COVID 19 Treatment Guide 6.0

By PRIC and AMS

Disclaimer: All information in this guide is merely for educational and informational purposes. It is not intended as a substitute for professional advice. Kindly seek consultation from your facility's physician for further management. We reserve the right to update this guide at any given time.

JABATAN FARMASI
HOSPITAL SUNGAI BULOH

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HSgB COVID-19 Treatment Guide - List of updates

Date	Updates	Description
December 2023 (Ver 6.0)	Nirmatrelvir/Ritonavir (Paxlovid) Drug Info Slide (amend)	<u>Revised:</u> • Paxlovid Off-label recommendation for eGFR < 30 • Paxlovid Off-label recommendation for NG Tube administration • Paxlovid Off-label recommendation for Pregnancy • Paxlovid Off-label recommendation for Breastfeeding
	Nirmatrelvir/Ritonavir (Paxlovid) in Severe Renal Impairment (amend)	• Can be prescribed upon approval by ID Consultant → changed to ID or Medical Specialist approval
	Nirmatrelvir/Ritonavir (Paxlovid) Administration via Enteral Feeding Tubes (new)	• Summary of administration of Paxlovid Administration via RT (Revised from Pfizer's recommendation)
	Remdesivir Drug Info Slide (amend)	• Recommended dose in renal impairment revision. • Remdesivir Off-label recommendation for Pregnancy revision
	Risk of Hospitalization & Treatment for People with COVID-19 (new)	• Summary of updated risk of Hospitalization & Treatment for People with COVID-19 by WHO, Nov 2023
	COVID 19 Treatment Guide in Pregnancy (amend)	<u>Revised:</u> • Paxlovid use in Pregnancy • Remdesivir use in Pregnancy <u>Added:</u> • Paxlovid use in Breastfeeding • Remdesivir use in Breastfeeding • Baricitinib use in Breastfeeding • Tocilizumab use in Breastfeeding

COVID 19 Treatment Guide in Adult Patients

By PRIC and AMS

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NIRMATRELVIR & RITONAVIR

PAXLOVID (separate tablets): Nirmatrelvir 150mg (2 film-coated tablets)
Ritonavir 100mg (1 film-coated tablet)

*** Can be prescribed by all ID/Medical/ED Specialists or Consultants**

Indication:

Patient diagnosed with COVID-19 Category 2 or 3

**as soon as possible after COVID-19 diagnosis and within 5 days of symptom onset.*

Dose:

Adult: 300 mg Nirmatrelvir (**TWO** 150 mg tablets) with 100 mg Ritonavir (**ONE** 100 mg tablet) **BD**

Duration: 5 days

Renal Impairment:

eGFR ≥60 to <90 mL/min: No dosage adjustment
eGFR 30-60 mL/min: Nirmatrelvir 150mg/ Ritonavir 100mg BD
eGFR <30 mL/min: Not recommended due to insufficient data.
** For eGFR < 30ml/min, off-label dosing may be considered after discussion with ID Consultant, done at the discretion of the healthcare professional – (Refer to next slide)* (link)

Hepatic Impairment:

Mild to moderate: No dosage adjustment

Severe: Not recommended

Missed Dose:

Within 8 hours - Take as soon as possible

More than 8 hours- Take at next scheduled time

Enteral administration:

Patient is advised to swallow the tablets whole and not to chew, break, or crush the tablets.

** For off-label administration of Paxlovid via NG Tube (done at the discretion of the healthcare professional), refer to:*

- *HSgB administration via Ryle's Tube* (link) *or*
- *Administration via Enteral Feeding Tubes by Pfizer* (link)

Pregnancy/Lactation: Paxlovid recommended, if indicated.

- *The consideration of Paxlovid should be based on a risk-benefit assessment (relevant risk factors and medical comorbidities).*
- *Clinicians are advised to engage in fully informed shared decision-making with patients regarding the potential use of Paxlovid.*
- *Ref: https://www.covid19treatmentguidelines.nih.gov/ & WHO Therapeutics and COVID-19: living guideline,Nov 2023)*

Precautions & Warnings:

- Hypersensitivity: Urticaria, angioedema, anaphylaxis, TEN and SJS
- Hepatotoxicity
- Not to be used for longer than 5 consecutive days
- **Not for pre- or post-exposure prophylaxis for prevention of COVID-19**

Adverse effect:

Dysgeusia (altered sense of taste), Diarrhoea, Hypertension, Myalgia

Drug-drug interaction:

Kindly refer to the next two pages for common drug interactions.

For full list of interactions, you may also refer to:

1. Liverpool Drug Interactions: Paxlovid Info Sheet (link)
2. EUA Fact Sheet for Healthcare Providers (link)
3. Liverpool COVID-19 Drug Interactions Website: https://www.covid19-druginteractions.org/checker (link)

Storage conditions: 15-25ºC

Dosing Guidance for Paxlovid (Nirmatrelvir/Ritonavir) in HSgB:

Renal Function	Drug Doses	How to order in eHIS	Remarks
eGFR > 60 ml/min	Nirmatrelvir 300mg + Ritonavir 100mg, twice daily	**3 tabs BD x 5/7**	
eGFR 30 - 60 ml/min	Nirmatrelvir 150mg + Ritonavir 100mg, twice daily	**2 tabs BD x 5/7**	
eGFR < 30 ml/min, not on dialysis	Nirmatrelvir 300mg + Ritonavir 100mg on Day 1, Nirmatrelvir 150mg + Ritonavir 100mg on Day 2-5	**3 tabs OD x 1/7, Then 2 tabs OD x 4/7**	**<u>Off-label Dose</u>** The dose is not in COVID guidelines & is based on: **Swapnil Hiremath et al. CJASN doi:10.2215/CJN.05270522** *The decision to initiate this off-label dosage should be made following discussion and approval by an ID or Medical Specialist.*
eGFR < 30 ml/min, on dialysis & weight ≥ 40kg	Nirmatrelvir 300mg + Ritonavir 100mg on Day 1, Nirmatrelvir 150mg + Ritonavir 100mg on Day 2-5	**3 tabs OD x 1/7, Then 2 tabs OD x 4/7** (On HD days, dose to be given after HD)	
eGFR < 30 ml/min, on dialysis & weight < 40kg	Nirmatrelvir 150mg + Ritonavir 100mg on Day 1, Nirmatrelvir 150mg + Ritonavir 100mg EOD x 2 doses	**2 tabs OD x 1/7, Then 2 tabs Q48H x 4/7** (On HD days, dose to be given after HD)	

Prepared by: Izyana Munirah Idham & Hannah Md Mahir (AMS Pharmacist). Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126/4114. Revised Dec 2023.

Paxlovid Renal Dose Adjustment: How to cut the Paxlovid strip

In patients with eGFR 30-60 mL/min, Paxlovid dose has to be **renal adjusted** to Nirmatrelvir 150mg/Ritonavir 100mg (= 2 tabs) BD.

Please cut away the extra tablet of **Nirmatrelvir (PF-07321332) 150mg** from each side of the strip before supplying Paxlovid to patients with renal dose adjustment.

Prepared by: Izyana Munirah Idham & Fong Siew Li (AMS Pharmacist). Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126/4114. Revised Dec 2023.

