KEMENTERIAN KESIHATAN MALAYSIA
(Ministry Of Health Malaysia)
Bahagian Perkhidmatan Farmasi
(Pharmacy Services Division)
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MALAYSIA

Tel: 03-7841 3200 / 03-7841 3320 /
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Ruj. Tuan :

Ruj. Kami : KKM-55/BPF/104/001/02 JLD.15(87)

Tarikh : 30 Disember 2014

Timbalan Pengarah Kesihatan Negeri (Farmasi)
Perlis/ Kedah/ Pulau Pinang/ Perak/ Selangor/ Pahang/ Terengganu/ Kelantan/ Sabah/ Sarawak/ Negeri Sembilan/ Melaka/ Johor/ W.P. KL & Putrajaya/ W.P. Labuan

Ketua Pegawai Farmasi
Hospital Kuala Lumpur/ Institut Kanser Negara/ Hospital Rehabilitasi Cheras

Y. Bhg. Datin/ Tuan/ Puan,

KEMASKINI SENARAI SEMAK PEMANTAUAN PENGGUNAAN TABLET DABIGATRAN & RIVAROXABAN DI FASILITI KEMENTERIAN KESIHATAN MALAYSIA

Saya dengan hormatnya merujuk kepada perkara di atas dan surat Ruj. Kami: KKM-55/BPF/104/001/02 JLD.13 (78) bertarikh 17 April 2013 dirujuk.

2. Seperti Y. Bhg. Datin/ Tuan/ Puan sedia maklum, Mesyuarat Panel Kajisemula Senarai Ubat-ubatan KKM Bil 2/2014 pada Julai 2014 telah meluluskan indikasi baru untuk ubat Rivaroxaban. Sehubungan dengan itu, Senarai Semak Pemantauan Penggunaan Tablet Dabigatran telah dikemaskini dengan memasukkan ubat Rivaroxaban ke dalam senarai semak ini agar pemantauan ke atas pesakit di fasiliti Kementerian Kesihatan Malaysia dapat dilaksanakan.

3. Bersama-sama ini dilampirkan garis panduan, carta alir serta senarai semak mempreskrib dan mendispen tablet Dabigatran dan Rivaroxaban yang terkini (**Lampiran A hingga D**). *Prescribing Information for Dabigatran/Rivoraxaban* juga disertakan sebagai rujukan (**Lampiran E**).

5. Sekiranya terdapat sebarang pertanyaan, sila hubungi Pn. Noraini binti Mohamad (emel: norainimohd@moh.gov.my/ 03-7841 3338) atau Pn. Shakirin binti Shaik Rahmat (emel: shakirin@moh.gov.my/03-7841 3634). Segala kerjasama untuk memastikan senarai semak ini digunakan di fasiliti di bawah jagaan Y. Bhg. Datin/ Tuan/ Puan amatlah dihargai.

Sekian, terima kasih.

"BERKHIDMAT UNTUK NEGARA"

Saya yang menurut perintah,

(ABIDA HAQ BINTI SYED M. HAQ)
Pengarah Bahagian Amalan dan Perkembangan Farmasi
Bahagian Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia
RMD/NM/ssr

s.k **Pengarah**
Bahagian Perkembangan Perubatan

Timbalan Pengarah
Cawangan Formulari & Farmakoekonomik
Bahagian Perkhidmatan Farmasi, IPKKM

KEMENTERIAN KESIHATAN MALAYSIA
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Ruj. Kami : KKM-55/BPF/104/012/01 JLD.15(88)

Tarikh : 30 Disember 2014

The Association of Private Hospitals of Malaysia (APHM)

National Heart Association of Malaysia (NHAM)

Malaysian Medical Association (MMA)

Y.Bhg. Dato'/Datin/Tuan/Puan,

KEMASKINI GARIS PANDUAN PEMANTAUAN PENGGUNAAN UBAT ANTIKOAGULASI: DABIGATRAN & RIVAROXABAN

Saya dengan hormatnya merujuk kepada perkara di atas dan surat Ruj. Kami:KKM-55/BPF/104/01 JLD. 11(89) bertarikh 29 Mac 2013.

