# Part VI: Summary of the risk management plan

## Summary of risk management plan for Rivaroxaban, 2.5 mg, film-coated tablets (rivaroxaban)

This is a summary of the risk management plan (RMP) for Rivaroxaban, 2.5 mg, film-coated tablets. The RMP details important risks of Rivaroxaban, 2.5 mg, film-coated tablets, how these risks can be minimised, and how more information will be obtained about Rivaroxaban, 2.5 mg, film-coated tablets' risks and uncertainties (missing information).

Rivaroxaban, 2.5 mg, film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Rivaroxaban, 2.5 mg, film- coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of Rivaroxaban, 2.5 mg, film-coated tablets' RMP.

### I. The medicine and what it is used for

Rivaroxaban, 2.5 mg, film-coated tablets is authorised for adults to prevent blood clots in the veins after a hip or knee replacement operation and/or to treat blood clots in the veins of legs (deep vein thrombosis) and in the blood vessels of lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels of legs and/or lungs (see SmPC for the full indication). It contains rivaroxaban as the active substance, and it is given by mouth (orally).

### II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Rivaroxaban, 2.5 mg, film-coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Rivaroxaban, 2.5 mg, film-coated tablets' risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Rivaroxaban, 2.5 mg, film-coated tablets, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Rivaroxaban, 2.5 mg, film-coated tablets is not yet available, it is listed under 'missing information' below.

### *II.A List of important risks and missing information*

Important risks of Rivaroxaban, 2.5 mg, film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Rivaroxaban, 2.5 mg, film-coated tablets. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | – Haemorrhage |
| Important potential risks | – Embryo-fetal toxicity |
| Missing information | – Patients with severe renal impairment (creatinine clearance < 30 mL/min)<br>– Remedial procoagulant therapy for excessive hemorrhage<br>– Patients receiving systemic treatment with Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors other than azole-antimycotics (e.g. ketoconazole) and Human immunodeficiency virus (HIV) protease inhibitors (e.g. ritonavir)<br>– Pregnant or breast-feeding women<br>– Patients with AF (atrial fibrillation) and a prosthetic heart valve<br>– Long term therapy with rivaroxaban for treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), stroke prevention in patients with nonvalvular atrial fibrillation (SPAF) and acute coronary syndrome (ACS) in real-life setting<br>– Patients with significant liver diseases (severe hepatic impairment/Child Pugh C) |

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| | – Patients <18 years of age |

***II.B Summary of important risks***

The safety information in the proposed Product Information is aligned to the reference medicinal product.

With reference to one safety concern, apart from routine risk minimisation measures, there are some additional risks minimisation measures:

| **Important identified risk: Hemorrhage** | |
|---|---|
| Risk minimisation measures | *Routine risk minimisation measures:*<br>*Routine risk communication:*<br>The safety information in the proposed product information is aligned to the reference medicinal product.<br>*Other routine risk minimisation measures beyond the Product Information:*<br>Legal status: medicinal product is subject to medical prescription<br>*Additional risk minimisation measures:*<br>– Prescriber Guide<br>– Patient Alert Card |

***II.C Post-authorisation development plan***

**II.C.1 Studies which are conditions of the marketing authorisation**

There are no studies which are conditions of the marketing authorisation or specific obligation of Rivaroxaban, 2.5 mg, film-coated tablets.

**II.C.2 Other studies in post-authorisation development plan**

There are no studies required for Rivaroxaban, 2.5 mg, film-coated tablets.

# Part VI: Summary of the risk management plan

## Summary of risk management plan for Rivaroxaban, 10 mg, film-coated tablets (rivaroxaban)

This is a summary of the risk management plan (RMP) for Rivaroxaban, 10 mg, film-coated tablets. The RMP details important risks of Rivaroxaban, 10 mg, film-coated tablets, how these risks can be minimised, and how more information will be obtained about Rivaroxaban, 10 mg, film-coated tablets' risks and uncertainties (missing information).

Rivaroxaban, 10 mg, film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Rivaroxaban, 10 mg, film-coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of Rivaroxaban, 10 mg, film-coated tablets' RMP.

### I. The medicine and what it is used for

Rivaroxaban, 10 mg, film-coated tablets is authorised for adults to prevent blood clots in the veins after a hip or knee replacement operation and/or to treat blood clots in the veins of legs (deep vein thrombosis) and in the blood vessels of lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels of legs and/or lungs (see SmPC for the full indication). It contains rivaroxaban as the active substance and it is given by mouth (orally).

