NHS
Bristol, North Somerset and South Gloucestershire
Integrated Care Board

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Prescriber Decision Support on Anticoagulation for Stroke Prevention in Non-valvular Atrial Fibrillation (NVAF)

Contents

Scope:

This document is intended as a prescriber decision support when prescribing anticoagulants for patients with non-valvular AF. The diagnosis and management of atrial fibrillation is beyond the scope of this document and prescribers are referred to the full NICE clinical guidance or NICE Pathway. For information on requesting an ECHO see Remedy.

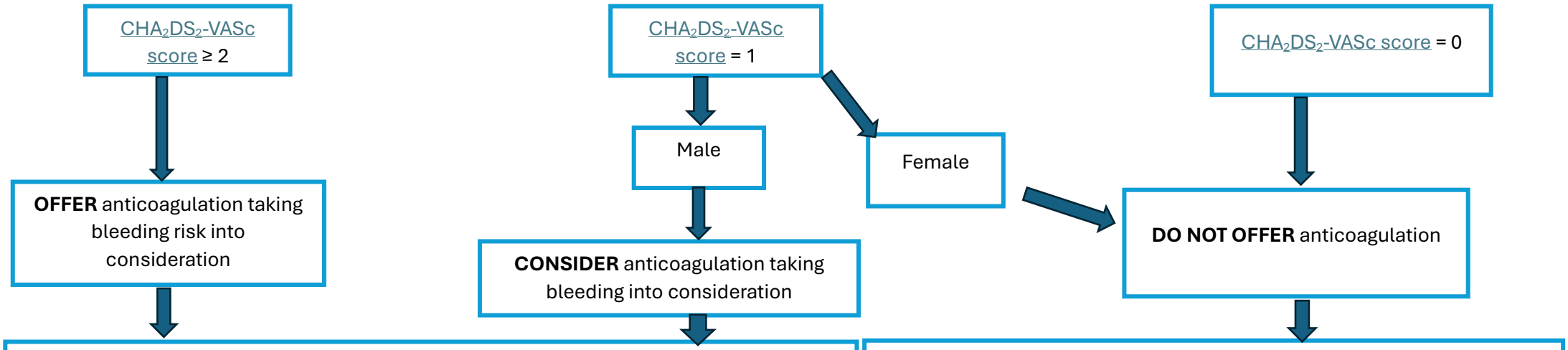
Some prescribing advice in this guidance, has been locally agreed with specialists from NBT and UHBW hospitals and may differ from the advice included by the manufacturers in the summary of product characteristics (SmPC).

There are currently four direct oral anticoagulants (DOACs) available and licensed in the UK for stroke prevention in NVAF; apixaban, rivaroxaban, edoxaban, and dabigatran. **Apixaban (twice daily dose)** and **Rivaroxaban (once daily dose)** tablets are now available as generic preparations, making them the best value treatment choice of DOACs and should be used first line unless there is a clinical reason for using another DOAC or anticoagulant. This is also reflected in the national commissioning recommendations for DOACs and aligns with the 2025/26 Planning Guidance which directs systems to optimise medicines value.

Adapted with permission from BSW ICB, by BNSSG Medicines Optimisation Team in collaboration with the ICS Anticoagulant Safety Group. Incorporates BNSSG Summary of considerations when prescribing a DOAC in non-valvular AF; BNSSG Guidance on switching between oral anticoagulant; BNSSG DOAC Decision Aid Tool for NVAF. Version 2.0 Approved at APMOC October 25, Review October 2028

Please note: ESC 2024 Guidelines refer to an updated CHA_2DS_2VA score for AF stroke risk which calculates stroke risk for patients with atrial fibrillation; similar to the CHA_2DS_2-VASc Score but without considering sex. We have used CHA2DS2-VASc score in this guidance to align with current NICE guidance and QOF

Flowchart 1 - Assessing stroke and bleed risk in NVAF



- Consider individual patient risk factors and patient preferences to guide treatment choices.
- Shared decision to be made with the individual about whether to start anticoagulation and about how to reduce modifiable risk factors for bleeds.
- For most people the benefit of anticoagulation outweighs the bleeding risk.