Nirmatrelvir/Ritonavir (Paxlovid) Administration via Enteral Feeding Tubes

INTRO:

- Both Nirmatrelvir (PF-07321332) and Ritonavir are immediate-release film-coated tablets designed to facilitate ease of swallowing and enhance the pharmaceutical elegance of the product. The decision to administer Paxlovid via Nasogastric Tube (NGT) is considered 'off-label' and is made at the discretion of the healthcare professional.

STEP 1: Prepare Nirmatrelvir (PF-07321332) and Ritonavir Liquid Suspensions

To ensure timely administration, prepare both Nirmatrelvir and Ritonavir liquid suspensions separately before administering through a NGT.

a) Nirmatrelvir (PF-07321332) Liquid Suspension Preparation:

1. Place the pink Nirmatrelvir (PF-07321332) tablet(s) into a 20mL syringe.
2. Draw 10mL of water & 5mL of air into the syringe.
3. Shake the syringe vigorously & continuously for 15 seconds.
4. Allow the syringe to lie flat for at least 3 minutes to allow the tablet(s) to disintegrate.

b) Ritonavir Liquid Suspension Preparation:

1. Gently crush the white Ritonavir tablet using a pill crusher until it becomes a fine powder, then carefully transfer the powder into a 20mL syringe.
2. If the pill crusher is washable, use 5 mL of water to rinse the tablet residue into the syringe.
3. Draw another 5mL of water & 5mL of air into the syringe
4. Shake the syringe vigorously & continuously for 15 seconds.
5. Allow the syringe to lie flat for at least 3 minutes to allow the powder to dissolve.

STEP 2: Administration of Nirmatrelvir and Ritonavir Liquid Suspensions via NGT

Administer both suspensions separately via NGT within a 5-minute interval.

1. Flush the NGT with 10mL of water.
2. Shake the syringe containing Nirmatrelvir (PF-07321332) vigorously up and down continuously for approximately 1 minute to ensure thorough mixing of the suspension.
3. Administer the entire contents of the syringe into the NGT.
4. Draw another 10mL of water into the syringe and flush it through the NGT (to rinse the syringe and ensure the complete dose is administered).
5. Repeat steps 2-4 for the Ritonavir liquid suspension.

Note: Ensure all steps are conducted sequentially, and the entire process is completed within a 4-hour period. The prepared suspensions remain stable for up to 4 hours at room temperature when stored in the syringe.

Revised from: Administration of Paxlovid via Enteral Feeding Tubes Recommendation by Pfizer (link)

Prepared by: Izyana Munirah Idham (AMS Pharmacist) & Mariah Zakaria (Clinical Pharmacist)
Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126/4114. Revised: Dec 2023.

NIRMATRELVIR & RITONAVIR

Drug-drug interaction:

AVOID USE

Inhibitory effect of ritonavir is expected to last up to 3 days after the last administered dose of nirmatrelvir/ritonavir
[avoid concurrent use during 5 days of Paxlovid PLUS 3 days after = 8 days]

Drugs	Alternatives
Amiodarone	Use Remdesivir to replace Paxlovid
Atorvastatin	If coadministration is necessary, reduce dose to 10 mg OD and resume the usual dose after 3 days upon completion of treatment.
Carbamazepine	Consider other AEDs.
Clopidogrel	Avoid Paxlovid in patients at very high-risk of thrombosis, e.g. at least within 6 weeks of coronary stenting. Alternatively, use Aspirin and Prasugrel
Clozapine	-
Colchicine	Consider NSAIDs for analgesia.
Erythromycin	Use Azithromycin
Ivabradine	-
Itraconazole	Use Fluconazole

Drugs	Alternatives
Phenobarbital	Consider other AEDs.
Phenytoin	Consider other AEDs.
Rifampicin	Use Rifabutin 150 mg OD
Rivaroxaban	Use Dabigatran
Rosuvastatin	If coadministration is necessary, do not exceed 10 mg rosuvastatin per day.
Ticagrelor	Use Aspirin, Prasugrel
Voriconazole	Consider to use if benefits outweigh the risks.

For full list of interactions, you may also refer to:

1. Liverpool Drug Interactions: Paxlovid Info Sheet (link)
2. EUA Fact Sheet for Healthcare Providers (link)
3. Liverpool COVID-19 Drug Interactions Website: https://www.covid19-druginteractions.org/checker

NIRMATRELVIR & RITONAVIR

Drug-drug interaction:

DOSE ADJUSTMENT

Inhibitory effect of ritonavir is expected to last up to 3 days after the last administered dose of nirmatrelvir/ritonavir
[dose adjustment required during 5 days of Paxlovid PLUS 3 days after = 8 days]

Drugs	Alternatives
Amlodipine	Reduce dose by 50%. Alternatively, maintain the same dose but monitor for symptoms of hypotension.
Apixaban	Reduce dose to 2.5mg if needed. Alternatively, consult a cardiologist/haematologist about the risks of stopping the anticoagulant and resume 3 days after the last dose of nirmatrelvir/ritonavir.
Aripiprazole	Reduce dose by 50%.
Clarithromycin	Normal renal function: usual dose CrCL 30-60 mL/min: reduce dose by 50% CrCL < 30 mL/min: reduce dose by 75%
Digoxin	Coadministration may increase digoxin concentrations. Monitor closely for symptoms of toxicity. **Dose adjustment based on TDM level (if needed).*
Quetiapine	Reduce dose by one sixth.
Rifabutin	150 mg OD

For full list of interactions, you may also refer to:
1. Liverpool Drug Interactions: Paxlovid Info Sheet (link)
2. EUA Fact Sheet for Healthcare Providers (link)
3. Liverpool COVID-19 Drug Interactions Website: https://www.covid19-druginteractions.org/checker

REMDESIVIR

Available as 100 mg for Inj (Lyophilized powder)

Dose:

Body weight ≥ 40kg:
Loading dose 200 mg on Day 1, followed by 100 mg OD

Body weight > 3.5kg to < 40kg:
Loading dose 5mg/kg on Day 1, followed by 2.5mg/kg/dose OD

Usual Duration: 3 to 5 days

Reconstitution & dilution:

Reconstitute 100mg (1 vial) in 19ml of sterile water for injection, then immediately dilute to either 100ml or 250ml with normal saline.

Route of administration:

IV infusion over 30 to 120 minutes.

Stability (after reconstitution):

Room temperature: Up to 4 hours
Fridge: Up to 24 hours

Stability (after dilution):

Room temperature: Up to 4 hours
Fridge: Up to 24 hours
This is inclusive of reconstitution time

Renal impairment:

Dose adjustments are not required for renally impaired patients, including those on HD
(FDA approved July 2023, based on REDPINE & CATCO Trials)

Liver impairment:

Discontinue if:
•ALT levels increases x 10 time of ULN
•ALT elevation is accompanied by signs or symptoms of liver inflammation

Pregnancy/Lactation:

Remdesivir recommended, if indicated.

- *The consideration of Remdesivir should be based on a risk-benefit assessment (relevant risk factors and medical comorbidities).*
- *Clinicians are advised to engage in fully informed shared decision-making with patients regarding the potential use of Remdesivir.*
- *Ref: https://www.covid19treatmentguidelines.nih.gov/ or WHO Therapeutics and COVID-19: living guideline,Nov 2023)*

Adverse effect: Nausea, increased ALT & AST

Precautions:

•Increased risk of transaminase elevations – perform LFT test at baseline & during treatment

Monitoring: Heart rate, LFT, serum creatinine

Drug interaction:

•Risk of reduced antiviral activity when coadministered with chloroquine or hydroxychloroquine

MOLNUPIRAVIR*

** Not available in HSgB starting Sept 2023*

Available as LAGEVRIO 200mg hard Capsule

Indication:

Patient diagnosed with COVID-19 Category 2 or 3.