### II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Rivaroxaban, 10 mg, film-coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Rivaroxaban, 10 mg, film-coated tablets' risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Rivaroxaban, 10 mg, film-coated tablets, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Rivaroxaban, 10 mg, film-coated tablets is notyet available, it is listed under 'missing information' below.

### *II.A List of important risks and missing information*

Important risks of Rivaroxaban, 10 mg, film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Rivaroxaban, 10 mg, film-coated tablets. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | – Haemorrhage |
| Important potential risks | – Embryo-fetal toxicity |
| Missing information | – Patients with severe renal impairment (creatinine clearance < 30 mL/min)<br>– Remedial procoagulant therapy for excessive hemorrhage<br>– Patients receiving systemic treatment with Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors other than azole-antimycotics (e.g. ketoconazole) and Human immunodeficiency virus (HIV) protease inhibitors (e.g. ritonavir)<br>– Pregnant or breast-feeding women<br>– Patients with AF (atrial fibrillation) and a prosthetic heart valve<br>– Long term therapy with rivaroxaban for treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), stroke prevention in patients with nonvalvular atrial fibrillation (SPAF) and acute coronary syndrome (ACS) in real-life setting<br>– Patients with significant liver diseases (severe hepatic |

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|---|---|
| | impairment/Child Pugh C)<br>– Patients <18 years of age |

***II.B Summary of important risks***

The safety information in the proposed Product Information is aligned to the reference medicinal product.

With reference to one safety concern, apart from routine risk minimisation measures, there are some additional risks minimisation measures:

| **Important identified risk: Hemorrhage** | |
|---|---|
| Risk minimisation measures | *Routine risk minimisation measures:*<br>*Routine risk communication:*<br>The safety information in the proposed product information is aligned to the reference medicinal product.<br>*Other routine risk minimisation measures beyond the Product Information:*<br>Legal status: medicinal product is subject to medical prescription<br>*Additional risk minimisation measures:*<br>– Prescriber Guide<br>– Patient Alert Card |

***II.C Post-authorisation development plan***

**II.C.1 Studies which are conditions of the marketing authorisation**

There are no studies which are conditions of the marketing authorisation or specific obligation of Rivaroxaban, 10 mg, film-coated tablets.

**II.C.2 Other studies in post-authorisation development plan**

There are no studies required for Rivaroxaban, 10 mg, film-coated tablets.

# Part VI: Summary of the risk management plan

## Summary of risk management plan for Rivaroxaban, 15 mg, film-coated tablets (rivaroxaban)

This is a summary of the risk management plan (RMP) for Rivaroxaban, 15 mg, film-coated tablets. The RMP details important risks of Rivaroxaban, 15 mg, film-coated tablets, how these risks can be minimised, and how more information will be obtained about Rivaroxaban, 15 mg, film-coated tablets' risks and uncertainties (missing information).

Rivaroxaban, 15 mg, film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Rivaroxaban, 15 mg, film-coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of Rivaroxaban, 15 mg, film-coated tablets' RMP.

### I. The medicine and what it is used for

Rivaroxaban, 15 mg, film-coated tablets is authorised for adults to prevent blood clots in brain (stroke) and other blood vessels in body in patients with a form of irregular heart rhythm called non-valvular atrial fibrillation, and to treat blood clots in the veins of legs (deep vein thrombosis) and in the blood vessels of lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels of legs and/or lungs (see SmPC for the full indication). It contains rivaroxaban as the active substance and it is given by mouth (orally).

### II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Rivaroxaban, 15 mg, film-coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Rivaroxaban, 15 mg, film-coated tablets' risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Rivaroxaban, 15 mg, film-coated tablets, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Rivaroxaban, 15 mg, film-coated tablets is not yet available, it is listed under 'missing information' below.

### *II.A List of important risks and missing information*

Important risks of Rivaroxaban, 15 mg, film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Rivaroxaban, 15 mg, film-coated tablets. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | – Haemorrhage |
| Important potential risks | – Embryo-fetal toxicity |
| Missing information | – Patients with severe renal impairment (creatinine clearance < 30 mL/min)<br>– Remedial procoagulant therapy for excessive hemorrhage<br>– Patients receiving systemic treatment with Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors other than azole-antimycotics (e.g. ketoconazole) and Human immunodeficiency virus (HIV) protease inhibitors (e.g. ritonavir)<br>– Pregnant or breast-feeding women<br>– Patients with AF (atrial fibrillation) and a prosthetic heart valve<br>– Long term therapy with rivaroxaban for treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), stroke prevention in patients with nonvalvular atrial fibrillation (SPAF) and acute coronary syndrome (ACS) in real-life setting<br>– Patients with significant liver diseases (severe hepatic impairment/Child Pugh C)<br>– Patients <18 years of age |

***II.B Summary of important risks***

The safety information in the proposed Product Information is aligned to the reference medicinal product.