2. Bahagian ini telah mengemaskini senarai semak pemantauan penggunaan ubat anti-koagulasi dengan memasukkan tablet Rivaroxaban. Ini adalah bagi memastikan keselamatan pesakit-pesakit di fasiliti Kementerian Kesihatan Malaysia (KKM) yang mengunakannya.

3. Sehubungan dengan itu, bersama-sama ini dilampirkan garis panduan, carta alir serta senarai semak mempreskrib dan mendispen tablet Dabigatran dan Rivaroxaban yang telah dikemaskini bagi kegunaan fasiliti kesihatan swasta agar keselamatan pesakit terjamin (**Lampiran A hingga D**). *Prescribing Information for Dabigatran/Rivaroxaban* juga disertakan sebagai rujukan (**Lampiran E**).

Sekian, terima kasih.

`BERKHIDMAT UNTUK NEGARA'

Saya yang menurut perintah,

(ABIDA HAQ BINTI SYED M. HAQ)
Pengarah Amalan dan Perkembangan Farmasi
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BAHAGIAN PERKHIDMATAN FARMASI
KEMENTERIAN KESIHATAN MALAYSIA

Garis Panduan Pemantauan Penggunaan Tablet Dabigatran/Rivaroxaban di Fasiliti Kementerian Kesihatan Malaysia

Edisi ke-2
Tahun 2014

LAMPIRAN A

PROSES KERJA MEMPRESKRIPSI DAN MENDISPEN TABLET DABIGATRAN/RIVAROXABAN DI FASILITI KEMENTERIAN KESIHATAN MALAYSIA

Bil.	Proses Kerja	Tanggungjawab
1	**MEMPRESKRIPSI**	
1.1	Isi *Checklist For Dabigatran/Rivaroxaban Prescribing* **(Lampiran C)** dalam 2 salinan ▪ 1 salinan disimpan dalam fail rekod pesakit ▪ 1 salinan dikepilkan pada preskripsi Senarai semak ini perlu diisi pada kali pertama dipreskrib dengan Dabigatran/Rivaroxaban bagi memantau risiko pendarahan dan status renal pesakit. Sila rujuk *Prescribing Information for Dabigatran dan Rivaroxaban Tablet* untuk panduan pendosan (**Lampiran E**).	Pakar Perunding
1.2	Kepilkan *Checklist For Dabigatran/Rivaroxaban Prescribing* **(Lampiran C)** bersama-sama preskripsi dan beri kepada pesakit untuk mendapat bekalan ubat di farmasi.	Pakar Perunding
2	**SARING DAN DISPEN**	
2.1	Terima dan saring preskripsi Dabigatran/Rivaroxaban serta *Checklist For Dabigatran/Rivaroxaban Prescribing* **(Lampiran C)**. Hubungi preskriber sekiranya terdapat masalah.	Pegawai Farmasi
2.2	Isi *Checklist For Dispensing Dabigatran/Rivaroxaban* (**Lampiran D**) dan dispens mengikut polisi pembekalan ubat hospital. Beri buku rekod antikoagulasi (seperti di **Lampiran B**) kepada pesakit.	Pegawai Farmasi

Bil.	Proses Kerja	Tanggungjawab
2.3	**<u>Kaunseling</u>** ❖ **Kaunseling Pertama** (untuk maklumat lanjut, sila rujuk **Lampiran E**-*Prescribing Information for Dabigatran/Rivaroxaban tablet.* • Beri kaunseling kepada pesakit apabila tablet Dabigatran/Rivaroxaban dibekal pada kali pertama • Isi *Checklist For Dispensing Dabigatran/Rivaroxaban* pada **Lampiran D (Bahagian A, B dan C).** ❖ **Kaunseling Susulan** • Nilai pengetahuan pesakit dan pantau status fungsi renal & hati pesakit serta kenalpasti sebarang kesan sampingan berdasarkan *Checklist For Dispensing Dabigatran/Rivaroxaban* pada **Lampiran D.** • Sekiranya didapati fungsi renal/hati pesakit merosot atau terdapat simptom-simptom pendarahan, hubungi preskriber untuk tindakan selanjutnya. • Laporkan *Adverse Drug Reaction* (ADR) jika perlu.	Pegawai Farmasi
	Pesakit Dalam: Isi borang CP4 dan hantar satu (1) salinan ke Farmasi Pesakit Luar berserta dengan *Checklist For Dispensing Dabigatran/Rivaroxaban* **(Lampiran D).**	
2.4	• Failkan semua dokumen ke dalam fail rekod pesakit **(Lampiran C, D & F)**. • Rekod dan kemaskini semua maklumat yang berkaitan ke dalam *masterlist* **(Lampiran G)**.	Pegawai Farmasi Pesakit Luar
2.5	Untuk bekalan susulan, semak *database* dan ulangi proses **SARING DAN DISPEN (2.3 & 2.4)**.	Pegawai Farmasi