*As soon as possible after COVID-19 diagnosis and within 5 days of symptoms onset.

Prescribing Criteria:

Patients contraindicated to *Paxlovid* due to:

•Significant drug-drug interactions

•Liver failure Child C

•Cannot tolerate *Paxlovid*

Dose:

Adult 18 years & above: 800mg (FOUR 200 mg capsules) BD

Duration: 5 days

Missed dose:

Within 10 hours – Take as soon as possible

More than 10 hours – Take at next scheduled dose

Enteral administration:

Capsule cannot be chewed, broken or crushed.

Renal impairment: No dosage adjustment

Hepatic impairment: No dosage adjustment

Adverse effect: Diarrhoea, nausea, dizziness.

Pregnancy: Not recommended.

Lactation: Not recommended. If used, breastfeeding should be interrupted during treatment and for **4 days** after the last dose.

Drug interaction: N/A

Warning & Precaution:

• **For female patients:** use effective contraception during treatment and for **4 days** after the last dose

•Not to be used for longer than 5 consecutive day

•Not for pre- or post- exposure prophylaxis for prevention of COVID-19

• Not for use in patients less than 18 years of age

Capsule ingredients:

•Croscarmellose sodium

•Hydroxypropyl cellulose

•Magnesium stearate

•Microcrystalline cellulose

•Hypromellose

•Titanium dioxide

•Red iron oxide

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised September 2023.

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TOCILIZUMAB

20 mg/ml inj (Available as 80 mg/4ml, 200 mg/10ml & 400 mg/20ml vial)
162mg /0.9ml pre-filled syringe (alternative formulation of vial)

Dose (vial): 400 mg as a single dose

•Supply as one 400 mg vial or five 80 mg vials

•Alternative dose: 4-8 mg/kg as a single dose (max 800 mg/dose)

Dose (pre-filled syringe):

A single dose, given according to body weight:

•20-39 kg: 162 mg (1 syringe)

•40-59 kg: 324 mg (2 syringes)

•60-79 kg: 486 mg (3 syringes)

• ≥ 80 kg: 648 mg (4 syringes)

***May go up to 5 syringes (810mg) for BW >100kg (to discuss with ID consultant)*

Route of administration: **IV Infusion** over 1 hour

Injection:

Do not infuse concomitantly in the same IV line with other medications

•≥ 30 kg: Dilute up to 100 ml with NS

•< 30 kg: Dilute up to 50 ml with NS

Pre-filled syringe:

•≥ 30 kg: Inject into 100ml NS IV drip

•< 30 kg: Dilute up to 50 ml with NS

Stability (after dilution):

Injection: Store in fridge up to 24 hours

Pre-filled syringe: 7 hours at room temperature

Pregnancy & Lactation: Probably Compatible

Renal impairment: No data

Adverse effect:

•Injection site reaction

•Infusion-related reaction (hypertension, headache, dizziness, rash) - monitor for next 24 hours

Precautions:

- ANC < 2 x 10^9/ L
- Platelet < 100 x 10^9 / L
- ALT or AST > 1.5x ULN

Monitoring: LFT, neutrophil and platelet

Contraindications:

- ANC < 0.5 x 10^9/ L
- Platelet < 50 x 10^9 / L
- ALT or AST > 5x ULN

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised Sept 2021.

BARICITINIB

Available as 2 mg & 4 mg tablet

Dose: 4 mg OD for 14 days, or until hospital discharge, whichever is first

Renal impairment:

eGFR ≥ 60 ml/min: No dosage adjustment

eGFR 30 to < 60ml/min: 2mg OD

eGFR 15 to < 30ml/min: 1mg OD

eGFR < 15ml/min: Use Tocilizumab

*(**wear gloves and N95** when halving tablets; administer the remaining half the next day)*

Hepatic impairment (before treatment initiation):

Mild to moderate: No dosage adjustment

Severe: Use is not recommended

Alternative oral administration:

Dissolve full tablet in 10ml water; serve via oral/Ryles tube.

Rinse container with 10ml water **to consume full dose.**

*Solution is **stable for 4 hours at room temperature**.*

Pregnancy: Limited data; use may be considered if potential benefits outweigh the possible risks

Lactation: Not recommended

Precautions:

• **Serious infection –** stop Baricitinib if develop serious infection, an opportunistic infection or sepsis until infection is controlled. Do not use in active TB.

•**Thrombosis –** monitor for PE/DVT symptoms

•**Gastrointestinal perforations –** new onset abdominal symptoms should be evaluated & treated

•**Laboratory abnormalities –** stop Baricitinib when:

- Neutropenia : ANC <1 x 10^9/ L
- Lymphopenia : ALC < 0.5 x 10^9/ L
- Anaemia : Haemoglobin < 8 g/dL
- ALT : ≥ 5x ULN
- AST: ≥ 10x ULN

Monitoring: Neutropenia, lymphopenia, anemia, LFT

Adverse effect: Infections, nausea, increased LFT

Drug interaction:

• **Live vaccines –** should not be given for at least 3 months after immunosuppressant

•**Biologic DMARDs and immunosuppressant–** may enhance immunosuppressive effects of Baricitinib

Only for internal circulation (HSgB).
For further enquires, kindly contact ext 03-6145 4126.
Revised Sept 2021.

DEXAMETHASONE

Available as 8 mg/2 ml Inj [equivalent to ≈ 6 mg dexa (base)] or 4 mg (base) Tablet

Usual dose:

IV: 8mg OD (or 12mg OD for if BMI >30kg/m^2)
[up to 20mg/day]

PO: 6-12 mg OD (max: 40mg/day)

Route of administration:

- Slow IV bolus over ≤ 1 min
- IV infusion over 5-15 min

Stability (after dilution):

Stable up to 24 hours at room temperature.

Pregnancy: Fetal risk cannot be ruled out

Lactation: Probably Compatible

Renal & hepatic impairment:

No adjustment required

Adverse effect:

Hyperglycemia, secondary infections, psychiatric effects, avascular necrosis

Precautions:

- Diabetes – monitor for hyperglycemia
- Renal impairment – monitor for fluid retention

Monitoring: BP, blood glucose

Contraindications:

Hypersensitivity to methylprednisolone & other corticosteroids

Drug interaction:

Phenytoin

Monitor for epileptic episodes

Warfarin

May enhance anticoagulant effect of vitamin K

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DEXAMETHASONE CONVERSION: IV TO PO

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- In order to reduce risk of bloodstream infection, the HSgB ID team has introduced an initiative to shorten the duration of IV access in patients.
- Recommendation: To step down IV Dexamethasone proactively once patient criteria is met.

PATIENT CRITERIA:

- Not on other IV drugs *
  **If patient is on IV Pantoprazole, can suggest to oralise it*
- Able to tolerate orally

HOW TO ORALISE:

IV Dexamethasone sodium phosphate **12 mg OD** (BMI > 30)	→	Tab Dexamethasone **8 mg** OD **OR** Tab Prednisolone **60 mg** OD
IV Dexamethasone sodium phosphate **8 mg OD**	→	Tab Dexamethasone **6 mg** OD **OR** Tab Prednisolone **40 mg** OD

Revision date 22 July 2021. For internal circulation only.