Bleeding Considerations:

- Using a bleed risk tool may help inform shared decision making: **ORBIT bleed risk tool.** (NB. Other bleed risk tools are available e.g. HAS-BLED)
- For people with a **high risk** of bleeding (ORBIT score ≥ 4), the benefit of anticoagulation **may** not always outweigh the bleeding risk. If the decision is to anticoagulate careful monitoring of bleeding risk is important.[20]
- For people with increased risk of bleeding address any modifiable risk factors such as: uncontrolled hypertension, concurrent medication (NSAIDs, Aspirin), harmful alcohol consumption.
- Do not withhold anticoagulation solely because of a person's age or their risk of falls.
- Consider prophylactic PPI for patients at high risk of GI bleeding. See BNSSG guidance on Optimising and reviewing Proton Pump Inhibitors.
- **Move to Flowchart 2** for decision making on choice of anticoagulant.

- Patient is not a candidate for anticoagulation based on above assessment or patient refuses treatment.
- Review stroke and bleeding risks annually, document outcome of assessment or patient decision in patient record.
- Review NVAF patients annually or when patient reaches 65 or develops any of the following at any age:
  - Hypertension
  - Diabetes mellitus
  - Heart failure
  - Peripheral vascular disease
  - Coronary artery disease
  - Stroke/TIA/systemic arterial embolism

Do not offer aspirin monotherapy solely for stroke prevention to people with AF. Review patients on existing antiplatelet therapy in line with local antiplatelet guidance.

Flowchart 2 - Decision making on choice of anticoagulant and patient factors

Patient is a candidate for and consents to anticoagulation to reduce risk of stroke in NVAF

- Discuss the options for anticoagulation with the person and base the choice on: ● clinical features (see flow chart below) ● patient preferences ● Baseline tests should be checked prior to initiation of anticoagulation: Body weight, FBC, U&Es (and Creatinine clearance (CrCl) calculated, **DO NOT USE eGFR**), LFTs, Clotting screen, BP.
- All patients should be involved in shared decision-making dialogue about the risks and benefits of anticoagulation. Further decision support tool can be found here: https://www.anticoagulation-dst.co.uk/

Does the patient have a contraindication to a DOAC?

Absolute Contraindications:

- Mechanical heart valve
- Moderate to severe mitral valve stenosis
- Antiphospholipid syndrome (APS) - **refer patient to Haematology**
- Pregnancy - **refer to specialist for advice**
- Hepatic disease associated with coagulopathy
- Known hypersensitivity to DOACs
- In renal failure:
  - with CrCl < 30 mls/min Dabigatran is contraindicated.
  - With CrCl < 15mls/min apixaban, rivaroxaban and edoxaban are contraindicated.
- History of inherited bleeding disorder – **seek Haematology advice**

Where Specialist input is needed:

- Intolerance to DOACs - **discuss with specialist if needed to review appropriateness in trying alternative DOACs**
- Breast feeding – **discuss with specialist if needed**
- Presence of malignant neoplasm at high risk of bleeding or significant risk of major bleeding - **discuss with Haematology or Oncology**
- Recent brain or spinal injury – **seek specialist advice**
- Recent brain, spinal or ophthalmic surgery – **seek specialist advice**
- Known or suspected oesophageal varices – **discuss with Hepatology if needed**
- Concomitant use of medicines which are not recommended with DOACs – **see SPCs and Notes Box below**
- Extremes of bodyweight >150kg or BMI>40 (NB. rivaroxaban and apixaban can be considered for patients up to 150kg[10,32]) or where bodyweight <50kg, **discuss options with specialist if patient can't tolerate warfarin**

NB. This list is not exhaustive, please refer to EMC for individual DOACs for further information on contraindications.