Lampiran B

CARTA ALIRAN

Wad atau Klinik: Memulakan Rawatan Antikoagulasi (Oleh Pakar atau Pakar Perunding)

Menyemak Indikasi untuk rawatan antikoagulasi

Memilih jenis ubat antikoagulasi yang sesuai.

Menjalankan ujian fungsi renal dan hati (baseline) serta menilai risiko pendarahan pesakit.

Mengisi *Checklist For Dabigatran/Rivaroxaban Prescribing* (Lampiran C)

Menyerahkan preskripsi dan *Checklist For Dabigatran/Rivaroxaban Prescribing* (Lampiran C) kepada pesakit.

Menentukan tarikh untuk rawatan susulan dan tarikh ujian darah.

Jika terdapat masalah : Rujuk kepada Pegawai Perubatan

Farmasi Pesakit Luar: Permulaan Rawatan/ Perjumpaan Susulan

1. Menerima dan menyemak *Checklist For Dabigatran/Rivaroxaban Prescribing* (Lampiran C) & preskripsi
2. Rujuk Pegawai Perubatan jika terdapat masalah
3. Isi *Checklist on Dispensing Dabigatran/Rivaroxaban Tablet* (Lampiran D)

   a. <u>Pesakit Baru</u>

   i. Rekod biodata pesakit, bacaan INR dan Serum Creatinine di Bahagian A

   ii. Lengkapkan maklumat ubat pesakit di Bahagian B

   iii. Berikan kaunseling seperti di Bahagian C.

   b. <u>Pesakit Lama</u>

   i. Nilai kefahaman pesakit berdasarkan kriteria di Bahagian C.

   ii. Semak tanda-tanda pendarahan, kegagalan buah pinggang dan kesan sampingan 'gastrointestinal' seperti di Bahagian D,E dan F.

   iii. Lengkapkan Bahagian G

4. Mengisi Buku Rekod Antikoagulasi dan menentukan tarikh susulan pengambilan ubat.
5. Mendispen Ubat
6. Mengisi semua maklumat yang diperlukan seperti di dalam proses kerja.

Perjumpaan susulan.

(3 bulan atau 6 bulan)

Ulang proses di atas bagi perjumpaan susulan untuk pengambilan baki ubat

Lampiran B

Contoh Buku Rekod Antikoagulasi

Informasi Pesakit

Nama:

R/N:

Alamat:

No Tel:

Nama Peg Perubatan:

Hospital/Klinik:

Jika berlaku sebarang kecemasan, sila hubungi:

Butiran Terapi Antikoagulan

(selain warfarin)

Indikasi:

Nama ubat antikoagulasi & dos:

Tarikh mula:

Catatan:

Rekod Lawatan Pesakit

Tarikh	Ubat & Dos	ClCr	TCA	Catatan

Rekod Lawatan Pesakit

Tarikh	Ubat & Dos	ClCr	TCA	Catatan

LAMPIRAN C

Reference No :

CHECKLIST ON PRESCRIBING DABIGATRAN / RIVAROXABAN TABLET

Patient's Name:	IC No & RN:	
INR Value & Date:	Age (Years):	Weight (Kg):
Serum Creatinine & Date(Baseline):	CrCl (ml/min):	
Liver Function & Date (Baseline):		

Please tick (√) at the relevant box

1. **Choice of Anticoagulant**

☐ Dabigatran	Dose:
☐ Rivaroxaban	Dose:

2. **Status of Anticoagulant Therapy**

	New Case
	Switch from Warfarin to Dabigatran / Rivaroxaban (Please state reason:)