METHYLPREDNISOLONE

Available as 500 mg Inj & 1000mg Inj

Dose: 1–2 mg/kg/day, tapered after 5 days
* Usual dose: 150-200mg OD (may go up to 500mg/day)

Reconstitution:

500mg in 7.8 ml (Solumedrol) / 500mg in 8ml (Medixon) or 1000mg in 15.6 ml (Solumedrol) of benzyl alcohol in WFI (provided solvent)

Route of administration:

•IV infusion for **< 250 mg** over 30-60 min (dilute with 50-100 ml NS or D5)
•IV infusion for **≥ 250 mg** over 30-60 min (dilute with 100-250 ml NS or D5)
Note: Administered separately from other drugs.

Stability (after reconstitution & dilution):

Solu-medrol & Medixon : Up to 48 h at room temperature (<25°C)

Pregnancy: Use in first trimester may cause oral cleft; treatment should not be withheld in pregnant patients when otherwise indicated.

Lactation: Compatible

Renal & hepatic impairment:

No adjustment required

Adverse effect:

Hyperglycemia, secondary infections, psychiatric effects, avascular necrosis

Precautions:

- Diabetes – monitor for hyperglycemia
- Renal impairment - monitor for fluid retention

Monitoring: BP, blood glucose, electrolytes (Na & K)

Contraindications:

Hypersensitivity to methylprednisolone & other corticosteroids

Drug interaction:

Quinolones

May enhance the adverse effect of quinolones. (eg. tendonitis and tendon rupture)

Warfarin

May enhance anticoagulant effect of vitamin K.

HSgB GUIDE ON THROMBOPROPHYLAXIS IN HOSPITALISED COVID-19 ADULTS

***COVID & non-COVID patients who are not on oxygen may still require anticoagulants.
Kindly refer to VTE Prophylaxis for Hospitalized Patients (as per MOH CPG on Prevention & Treatment of VTE)***

Oxygen requirement

Low-flow Oxygen

Start *therapeutic dose prophylaxis* anticoagulant if:

- Oxygen support – Nasal Prong or Face Mask
- Not receiving ICU level of care
- D-Dimer > ULN (>500ng/ml)
- No increased ***bleeding risk****

Therapeutic dose
for 14 days or till discharge
(whichever comes first):

SC Enoxaparin 1mg/kg BD or 1.5mg/kg OD

- *If BMI ≥40kg/m²*: 0.75mg/kg BD *(round up)*
- *If CrCl <30ml/min*: 1mg/kg OD

OR

IVI Unfractionated Heparin
(Refer to IV Heparin Infusion Protocol for VTE)

THEN
Switch back to standard dose prophylaxis if completed 14 days or patient require high-flow oxygen / transfer to ICU

High-flow Oxygen

Start *standard dose prophylaxis* dose anticoagulant if:

- Oxygen support - HFM, HFNC, CPAP, BiPAP, Mechanical ventilation
- Receiving ICU level of care [±vasopressor]

Standard dose till discharge:

SC Enoxaparin 40mg OD

- *If BMI ≥ 40kg/m2*: 80mg per day
- *If CrCl < 30ml/min*: 20mg OD

OR

SC Unfractionated Heparin 5000 units BD or TDS

- If BMI >40 kg/m2: 7500units BD

OR

SC Fondaparinux 2.5mg OD
(Not for ICU patients, underweight <50kg, renal impaired CrCl <30ml/min, pregnant women)

If patient not suitable for therapeutic dose anticoagulant

Note:
Current preferred regimen in view of enoxaparin stock

***Checklist for increased risk of bleeding:**
Check if any contraindication(s) to start therapeutic dose anticoagulant:

- Platelet count <50x10^9/L
- Hb <8g/dL
- Active bleeding or Hb drop >2g/dL
- INR >2 or aPTT >50secs
- Bleeding within 30 days requiring emergency visit or hospitalization
- Requiring dual antiplatelet therapy (DAPT)
- Inherited or active acquired bleeding disorder
- Any other risk factor(s) for bleeding

Thromboprophylaxis for Pregnant Women:

Please refer to ***VTE Prophylaxis in Pregnancy*** section

1. Statement on Anticoagulation in Hospitalized Patients with COVID-19. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed [9th Jan 2022]
2. Leentjens J, van Haaps TF, Wessels PF et al. 2021. COVID-19-associated coagulopathy and antithrombotic agents—lessons after 1 year. https://doi.org/10.1016/S2352-3026(21)00105-8
3. Viggiano GV, Cardillo G, Russo V et al. FONDENOXAVID: A Retrospective Analysis on Utility of Thromboprophylaxis with Fondaparinux and Enoxaparin in Patients with COVID19 Infection in Italy. Preprints 2020, 2020050309 (doi: 10.20944/preprints202005.0309.v1).
4. Royal College of Obstetricians & Gynaecologists. 2020. Coronavirus (COVID-19) Infection in Pregnancy

HSgB ANTICOAGULANT CHART FOR COVID-19 CASES

BY: AMS Pharmacists (Izyana & Hannah), Clinical Unit (Sia) & PRIC (Abby) HSgB. Only for internal circulation (HSgB). For further enquires, kindly contact ext 4126. Revised 17th Jan 2022.

This guide is NOT intended for ICU / Pregnant / Paediatric Patients

Indication / Anti coagulant		Thromboprophylaxis Dose				Treatment Dose	
		High-flow Oxygen: • HFM, HFNC, CPAP, BiPAP or Intubated • ICU level of care (± on vasopressor/inotrope)		**Low-flow Oxygen:** • Low flow Oxygen: NP or FM • Duration: 14 days or until hosp discharge		**Suspected or Confirmed DVT/PE**	
S/C ENOXAPARIN (CLEXANE) *(CrCl < 15 ml/min – Limited data)*		**Standard Dose Prophylaxis**		**Therapeutic Dose Prophylaxis** *1.5 mg/kg OD or 1 mg /kg BD*		**DVT/PE Treatment Dose** *1 mg /kg BD*	
	BW (kg)	**Normal Renal Function**	**Renal Adj Dose (CrCl 15 – 30 ml/min)**	**Normal Renal Function**	**Renal Adj Dose (CrCl 15 – 30 ml/min)**	**Normal Renal Function**	**Renal Adj Dose (CrCl 15 – 30 ml/min)**
	40 – 49	40 mg OD	20 mg OD	60 mg OD *(or 40 mg BD)*	40 mg OD	40 mg BD	40 mg OD
	50 - 69			*80 mg OD *(or 60 mg BD)*	60 mg OD	60 mg BD	60 mg OD
	70 - 99			*100-120 mg OD *or* 80 mg BD	80 mg OD	80 mg BD	80 mg OD
	100 - 120	60 mg OD	30 mg OD	*80-120 mg BD	*80-120 mg OD	100 - 120 mg BD	100 - 120 mg OD
	BMI ≥ 40 kg/m^2:	80 mg/day	40 mg OD	0.75 mg/kg BD *(Up to 160 mg BD)*	0.75 mg/kg OD *(Up to 160 mg OD)*	0.75 mg/kg BD *(Up to 160 mg BD)*	0.75 mg/kg OD *(Up to 160 mg OD)*
S/C FONDAPARINUX (ARIXTRA)	**BW (kg)**	**Standard Risk Prophylaxis**		**Therapeutic Dose Prophylaxis**		**DVT/PE Treatment Dose**	
	< 50	*Not recommended*	*(CrCl< 30 ml/min - Contraindicated)*	*No data*		5 mg OD	*(CrCl< 30 ml/min - Contraindicated)*
	50 – 100	2.5 mg OD				7.5 mg OD	
	> 100					10 mg OD	
UNFRACTIONATED HEPARIN	**BMI (kg/m^2):**	**Standard Risk Prophylaxis**		**Therapeutic Dose Prophylaxis**		**DVT/PE Treatment Dose**	
	< 40	S/C Heparin 5000 units BD or TDS		IVI Unfractionated heparin *(Click here to refer to HSgB IV Heparin Infusion Protocol for VTE)*		IVI Unfractionated heparin *(Click here to refer to HSgB IV Heparin Infusion Protocol for VTE)*	
	≥ 40	S/C Heparin 7500 units BD					