YES

Consider warfarin or LMWH or no anticoagulation (Seek Specialist advice where needed)

NO

Consider a DOAC

Move to Flowchart 3 for decision making on choice of DOAC

Flowchart 3 – Anticoagulant treatment options in Non-Valvular Atrial Fibrillation (NVAF)

Patient assessed as eligible for DOAC (see previous flowchart 1 and 2)
Apixaban and **Rivaroxaban** are first choice DOACs for NVAF in BNSSG **other than those patients with previous intolerance to apixaban or rivaroxaban or on the advice of a specialist**. In line with NICE guidance, other DOACs can be considered.

Use the Cockcroft Gault method to determine creatinine clearance (CrCl) and prescribe licensed DOAC dose according to result. **Actual body weight** should be used to calculate CrCl unless a patient is obese, BMI>30, in which case adjusted body weight should be used. MDcalc tool can be used to calculate adjusted body weight.

Seek advice from your local Anticoagulant Specialist in the event of any uncertainty regarding which dose is best to use.

CrCl < 15ml/min

DOACs are contraindicated

Discuss with Renal Team

Can patient tolerate and comply with Twice Daily dosing?

Yes

No

Apixaban (where **Twice Daily** dosing appropriate)
Does the patient have **2 out of the 3** of the following?

1. **Age** ≥ 80 years
2. **Body weight** ≤ 60 kg
3. **Serum creatinine** ≥ 133 micromol/L

OR CrCl 15-29 mL/min renal impairment

YES

NO

Apixaban 2.5mg BD

Apixaban 5mg BD

Rivaroxaban (where **Once Daily** dosing appropriate)

Moderate – severe (CrCl 15-49 ml/min) renal impairment?
(NB. Rivaroxaban 15mg and 20mg should be taken with/after food)[5]

NO

YES

Rivaroxaban 20mg OD

Rivaroxaban 15mg OD

NB: Where a patient has a poor diet, **Apixaban** or **Edoxaban** may be considered as alternatives as can be taken with or without food (see EMC where dose reduction needed)

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Notes

Medication non-adherence: Apixaban is the preferred choice DOAC if a twice daily dose (BD) is acceptable and Rivaroxaban if a once daily dose (OD) is preferred. For patients unlikely to comply with BD dosing and where Rivaroxaban is not appropriate, consider Edoxaban (if no previous intolerance).

Drug Interactions: DOACs have several clinically significant interactions with other medicines, some of which may increase risk of bleeding or may reduce the DOAC levels in the body and increase risk of thrombosis. Consult EMC, BNF and SPS for drug-drug interactions and dosing guidance. Key drug interactions include CYP450 enzyme inducers e.g. carbamazepine or CYP450 enzyme inhibitors e.g. itraconazole.

Where an interaction presents, review to see if an alternative anticoagulant or interacting medicine can be used – **seek Specialist advice where needed.** Warfarin would be 1st line with strongly interacting P-gp inducers/inhibitors as it can be monitored with INR testing and the dose adjusted in response to the interaction to ensure sufficient anticoagulation[30]. If warfarin is deemed inappropriate for the patient, it must be discussed with them (patient) and a DOAC used with caution.

Where concomitant use of an interacting drug such as carbamazepine and a DOAC is necessary, edoxaban is the preferred choice of DOAC locally if clinically appropriate for the patient (the interaction has been deemed to be a moderate interaction in the BNF where carbamazepine is predicted to decrease exposure to edoxaban. Manufacturer advises caution). [11] It is worth noting the SPC for apixaban states that the concomitant use of apixaban with strong CYP3A4 and P-gp inducers (e.g. carbamazepine) may lead to a ~50% reduction in apixaban exposure.[13] The EMC for Rivaroxaban advises that concomitant administration of strong CYP3A4 inducers should be avoided.[14]

Diet considerations: Consider patients diet when prescribing DOACs: Rivaroxaban 15mg & 20mg should be taken with food as per MHRA Drug Safety Update. Where poor diet, consider Apixaban or Edoxaban as they can be taken with or without food as per SPC.