3. **Indication**

	Prevention of Stroke and Systemic Embolism in Non-Valvular Atrial Fibrillation ***(Indicated for Dabigatran 110mg & Dabigatran 150mg, Rivaroxaban 15mg & Rivaroxaban 20mg)***
	Prevention of VTE events in total knee replacement or total hip replacement surgery patient ***(Indicated for Dabigatran 75mg & Dabigatran 110mg, Rivaroxaban 10mg)***
	Prevention and Treatment of Recurrent DVT / PE in Acute DVT ***(Indicated for Rivaroxaban 15mg & Rivaroxaban 20mg)***

4. **DO NOT start anticoagulant agent if patient has condition(s) as stated below (Contraindication)**

	Insufficiency renal function CrCl <30ml/min : Dabigatran CrCl <15ml/min : Rivaroxaban		Abnormal hepatic function Child-Pugh B & C : Rivaroxaban Elevated liver enzymes >3 times ULN : Dabigatran
	Active bleeding (< 6 months) (e.g: intracranial hemorrhage, Recent GI bleed)		Planned for neuraxial anesthesia or spinal puncture
	Pregnancy		Lactation

5. **Special Warnings & Precautions**

	Active ulcerative GI disease		Congenital or acquired coagulation disorder
	Bacterial endocarditis		Recent biopsy or major trauma (< 6 months)
	Brain, spinal or ophthalmic surgery		Extreme body weight: >110 kg
	Low body weight: <50 kg		Thrombocytopenia or function platelet defect

6. **Checklist when Switching patient from warfarin to Dabigatran or Rivaroxaban:**

	Dabigatran	**Rivaroxaban**
1. Indication **a) Treatment and Recurrent of DVT**	☐INR must be < 2	☐INR must be ≤ 2.5
b) Prevention of Stroke and Systemic Embolism in Non-Valvular Atrial Fibrillation	☐INR must be < 2	☐INR must be ≤ 3
2. Patient has been informed to discontinue warfarin immediately		
3. The bleeding risk and symptoms has been informed to the patient including the necessity for frequent renal function monitoring		

(Specialist's signature) Date:
Name:
Designation and Stamp:

Reference no.: ☐

CHECKLIST ON DISPENSING DABIGATRAN/RIVAROXABAN TABLET
(Please use one checklist per patient)

Please tick (√) at the relevant box

First visit ☐
Follow up ☐

A. Patient's Biodata and Baseline Renal/Liver Function

Patient's Name:	IC No & RN:	
INR Value & Date:	Age (Years):	Weight (Kg):
Serum Creatinine & Date:	CrCl (ml/min):	
Liver Function & Date:		

B. Concurrent Medications (inclusive of traditional products and supplements)

Drug Name / Dose / Frequency

C. Patient counselling

Drug Dabigatran				
Visit no.:				
Date:				
Take the capsule twice daily at about the same time every day.				
Remind patients not to discontinue Dabigatran without informing the health provider who prescribe it.				
Keep Dabigatran in the original blister pack to protect from moisture. Do not put Dabigatran in pill boxes. **(Dabigatran deteriorates immediately when exposed to humidity).**				
Instruct patient to remove only one capsule from the blister pack at the time of use.				
Do not chew or break the capsule before swallowing. Swallow capsules whole with water. Dabigatran can be taken with or without food.				
If a dose of Dabigatran is not taken at the scheduled time, take it as soon as possible on the same day.				
The missed dose can still be taken up to 6 hours prior to the next dose.				
Do not double dose to make up for the missed dose.				
Do not run out of Dabigatran. Refill the prescription before it finished.				
Inform healthcare provider if there is new drugs prescribed, procedures planned or pregnancy.				
Please explain the possible side effects (**Refer to D,E & F**)				

Rivaroxaban				
Visit no.:				
Date:				
Advise patients to take Rivaroxaban exactly as prescribed. Take the tablet about the same time every day (advisable with the evening meal)				
Remind patients not to discontinue Rivaroxaban without informing the health provider who prescribe it.				
The 15 mg and 20 mg Rivaroxaban tablets should be taken with food, while the 10 mg tablet can be taken with or without food.				
If a dose of Rivaroxaban is not taken at the schedule time, administer the dose as soon as possible on the same day as follows; 1. For patients receiving **15 mg twice daily**: The patient should take the dose immediately to ensure intake of **30 mg daily**, two 15 mg tablets may be taken at once. 2. For patients receiving 20 mg, 15 mg or 10 mg once daily: The patient should take the missed dose immediately on the same day (by 12 midnight).				
Do not run out of Rivaroxaban. Refill the prescription before it finished.				
Inform healthcare provider if there is new drugs prescribed, procedures planned or pregnancy.				
Please explain the possible side effects (**Refer to D,E & F**)				

For initial visit, pharmacist has to counsel based on these points. For 2nd visit onwards, pharmacist has to assess patient's knowledge.

