurrence in high risk patients: Rivaroxaban Viatris 20mg once daily** for extended prevention of recurrence, after at least 6 months treatment, in patients at high risk of recurrent DVT or PE, such as those:<br>- With complicated comorbidities<br>- Who have developed recurrent<br>DVT or PE on extended prevention with Rivaroxaban 10 mg |
| Children – dosing is based on body weight | Rivaroxaban Viatris is not recommended for use in children less than 6 months of age who:<br>- at birth had <37 weeks gestation, or<br>- have a body weight of less than<br>2.6kg, or<br>- who have had less than 10 days of oral feeding.<br>The dose of Rivaroxaban Viatris cannot be reliably determined in these children and has not been studied.<br>For all other children, Rivaroxaban Viatris treatment should be initiated following ≥5 days of initial anticoagulation treatment with parenteral heparins. | |



| | | |
|---|---|---|
| | Dosing is based on body weight. To ensure that a therapeutic dose is maintained, the weight of the child should be monitored and the dose reviewed regularly, especially for children below 12 kg. Dose adjustments should be made based on changes in body weight only.<br>Rivaroxaban Viatris 15 mg Tablets, Rivaroxaban Viatris 20mg Tablets or Rivaroxaban Viatris 1mg/mL granules for oral suspension can be used to achieve the appropriate weight-based dose.<br>For children weighing >2.6kg and <30kg, use the granules for oral suspension.<br>For children and adolescents weighing ≥30 and <50kg, use the 15mg tablet or granules for oral suspension.<br>For children and adolescents weighing ≥50kg, use the 20mg tablet or granules for oral suspension. | |
| Prevention of VTE in adults undergoing elective **hip or knee replacement surgery** | **Rivaroxaban Viatris 10 mg once daily**<br>**Hip Replacement Surgery** 5 weeks treatment duration<br>**Knee Replacement Surgery** 2 weeks treatment duration | |

| | | |
|---|---|---|
| Prevention of atherothrombotic events in adult patients with **CAD** or **symptomatic PAD** at high risk of ischaemic events | **Rivaroxaban Viatris 2.5 mg twice daily** in combination with ASA 75–100 mg/day | |
| Prevention of atherothrombotic events in adult patients **after an ACS** with elevated cardiac biomarkers | **Rivaroxaban Viatris 2.5 mg twice daily in combination with standard antiplatelet therapy** (ASA 75–100 mg/day alone or ASA 75–100 mg/day plus clopidogrel 75 mg/day or a standard dose of ticlopidine) | |

**Rivaroxaban Viatris 15 mg and 20 mg should be taken with food**
For patients who are unable to swallow whole tablets, 'Rivaroxaban Viatris' tablet may be crushed and mixed with water or apple puree immediately prior to use and administered orally.

[a] With one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.
[b] Use with caution in patients with creatinine clearance 15–29 ml/min and in patients with renal impairment when concomitantly receiving other medicinal products that increase rivaroxaban plasma concentration.
[c] Not recommended as an alternative to unfractionated heparin in patients with PE who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy.

**Reference: 1.** Rivaroxaban Viatris (rivaroxaban). Summary of Product Characteristics, as approved by the European Commission.