**** Dose has been capped conservatively in view of Enoxaparin stock shortage.***

HSgB GUIDE ON VENOUS THROMBOEMBOLISM TREATMENT IN COVID-19 ADULTS

Suspected Venous Thromboembolism (VTE):
Treatment dose of S/C Enoxaparin or **S/C Fondaparinux**

CTPA/US Doppler → No Evidence of VTE: **Change to Prophylactic Dose**

Confirmed VTE

Stable/ Tolerating Orally? → **NO** → Continue treatment dose of **S/C Enoxaparin** or **S/C Fondaparinux** or **IVI Unfractionated Heparin**

YES ← **STABLE**

Discuss on choice of oral anticoagulant and make decision

WARFARIN

IN-PATIENT:
Bridge with treatment dose **S/C Enoxaparin** or **S/C Fondaparinux**
+
T. Warfarin :
- Usual initial dose: **5 mg / 5 mg / 3 mg**, then adjust based on INR
- Initial dose for **sensitive patients**: **3 mg / 2 mg / 2 mg**, then adjust based on INR

DOAC

Refer to DOAC Checklist before initiation *[click here]*

Supply Methods (In-Patient/Discharge):
1. Self-purchase 2. Pesara
3. Quota HSgB (to get Dr Suresh's approval)

DISCHARGE:
T. Warfarin (dose based on latest INR)

PARENTERAL ANTICOAGULANT TREATMENT DOSE

Normal renal function:
S/C Enoxaparin 1 mg/kg BD ***OR***
S/C Fondaparinux:
- < 50 kg : 5 mg OD
- 50-100 kg: 7.5 mg OD
- > 100 kg : 10 mg OD

Renally Impaired (CrCl <30ml/min or HD patients):
S/C Enoxaparin 1 mg/kg OD

Normal/ impaired renal function:
IVI Unfractionated heparin
(Refer to IV Heparin Infusion Protocol for VTE)

1. Self-purchase	2. Pesara (Government pensioner/spouse)	3. Quota HSgB (To get Dr Suresh's approval)
• Any choice of DOAC • To prescribe in eHIS and provide patient with prescription *[click here]* for self purchase	• **Dabigatran (*Preferable*)** or Apixaban • Fill in Borang Permohonan Ubat Untuk Pesara Awam Persekutuan Hospital Sungai Buloh *[click here]* • Prescription • Photocopy of pensioner's IC and pensioner card • Pharmacy will supply full treatment course	• **Dabigatran (*Preferable*)** or Apixaban (*Only if Dabigatran is contraindicated due to renal impairment, on nasogastric tube and/or extremes of weight*) • Pharmacy will supply full treatment course

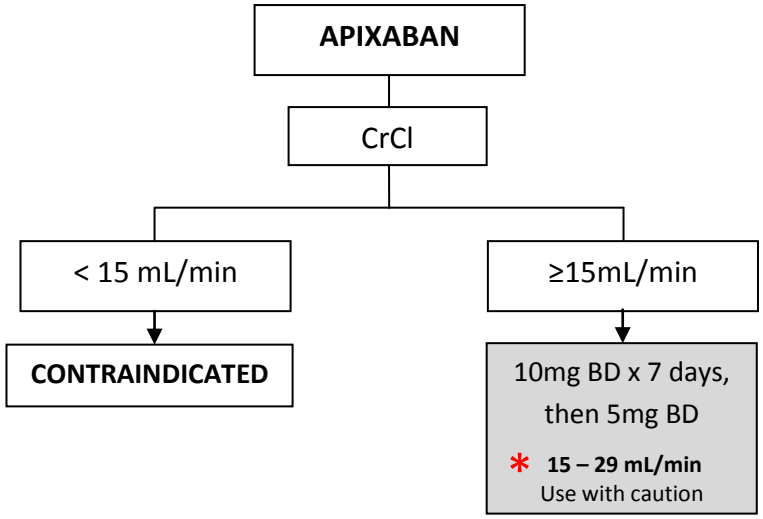
DO NOT SWITCH choice of oral anticoagulant in the middle of treatment UNLESS patient develop ALLERGIC/ ADVERSE REACTION or only UNDER SPECIAL CIRCUMSTANCES. This is to prevent MEDICATION ERROR. Decide WISELY before initiation.

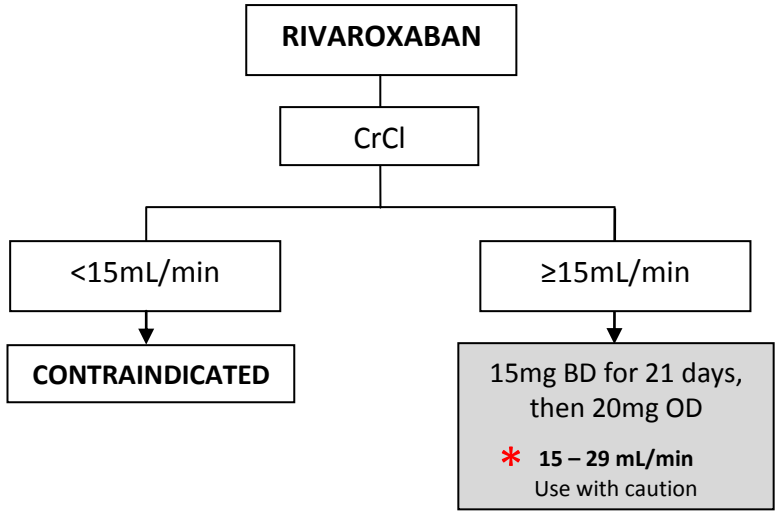
Prepared by Pharmacy Dept. Revised 7th July 2021. For internal circulation only.