Patient counselling: Refer to the BNSSG ICS DOACs Counselling Checklist.

DOAC monitoring: FBCs, LFTs, U&Es, Serum creatinine (for creatinine clearance), weight. Age ≥ 75 years or frail – every 4 months. If CrCl is ≤ 60ml/min, the CrCl divided by 10 is the minimum DOAC monitoring interval (in months). e.g. CrCl ≤ 60 ml/min, recheck every 6 months, CrCl ≤ 30ml/min recheck every 3 months etc. Clinicians may consider DOAC review 1 month after initiation especially if higher bleeding risk. [9] All other patients may be reviewed annually.

Patients (particularly those with an increased bleeding risk) should be made aware of the risk of bleeding and be routinely examined clinically for signs of bleeding or anaemia. Bleeding can occur at any site during treatment with DOACs. Treatment with DOACs should be discontinued if severe bleeding occurs.[31] (see MHRA Drug Safety Update)

Advice and Guidance should be sought from the relevant specialist for any patient presenting with adverse effects to a DOAC such as active bleeding. The decision to stop a DOAC is complex and dependent on individual assessment considering bleeding and extent/ severity/location and thrombotic risk. Any adverse effects should be reported to the MHRA via the Yellow Card scheme.

Duration of treatment: **It's crucial that patients are advised to continue anticoagulation for any indication until explicitly told to stop by a clinician.** For an indication of Atrial Fibrillation (AF): anticoagulant treatment will be **lifelong**.

Queries and Support:

Where **patients** have queries about their DOACs they should speak to their GP or Specialist in the first instance.

Where **clinicians** need additional support Specialist Anticoagulant Advice can be obtained from local hospitals:

- **UHBW Anticoagulation Monitoring Service (warfarin clinic)** - 011734 23874 (Mon-Fri 9:00-17:30), email: warfarin.helpline@uhbw.nhs.uk
- **NBT Anticoagulation Monitoring Service (warfarin clinic)** - 0117 414 8405 (Mon-Fri 9:00-17:00), email: ams@nbt.nhs.uk

Both clinics are closed on Bank Holidays.

Medicines Information Teams:

- **NBT** — please use Care flow Connect platform where available, alternatively please email your enquiry to Medicines.Information@nbt.nhs.uk
- **UHBW** - please use Care Flow Connect platform
- **Sirona medicines advice** -please use SIRCH.pharmacist@nhs.net (telephone number 07970 778499 which is open

Monday – Friday 9am – 4pm (excluding bank holidays)

- **Spire Bristol pharmacy** via bristolhosppharmacyteam@spirehealthcare.com

Switching between oral anticoagulants for Non-valvular AF (NVAF)

When switching between different oral anticoagulant therapies, it is important to ensure the continuation of anticoagulant therapy while minimizing the risk for bleeding. This requires insights into the pharmacokinetics and dynamics of different anticoagulation regimens, interpreted in the context of the individual patient.[19]

<table>
<tr><th>To →
From ↓</th><th>Warfarin</th><th>Apixaban</th><th>Rivaroxaban</th><th>Edoxaban</th><th>Dabigatran</th></tr>
<tr><td>Warfarin</td><td></td><td colspan="4">SPCs recommend different INRs at which to initiate DOACs after stopping warfarin:
Apixaban and Dabigatran*: Start when INR < 2
Edoxaban: Start when INR < 2.5
Rivaroxaban: Start when INR < 3
This approach would require repeat INR checks daily until the required INR is achieved.