D. Symptoms of bleeding	**Visit no.:**				
	Date:				
Bruises					
Gum, nose bleed					
Headaches, dizziness or weakness					
Haemoptysis					
Haematuria					
Melaena					
Red or black, tarry stools					
E. Symptoms of renal failure					
Excessive or rapid weight gain					
Oedema					
Dehydration					
Nausea & vomiting					
Pruritus					
F. Gastrointestinal adverse reaction (if applicable)					
Dyspepsia, burning or nausea					
Abdominal pain or discomfort					
Epigastric discomfort, GERD					

G. Comment

Visit no.	Date	Comment	Sign & stamp

PRESCRIBING INFORMATION FOR DABIGATRAN / RIVAROXABAN TABLET

Indication and dose:

<table>
<tr><th>Drug</th><th>Dabigatran</th><th>Rivaroxaban</th></tr>
<tr><td rowspan="3">Indication and dose</td><td>• Prevention of venous thromboembolic events in patients who have undergone total knee replacement or total hip replacement surgery (75 mg & 110 mg tablet).

Dose:
Initiate orally within 1–4 hours of completed surgery as a single capsule (110 mg). Thereafter,
<u>Hip replacement</u>:
220mg (2 capsules of 110mg) once daily for 28 - 35 days
<u>Knee replacement</u>:
220mg (2 capsules of 110mg) once daily for 10 days</td><td>• Prevention of venous thromboembolism in patients undergoing elective hip or knee replacement surgery (10mg tablet)

Dose:
<u>Hip replacement</u>:
10 mg once daily for 35 days
<u>Knee replacement</u>:
10 mg once daily for 12 days
(with or without food)</td></tr>
<tr><td>• Reduction of the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (AF)
(110 mg & 150 mg tablet).

Dose:
The recommended daily dose is 300 mg taken as one 150 mg capsule twice daily. Therapy should be continued long term</td><td>• Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factor, such as congestive heart failure, hypertension, age≥ 75 yrs, diabetes mellitus, prior stroke or transient ischaemic attack (15 & 20mg)

Dose:
20 mg once daily with the evening meal. Therapy should be continued long term</td></tr>
<tr><td></td><td>• Treatment of deep vein thrombosis (DVT), and prevention of recurrent DVT and pulmonary embolism (PE) following and acute DVT in adults (15 & 20mg)

Dose:
15 mg twice daily with food, for first 21 days

▼on day 22, transition to

20mg once daily with food, for remaining treatment</td></tr>
</table>

Dosing modification and consideration:

<table>
<tr><th>Drug</th><th>Dabigatran</th><th>Rivaroxaban</th></tr>
<tr><td rowspan="3">Dosing modification and consideration</td><td>Prophylaxis of DVT following hip or knee replacement surgery:
Special patient populations with a reduced daily dose:
• Patients aged 75 years or older
• Moderate renal impairment (creatinine clearance 30–50 mL/min)
• Concomitant use of verapamil or amiodarone or quinidine
Dose recommendation for special patient populations:
Initiate orally within 1–4 hours of completed surgery as a single capsule (75 mg). Thereafter,
<u>Hip replacement</u>:
150mg (2 capsules of 75mg) once daily for 28 - 35 days
<u>Knee replacement</u>:
150mg (2 capsules of 75mg) once daily for 10 days</td><td>Prophylaxis of DVT following hip or knee replacement surgery:

Renal impairment
<u>CrCl <30 mL/min:</u> Avoid use

Observe closely and prompt evaluate any signs or symptom of blood loss in patients with CrCl 30 to 50 mL/min. Discontinue rivaroxaban in patients who develop acute renal failure while on rivaroxaban</td></tr>
<tr><td>Non-valvular Atrial Fibrillation:
Special patient populations with a reduced daily dose (220 mg taken as one 110 mg capsule twice daily):
• Patients aged 80 years or above
• Concomitant use of verapamil
For the following groups, the daily dose of 300 mg or 220 mg should be selected based on an individual assessment of the thromboembolic risk and the risk of bleeding:
• Patients between 75-80 years
• Patients with moderate renal impairment (CrCL 30-50 ml/min)
• Patients with gastritis, esophagitis or gastroesophageal reflux
• Other patients at increased risk of bleeding</td><td>Non-valvular Atrial Fibrillation:

Renal impairment
<u>CrCl15 to 50 mL/min</u>: 15 mg once daily with the evening meal
<u>CrCl <15 mL/min:</u> Avoid use

Periodically assess renal function as clinically indicated (i.e.more frequently in situations in which renal function may decline) and adjust therapy accordingly. Discontinue rivaroxaban in patients who develop acute renal failure while on rivaroxaban</td></tr>
<tr><td></td><td>• Treatment DVT, and prevention of recurrent DVT and PE following an acute DVT in adults

Renal impairment
<u>CrCl <30 mL/min:</u> Avoid use</td></tr>
</table>

Switching to and from Dabigatran or Rivaroxaban:

Drug	Dabigatran	Rivaroxaban
Switching warfarin to and from dabigatran or rivaroxaban	<u>Switching from Warfarin to Dabigatran</u> -Discontinue Warfarin and take Dabigatran when the INR is below 2. Do not supply Dabigatran if INR is above 2. <u>Switching from injectable anticoagulant to Dabigatran</u> - Start dabigatran 0 to 2 hours prior to the time that the next dose of an injectable anticoagulant would be due <u>Switching from continuous treatment (e.g IV Unfractianated Heparin) to Dabigatran</u> - Dabigatran should be given at the time of discontinuation of the continuous treatment <u>Switching from Dabigatran to injectable anticoagulant or continuous treatment</u> –An injectable anticoagulant should be given 12 hours after the last dose of dabigatran	<u>Switching patients with AF on Warfarin to Rivaroxaban</u> –Discontinue warfarin and start Rivaroxaban when the INR is ≤ 3.0 <u>Switching patients with DVT or PE on Warfarin to Rivaroxaban</u> –Discontinue warfarin and start Rivaroxaban when the INR is ≤ 2.5 <u>Switching patients with DVT or PE on LMWH to Rivaroxaban</u> – Start rivaroxaban 0 to 2 hours prior to the next scheduled administration of LMWH. If patient in the initial phase (first 21 days), continue rivaroxaban 15 mg twice daily for first 21 days, then switch to 20mg once daily with food for remaining treatment. If patients on LMWH for more than 21 days, start rivaroxaban 20mg od 0 to 2 hours before the time of the next scheduled administration of LMWH <u>Switching patients following orthopaedic surgery on LMWH to Rivaroxaban</u> – Start rivaroxaban 0 to 2 hours prior to the next scheduled administration of LMWH.

Cautions:

Drug	Dabigatran	Rivaroxaban
Cautions/ Special warning for use	**Use in renal impairment:** Clearance of dabigatran in patients with renal insufficiency may take longer. Please make sure patients have done renal function test prior to initiation of treatment with Dabigatran. Close clinical surveillance is recommended in patients with renal impairment. **Use in hepatic impairment:** Patients with elevated liver enzymes > 2 ULN should not be prescribed dabigatran. **Risk of bleeding:** Use with caution in conditions with an increased risk of bleeding. Bleeding may occur at any site during therapy with Dabigatran. An unexplained fall in haemoglobin and/or hematocrit or blood pressure should lead to a search for a bleeding site. When clinically relevant bleeding occurs, treatment should be interrupted	**Increased risk of thrombotic events after Premature Discontinuation:** An increased rate of stroke was observed during the transition from Rivaroxaban to warfarin in clinical trials in atrial fibrillation patients. If Rvaroxabani is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant **Risk of bleeding:** Rivaroxaban can cause serious and fatal bleeding. Promptly evaluate signs and symptoms of blood loss. **Spinal/ epidural anesthesia or Puncture:** When neuraxial anesthesia (spinal/epidural anesthesia) or spinal puncture is employed, patients treated with anticoagulant agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis. An epidural catheter should not be removed earlier than 18 hours after the last administration of Rivaroxaban. The next Rivaroxaban dose is not to be administered earlier than 6 hours after the removal of the catheter. If traumatic puncture occurs, the administration of Rivaroxaban is to be delayed for 24 hours **Pregnancy-related hemorrhage:** Use Rivaroxaban with caution in pregnant women due to the potential for obstetric haemorrhage and/or emergent delivery. Promptly evaluate signs and symptoms of blood loss. **Prosthetic heart valves:** Rivaroxaban use not recommended