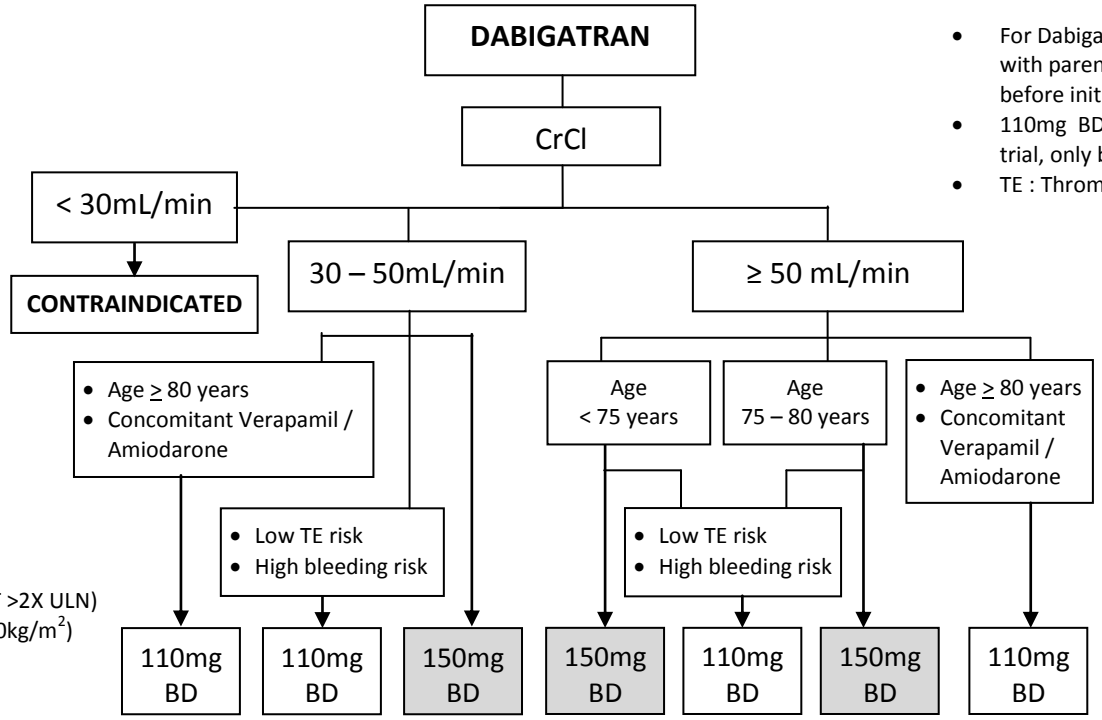
DOAC DOSING GUIDE FOR VENOUS THROMBOEMBOLISM (DVT/PE)

PREPARED BY PHARMACY DEPT HOSP SG BULOH. UPDATED 8TH JULY 2021

FOR INTERNAL CIRCULATION ONLY







- For Dabigatran, min 5 days of treatment with parenteral anticoagulant is required before initiation
- 110mg BD dose is not studied in clinical trial, only based on PKPD analyses
- TE : Thromboembolic

FOOTNOTE FOR ALL DOAC

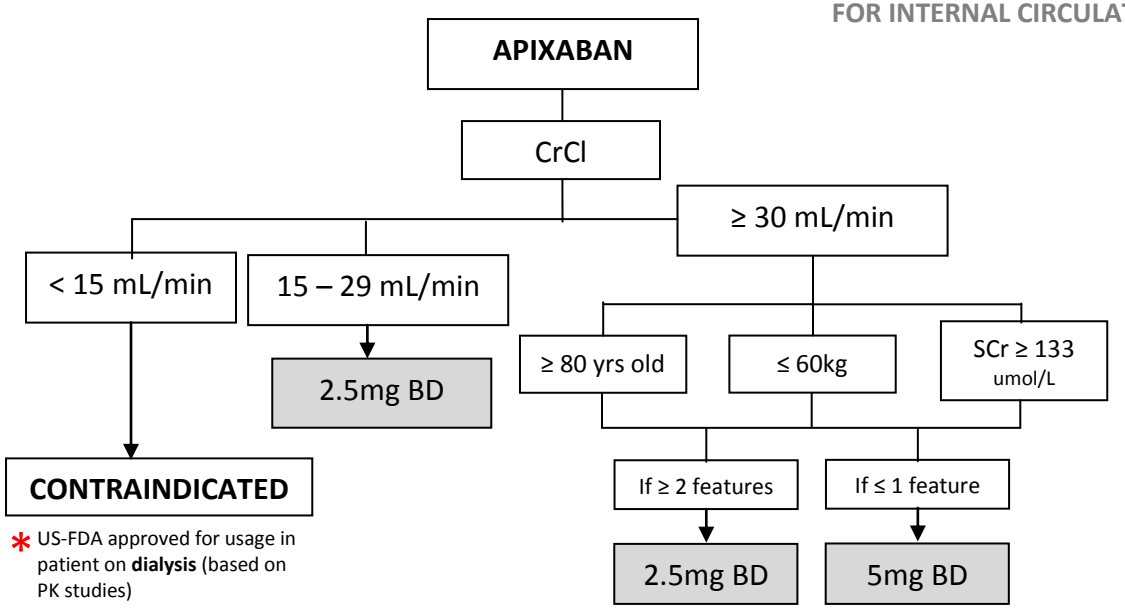
- Not recommended in pregnancy/lactation
- Not recommended when liver enzyme elevated (ALT/AST >2X ULN)
- For extremes of body weight (< 50kg, > 120kg or BMI > 40kg/m^2) please consult your pharmacist.
- For further enquiries, please contact Pharmacy.

DOAC DOSING GUIDE FOR ATRIAL FIBRILLATION (AF)