With reference to one safety concern, apart from routine risk minimisation measures, there are some additional risks minimisation measures:

| **Important identified risk: Hemorrhage** | |
|---|---|
| Risk minimisation measures | *Routine risk minimisation measures:*<br>*Routine risk communication:*<br>The safety information in the proposed product information is aligned to the reference medicinal product.<br>*Other routine risk minimisation measures beyond the Product Information:*<br>Legal status: medicinal product is subject to medical prescription<br>*Additional risk minimisation measures:*<br>– Prescriber Guide, Patient<br>– Alert Card |

***II.C Post-authorisation development plan***

**II.C.1 Studies which are conditions of the marketing authorisation**

There are no studies which are conditions of the marketing authorisation or specific obligation of Rivaroxaban, 15 mg, film-coated tablets.

**II.C.2 Other studies in post-authorisation development plan**

There are no studies required for Rivaroxaban, 15 mg, film-coated tablets.

# Part VI: Summary of the risk management plan

## Summary of risk management plan for Rivaroxaban, 20 mg, film-coated tablets (rivaroxaban)

This is a summary of the risk management plan (RMP) for Rivaroxaban, 20 mg, film-coated tablets. The RMP details important risks of Rivaroxaban, 20 mg, film-coated tablets, how these risks can be minimised, and how more information will be obtained about Rivaroxaban, 20 mg, film-coated tablets' risks and uncertainties (missing information).

Rivaroxaban, 20 mg, film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Rivaroxaban, 20 mg, film-coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of Rivaroxaban, 20 mg, film-coated tablets' RMP.

### I. The medicine and what it is used for

Rivaroxaban, 20 mg, film-coated tablets is authorised for adults to prevent blood clots in brain (stroke) and other blood vessels in body in patients with a form of irregular heart rhythm called non-valvular atrial fibrillation, and to treat blood clots in the veins of legs (deep vein thrombosis) and in the blood vessels of lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels of legs and/or lungs (see SmPC for the full indication). It contains rivaroxaban as the active substance and it is given by mouth (orally).

### II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Rivaroxaban, 20 mg, film-coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Rivaroxaban, 20 mg, film-coated tablets' risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Rivaroxaban, 20 mg, film-coated tablets, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Rivaroxaban, 20 mg, film-coated tablets is not yet available, it is listed under 'missing information' below.

***II.A List of important risks and missing information***

Important risks of Rivaroxaban, 20 mg, film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Rivaroxaban, 20 mg, film-coated tablets. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | – Haemorrhage |
| Important potential risks | – Embryo-fetal toxicity |
| Missing information | – Patients with severe renal impairment (creatinine clearance < 30 mL/min)<br>– Remedial procoagulant therapy for excessive hemorrhage<br>– Patients receiving systemic treatment with Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors other than azole-antimycotics (e.g. ketoconazole) and Human immunodeficiency virus (HIV) protease inhibitors (e.g. ritonavir)<br>– Pregnant or breast-feeding women<br>– Patients with AF (atrial fibrillation) and a prosthetic heart valve<br>– Long term therapy with rivaroxaban for treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), stroke prevention in patients with nonvalvular atrial fibrillation (SPAF) and acute coronary syndrome (ACS) in real-life setting<br>– Patients with significant liver diseases (severe hepatic impairment/Child Pugh C) |

| List of important risks and missing information | |
|---|---|
| | – Patients <18 years of age |

***II.B Summary of important risks***

The safety information in the proposed Product Information is aligned to the reference medicinal product.

With reference to one safety concern, apart from routine risk minimisation measures, there are some additional risks minimisation measures:

| Important identified risk: Hemorrhage | |
|---|---|
| Risk minimisation measures | *Routine risk minimisation measures:*<br>*Routine risk communication:*<br>The safety information in the proposed product information is aligned to the reference medicinal product.<br>*Other routine risk minimisation measures beyond the Product Information:*<br>Legal status: medicinal product is subject to medical prescription<br>*Additional risk minimisation measures:*<br>– Prescriber Guide, Patient<br>– Alert Card |

***II.C Post-authorisation development plan***

**II.C.1 Studies which are conditions of the marketing authorisation**

There are no studies which are conditions of the marketing authorisation or specific obligation of Rivaroxaban, 20 mg, film-coated tablets.

**II.C.2 Other studies in post-authorisation development plan**

There are no studies required for Rivaroxaban, 20 mg, film-coated tablets.