		Nursing mothers: Discontinue drug or discontinue nursing

Contraindication:

Drug	Dabigatran	Rivaroxaban
Contraindication	• Hypersensitivity to the active substance or to any of the excipients • Patients with severe renal impairment (CrCL < 30 ml/min) • Active clinically significant bleeding • Organic lesion at risk of bleeding • Spontaneous or pharmacological impairment of haemostasis • Hepatic impairment or liver expected to have any impact survival • Concomitant treatment with systemic ketoconazole, cyclosporine, itraconazole, tacrolimus	• Hypersensitivity to the active substance or to any of the excipients. • Clinically significant active bleeding. • Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C • Patients with severe renal impairment (refer dosing consideration) • Pregnancy and breastfeeding • Lesion or condition at significant risk of major bleeding • Concomitant treatment with any other anticoagulant agent except under the circumstances of switching therapy to or from rivaroxaban or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter.

Monitoring:

Drug	Dabigatran	Rivaroxaban
Monitoring	Visible monitoring of patient for signs of bleeding and anaemia (no clinical monitoring available – INR not able to be used as different pathway of action)	Visible monitoring of patient for signs of bleeding and anaemia (no clinical monitoring available – INR not able to be used as different pathway of action)

Drug interactions:

Drug	Dabigatran	Rivaroxaban
Drug interactions	**Generally interactions lead to an increase bleeding risk – patients should be monitored closely for signs of bleeding and anaemia.** • Caution with concomitant other anticoagulants • Systemic azoleantimycotics e.g.ketoconazole, ciclosporin, itraconazole, tacrolimus are contraindicated • Caution with concomitant strong P-gp inhibitors e.g. amiodarone, quinidine, verapamil • Caution concomitant use of amiodarone (amiodarone has a long half-life and interaction may exist for weeks after discontinuation, especially in patients with mild-moderate renal impairment) • Caution concomitant use of quinidine especially in patients with mild to moderate renal impairment • Caution concomitant use of verapamil • Caution concomitant use of clarithromycin, especially in patients with mild-moderate renal impairment. • Protease inhibitors (e.g. ritonavir containing products) should not be prescribed concomitantly (due to lack of available safety data for this combination) **Interactions below lead to a decrease in anticoagulant concentration therefore treatment may be suboptimal** • Caution concomitant use of strong CYP3A4 inducers e.g. rifampicin, St. John's Wort, carbamazepine, phenytoin	**Interactions below lead to an increase bleeding risk – patients should be monitored closely for signs of bleeding and anaemia.** • Concomitant use of systemic azoleantimycotics e.g. ketoconazole, itraconazole, voriconazole, posaconazole, • HIV protease inhibitors • Concomitant use of dronedarone should be avoided • Caution with concomitant anticoagulants • Caution with concomitant NSAIDs and platelet aggregation inhibitors (e.g. clopidogrel) **Interactions below lead to a decrease in anticoagulant concentration therefore treatment may be suboptimal** • Caution concomitant use strong CYP3A4 inducers e.g. phenytoin, carbamazepine, phenobarbital, St. John's Wort

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Patient Follow-Up Sheet

Name : **IC/RN** :

Initiation Date : **Initiated by** :

Indication : **Drug Dosage** :

Duration of treatment :

Date	Next TCA (Pharmacy)	Next TCA (Clinic)	CrCl (ml/min) (if applicable)	Remarks

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Masterlist for Patients on Dabigatran/Rivaroxaban tablet

No	Ref. No	Name	I/C No	Dose	Initiate by	Treatment Initiation Date	Notes