PREPARED BY PHARMACY DEPT HOSP SG BULOH. UPDATED 8TH JULY 2021

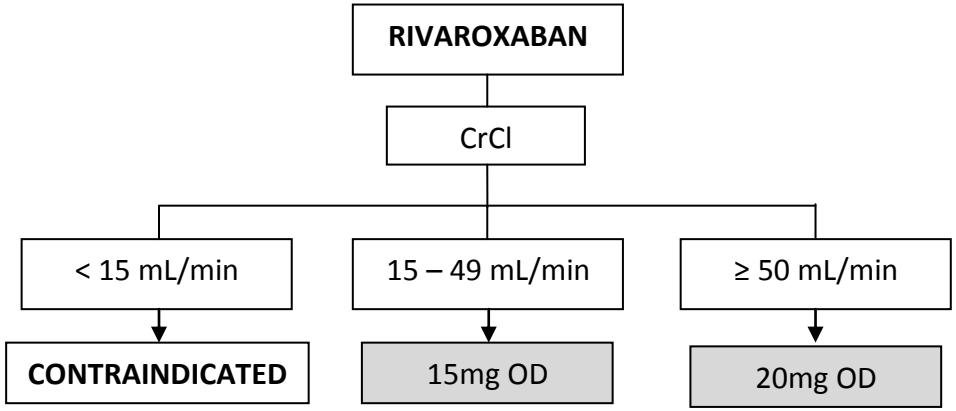
FOR INTERNAL CIRCULATION ONLY

APIXABAN

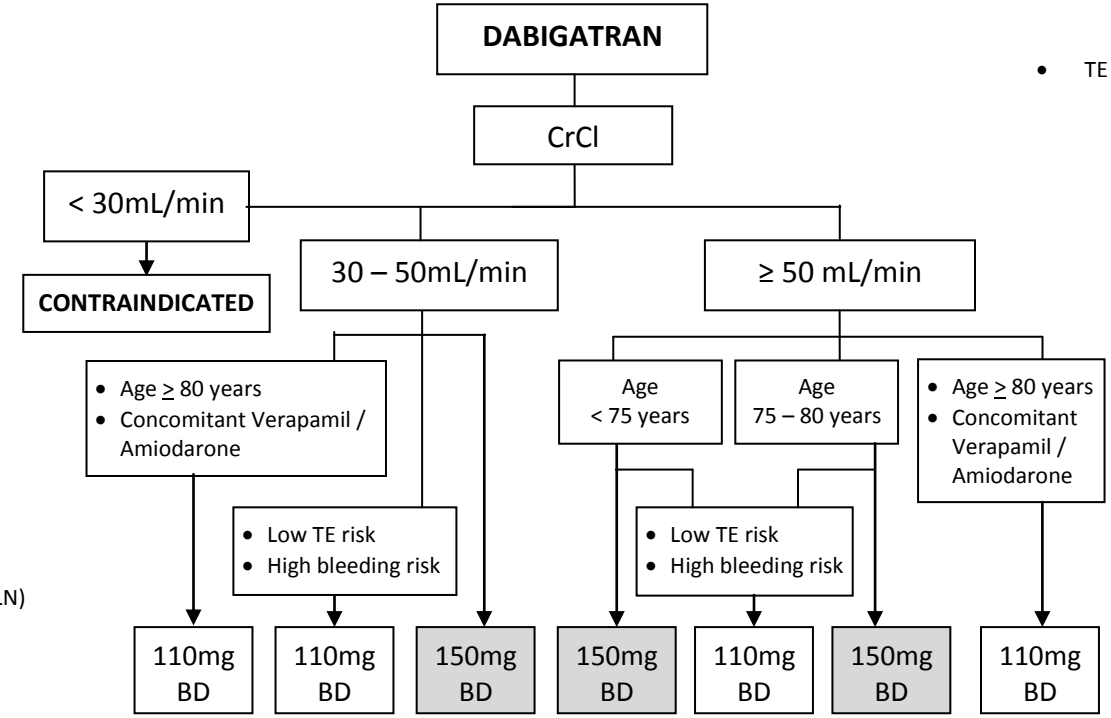


* US-FDA approved for usage in patient on **dialysis** (based on PK studies)

RIVAROXABAN



DABIGATRAN



- TE : Thromboembolic

FOOTNOTE FOR ALL DOAC

- Not recommended in pregnancy/lactation
- Not recommended when liver enzyme elevated (ALT/AST >2X ULN)
- For extremes of body weight (< 50kg, > 120kg or BMI > 40kg/m^2) please consult your pharmacist.
- For further enquiries, please contact Pharmacy.

DOAC Checklist for AF & VTE

Prepared by PRIC HSgB.
For internal circulation only. To consult physician if needed.

CHECKLIST	DABIGATRAN	APIXABAN	RIVAROXABAN
☐ **INDICATION: STROKE PREVENTION IN AF (SPAF)**	**Usual dose**[1,4] 150mg BD **Dosing Adjustment** [1,4] • 110mg BD if fulfill any of the following risk factors: i) Patients aged ≥80 years ii) Concomitant use of Verapamil / Amiodarone **Please refer to bottom of the table for further dosing consideration*	**Usual dose**[2] 5mg BD **Dosing Adjustment**[2] • 2.5mg BD if fulfill **TWO** of the following criteria: i) Patients aged ≥80 years ii) Body weight ≤60kg iii) Serum Creatinine ≥133 umol/L • 2.5mg BD if CrCl 15-29ml/min	**Usual Dose**[3] 20mg OD **Dosing Adjustment**[3] • 15 mg OD if CrCl 15-49 ml/min
☐ **INDICATION: VTE** **Not applicable for prevention of VTE in patient undergoing hip or knee replacement surgery* ***Duration for treatment:** at least 3 months*	**Treatment / Prevention**[1,4] PARENTERAL ANTICOAGULANT for at least 5 days **THEN** 150mg BD **OR** 110mg BD if fulfill any of the following risk factors i) Patients aged ≥80 years ii) Concomitant use of Verapamil / Amiodarone iii) High bleeding risk **AND** CrCl: 30-50 ml/min **Please refer to bottom of the table for further dosing consideration*	**Treatment**[2] 10mg BD for 7 days **THEN** 5mg BD **Prevention of Recurrent VTE**[2] 2.5mg BD *(after at least 6 months of therapeutic dose of anticoagulant)*	**Treatment**[3] 15mg BD for 21 days **THEN** 20mg once daily **Prevention of Recurrent VTE**[3] 10 mg OD *(after at least 6 months of therapeutic dose of anticoagulant)*
☐ **RENAL FUNCTION**	**<30 ml/min**: Contraindicated[1,4]	**<15 ml/min** : Contraindicated **15 – 29 ml/min** : Use with caution[2]	**<15 ml/min** : Contraindicated **15 – 29 ml/min** : Use with caution[3]

*** FOR DABIGATRAN: May consider adjustment to 110mg BD** based on individual thromboembolic and bleeding risk assessment for the following groups:
i) Age: 75-80 years, ii) Moderate renal impairment (30 – 50ml/min), iii) Hx of gastritis, esophagitis or gastroesophageal reflux, iv) Patients with increased risk of bleeding

Revised May 2021

References.

1. Pradaxa [Product Insert].Ingelheimam Rhein: Boehringer Ingelheim; 07 February 2020.
2. Eliquis [Product Insert]. New York: Pfizer; 03 September 2020.
3. Xarelto [Product Insert]. Leverkusen: Janssen Pharmaceuticals; March 2020.
4. *(2020). Anticoagulant MTAC (AC-MTAC) Protocol. 2nd Ed.* Selangor: Ministry of Health Malaysia.
5. Chen, A., Stecker, E., & Warden, B. A. (2020). Direct Oral Anticoagulant Use: A Practical Guide to Common Clinical Challenges. *Journal of the American Heart Association*, 1-18.
6. Rivaroxaban—Once daily, oral, direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation: Rationale and Design of the ROCKET AF study. (2010). *American Heart Journal*, *159*(3). https://doi.org/10.1016/j.ahj.2009.11.025

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JABATAN FARMASI
HOSPITAL SUNGAI BULOH

DOAC Checklist for AF & VTE

Prepared by PRIC HSgB.
For internal circulation only. To consult physician if needed.

CHECKLIST	DABIGATRAN	APIXABAN	RIVAROXABAN
☐ **HEPATIC FUNCTION**	Child Pugh **A**: No dosage adjustment. Child Pugh **B**: No dosage adjustment. Use with caution. Child Pugh **C**: Contraindicated. [4-5] ***Not recommended when elevated liver enzymes > 2 ULN***[1,4]	Child Pugh **A**: No dosage adjustment. Child Pugh **B**: No dosage adjustment. Use with caution. Child Pugh **C**: Contraindicated ***Use with caution when elevated liver enzymes > 2 ULN***[2,4,5]	Child Pugh **A**: No dosage adjustment. Child Pugh **B**: Contraindicated Child Pugh **C**: Contraindicated[3-5] ***No data for elevated liver enzymes > 3 ULN***[6]
☐ **WEIGHT CONSIDERATION** ** Low body weight: ↑bleeding risk* ** Obesity: ↓ drug exposure*	• **Wt <50kg**: Use with caution.[1] • **BMI >40kg/m² or Wt >120 kg:** Avoid use. Suggest to use alternative.[5]	• **Wt <50kg**: Use with caution. **For NVAF:** Adjust dose if other criteria are met. **For VTE :** No dosage adjustment. [2] • **BMI >40kg/m² or Wt >120 kg**: Use with caution. Consult physician.[5]	• **Wt <60kg**: Avoid use.[5] • **BMI >40kg/m² or Wt >120 kg:** Use with caution. Consult physician.[5]
☐ **PREGNANCY & LACTATION**	Not recommended.[1-5]		
☐ **ADMINISTRATION**	Swallow whole. Do **not** break, chew or open capsules.[1]	Swallow whole or crush the tablet and suspend in 60mL of water / D5.[2]	Swallow whole or crush the tablet and suspend in 50mL of water / D5. To be taken with food.[3]
PHYSICAL APPEARANCE *Only the product that are available in HSgB are shown	 **Pradaxa hard cap 150mg**  **Pradaxa hard cap 110mg**	 **Eliquis FC Tab 5mg**  **Eliquis FC Tab 2.5mg**	 **Xarelto FC Tab 20mg**

Revised May 2021

References.