* If the patient has a higher clot risk/CHA_2 DS_2 VASC, consider using the EHRA advice instead:
EHRA guidance[17,18] gives pragmatic guidance on when to start DOACs after stopping warfarin:
If INR ≤ 2: Commence DOAC that day
If INR between 2 and 2.5: Commence DOAC the next day (ideally) or the same day
If INR between 2.5 and 3: Withhold warfarin and recheck INR in 1-2 days and start DOAC as above.</td></tr>
<tr><td>Apixaban</td><td>Give Warfarin in combination with Apixaban until INR is ≥ 2.0. Check INR after 2 days of the combination. INRs to be monitored at least twice a week whilst taking both anticoagulants, with blood sample to be preferably taken prior to taking the dose of Apixaban. Apixaban should be discontinued when INR is ≥ 2.0.[13]</td><td colspan="3">Stop Apixaban and start the alternative DOAC when the next dose of Apixaban is due, except in situations where higher than therapeutic plasma concentrations are expected (e.g. in a patient with impaired renal function). In such situations, a longer interval in between DOACs is recommended.[17] Patient should still have their morning and evening Apixaban dose, then the next scheduled day they start their new DOAC.
NB. Rivaroxaban and Edoxaban are contraindicated where CrCl < 15 ml/min, Dabigatran is contraindicated where CrCl <30ml/min.</td></tr>
</table>

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Rivaroxaban	Warfarin should be given in combination with Rivaroxaban until the INR is ≥ 2.0. INRs to be monitored at least twice a week whilst taking both anticoagulants Take INRs immediately before Rivaroxaban dose is due. Once rivaroxaban is discontinued, the next INR should be taken at least 24hrs later for a reliable result.[14]	Stop Rivaroxaban and start alternative DOAC when the next dose of Rivaroxaban is due, except in situations where higher than therapeutic plasma concentrations are expected (e.g. in a patient with impaired renal function). In such situations, a longer interval in between DOACs is recommended.[17] **NB. Apixaban is contraindicated where CrCl < 15 ml/min.**		Stop Rivaroxaban and start alternative DOAC when the next dose of Rivaroxaban is due, except in situations where higher than therapeutic plasma concentrations are expected (e.g. in a patient with impaired renal function). In such situations, a longer interval in between DOACs is recommended.[17] **NB. Edoxaban is contraindicated where CrCl < 15 ml/min, Dabigatran is contraindicated where CrCl <30ml/min.**	
Edoxaban	**Patients on 60 mg dose:** administer Edoxaban 30 mg once daily with warfarin. **Patients on a 30 mg dose:** administer Edoxaban 15 mg once daily with warfarin. Once INR ≥ 2.0 or after 14 days (whichever is sooner), Edoxaban should be discontinued. Take INRs immediately before Edoxaban dose is due. INRs to be monitored at least twice a week whilst taking both anticoagulants.	Stop Edoxaban and start the alternative DOAC when the next dose of initial DOAC is due, except in situations where higher than therapeutic plasma concentrations are expected (e.g. in a patient with impaired renal function). In such situations, a longer interval in between DOACs is recommended.[17] **NB. Apixaban and Rivaroxaban is contraindicated where CrCl < 15 ml/min.**			Stop Edoxaban and start the alternative DOAC when the next dose of initial DOAC is due, except in situations where higher than therapeutic plasma concentrations are expected (e.g. in a patient with impaired renal function). In such situations, a longer interval in between DOACs is recommended.[17] **NB. Dabigatran is contraindicated where CrCl <30ml/min.**
Dabigatran	**Conversion protocol depends on renal function:**	Stop Dabigatran and start the alternative DOAC when the next dose of initial DOAC is due, except in situations where higher than therapeutic plasma concentrations			

	CrCL ≥ 50 mL/min, start warfarin 3 days before discontinuing Dabigatran. **CrCL ≥30 - 50 mL/min**, start warfarin 2 days before discontinuing Dabigatran. Interpret INR values with caution until Dabigatran has been discontinued for at least 2 days as Dabigatran can impact INR.	are expected (e.g. in a patient with impaired renal function). In such situations, a longer interval in between DOACs is recommended. [17] **NB. Apixaban, Rivaroxaban and Edoxaban are contraindicated where CrCl < 15 ml/min.**	

DOAC Prescribing Dosing Table for Non-Valvular AF (NVAF)

DOAC	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
Dosing in NVAF	Prescribe Apixaban **5mg twice daily** Reduce dose to 2.5 mg twice daily if at least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL (133 micromole/L) Or CrCl 15-29 mL/min renal impairment. Therapy should be continued long term.[13]	Prescribe Rivaroxaban **20mg once daily** Reduce dose to 15mg once daily if CrCl< 50mL/min in NVAF patients only. Therapy should be continued long term.	Prescribe Edoxaban **60mg once daily** Reduce dose to 30mg once daily in patients with one or more of the following: Body weight ≤ 60kg, or CrCl< 50ml/min, or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole. Therapy should be continued long term.	Prescribe Dabigatran **150mg twice daily** if aged <75 years, CrCl> 50mL/min, low risk of bleeding (weight <50kg with close clinical surveillance) Reduce dose to 110mg twice daily if aged > 80 years or prescribed verapamil. Consider 110mg twice daily based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80years or with CrCl <50mL/min or with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux). Therapy should be continued long term.
Weight considerations	Can be considered for patients up to 150kg (but not stated in any guidance)[10]	Can be considered for patients up to 150kg (but not stated in any guidance).[10]	Bodyweight <50kg use DOACs with caution and discuss options with specialist. Weight >120kg - avoid	Bodyweight <50kg use DOACs with caution and discuss options with specialist. Weight >120kg - avoid

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	Bodyweight <50kg use DOACs with caution and discuss options with specialist	Bodyweight <50kg use DOACs with caution and discuss options with specialist		
Contraindicated/not recommended	CrCl < 15 ml/min	CrCl < 15 ml/min	CrCl <15ml/min	**CrCl <30ml/min**
Cautions **See also individual SPC**		CrCl <30ml/min. Take with or after food (15mg and 20mg doses).	CrCl >95ml/min	Do not use in a standard medication compliance aids (MCA) or store outside of original packaging. Peel off backing foil to expose capsule (do not push through)
Interactions **Check BNF:** https://bnf.nice.org.uk/ **SPC:** https://www.medicines.org.uk/emc#gref **SPS:** https://www.sps.nhs.uk/articles/understanding-interactions-with-direct-oral-anticoagulants-doac/	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir - **not recommended**. (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St.John's Wort – **use with caution**.	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, dronedarone – **not recommended** (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – **should be avoided**	Rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort – **use with caution** (see SPC for full details) Ciclosporin, dronedarone, erythromycin, ketoconazole – **reduce dose as above.**	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone -**contraindicated** (See SPC for full details) Rifampicin, St John's Wort, carbamazepine, phenytoin **–should be avoided.** Amiodarone, quinidine, ticagrelor, posaconazole – **use with caution.** Verapamil **(use reduced dose).** Antidepressants: SSRIs and SNRIs**- increased bleeding risk**
Missed doses	Take the dose immediately then continue with twice daily administration as before. A double dose should not be taken to make up for a missed tablet.	Take as soon as remembered. Do not take more than one tablet in a single day. Carry on with usual dose the following day.	Take as soon as remembered. Do not take more than one tablet in a single day to make up for missed doses. Carry on with the usual dose the following day.	If **less than 6 hours** until next dose, then omit and continue with scheduled dose. If **more than 6 hours** until next dose, take at once.

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Intake with food	With or without food	Take with or after food (15mg and 20mg doses).[5]	With or without food	With or without food
Lactose/wheat content	Lactose; No wheat	Lactose; No wheat	No lactose; maize starch	No lactose
Nasogastric (NG) and PEG administration/ crushing & dispersing	Yes	Yes	Yes	No
Nasojejunal (NJ) and PEJ	Discuss with Specialist	Not suitable.[28,33]	Discuss with Specialist	Not suitable.[28,33]

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