1. Pradaxa [Product Insert].Ingelheimam Rhein: Boehringer Ingelheim; 07 February 2020.
2. Eliquis [Product Insert]. New York: Pfizer; 03 September 2020.
3. Xarelto [Product Insert]. Leverkusen: Janssen Pharmaceuticals; March 2020.
4. *(2020). Anticoagulant MTAC (AC-MTAC) Protocol. 2nd Ed.* Selangor: Ministry of Health Malaysia.
5. Chen, A., Stecker, E., & Warden, B. A. (2020). Direct Oral Anticoagulant Use: A Practical Guide to Common Clinical Challenges. *Journal of the American Heart Association*, 1-18.
6. Rivaroxaban—Once daily, oral, direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation: Rationale and Design of the ROCKET AF study. (2010). *American Heart Journal*, *159*(3). https://doi.org/10.1016/j.ahj.2009.11.025

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DABIGATRAN

Available as 110 mg and 150 mg capsule

Dose – **Treatment of DVT & PE**:

150mg BD, after 5-10 days of parenteral anticoagulant[#] (treatment duration: ≥ 3 months)

[#]Start Dabigatran at the next scheduled dose of parenteral anticoagulation when converting

110mg BD is recommended for:

- Patients aged 80 years or above
- Patients who receive concomitant Verapamil

Obese (BMI > 40 kg/m^2 or > 120 kg): Use not supported

Other dosing considerations:

Regime of **150mg BD or 110mg BD** is selected based on an individual assessment of thromboembolic risk and the risk of bleeding for:

- Patients between 75-80 years
- Patients with moderate renal impairment
- Patients with gastritis, esophagitis or gastroesophageal reflux
- Other patients at increased risk of bleeding

Enteral administration (e.g. Ryle's tube):

Do not use.

Method of supply:

Quota*, *pesara* or self-purchase^

**Criteria to supply for quota:*

- *Seen by a medical specialist or neuromedical*
- *Failed warfarin or not a candidate for warfarin*
- *Under follow-up at HSgB*

^Estimated retail price for a box of 28's: RM 152

Pregnancy & lactation: Avoid use

Renal impairment – **Treatment of DVT & PE**:

CrCl > 30 ml/min: 150mg BD

CrCl 30-50 ml/min: 150mg BD;
110mg BD for high risk of bleeding

CrCl < 30 ml/min: Contraindicated

Liver impairment: Not recommended when elevated liver enzymes > 2 ULN

Monitoring: aPTT

Contraindication:

- Active clinically significant bleeding
- Lesion or condition, if considered a significant risk factor for major bleeding (eg. GI ulcer)
- Mechanical heart valves

Adverse effect: Bleeding

Drug interaction:

P-glycoprotein inducers: ↓ Dabigatran level
Rifampicin

P-glycoprotein inhibitors: ↑ Dabigatran level
Amiodarone, Verapamil, Quinidine, systemic Ketoconazole, Ticagrelor, Clarithromycin

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised Sept 2021.

APIXABAN

Available as 2.5 mg and 5 mg tablet

Dose – **Treatment of DVT &/or PE**:

10 mg BD for 7 days, followed by 5 mg BD

(refer to *"HSgB Venous Thromboembolism Guideline for COVID-19 Patients"* for more details)

Enteral administration (e.g. Ryle's tube):

May crush and suspend in 60 ml of water or D5W; administer immediately - suspension stable up to 4h

Method of supply:

Inpatient: Supplied by HSgB

Outpatient: Self purchase^ / pesara / quota*

^Estimated retail price for a box of 60's: ~RM 315

**Criteria to supply for quota:*

- *Seen by a medical specialist or neuromedical*
- *Failed warfarin or not a candidate for warfarin*
- *On NG tube feeding and requiring anticoagulant*

Pregnancy & lactation: Not recommended

Renal impairment:

≥ 30ml/min: No dose adjustment

15-29ml/min: Use with caution

< 15ml/min: Contraindicated

Liver impairment:

Child-Pugh A: No dose adjustment

Child-Pugh B: No dose adj; use with caution

Child-Pugh C: Contraindicated

Use with caution when ↑ ALT/AST >2 x ULN

Contraindications:

- Active clinically significant bleeding
- Lesions or conditions at increased risk of clinically significant bleeding
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk
- Concomitant systemic treatment with strong inhibitors of both CYP3A4 and p-glycoprotein, or any other anticoagulants

Precautions:

- **Body weight considerations:** Use with caution in BW < 50kg, or BW > 120kg / BMI > 40kg/m^2
- **Active cancer:** Efficacy & safety for treatment of VTE not established

Adverse reaction: Haemorrhage

Monitoring: CBC, aPTT, PT, serum creatinine, LFT

Drug interactions:

- **Strong inhibitors of CYP3A4 & P-glycoprotein**: ↑ Apixaban. eg. Azoles & HIV protease inhibitors
- **Other anticoagulants:** May enhance anticoagulant effect. eg. UFH, LMWH, Fondaparinux & oral anticoagulants
- **Strong inducers of CYP3A4 & P-glycoprotein**: ↓ Apixaban - not recommended for VTE treatment as efficacy may be compromised. E.g. Rifampicin, Phenytoin

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised Sept 2021.

JABATAN FARMASI HOSPITAL SUNGAI BULOH

HOSPITAL SUNGAI BULOH

RIVAROXABAN

Available as 20 mg tablet

Dose **– Treatment of DVT &/or PE**:
15 mg BD for 21 days, followed by 20 mg OD

Enteral administration (e.g. Ryle's tube):
Swallow whole or crush the tablet and suspend in 50mL of water / D5. To be taken with food.

Method of supply: Self purchase^ / pesara
^Estimated retail price for a box of 28's: RM 258

Pregnancy & lactation: Not recommended

Renal impairment:
≥ 30ml/min: No dose adjustment
15-29ml/min: Use with caution
< 15ml/min: Contraindicated

Liver impairment:
Child Pugh A: No dosage adjustment.
Child Pugh B & C: Contraindicated
No data for elevated liver enzymes > 3 ULN

Contraindications:
- Active clinically significant bleeding
- Lesions or conditions at increased risk of clinically significant bleeding
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk

Precautions:
- **Body weight considerations:** Use with caution in BW < 50kg, or BW > 120kg / BMI > 40kg/m^2

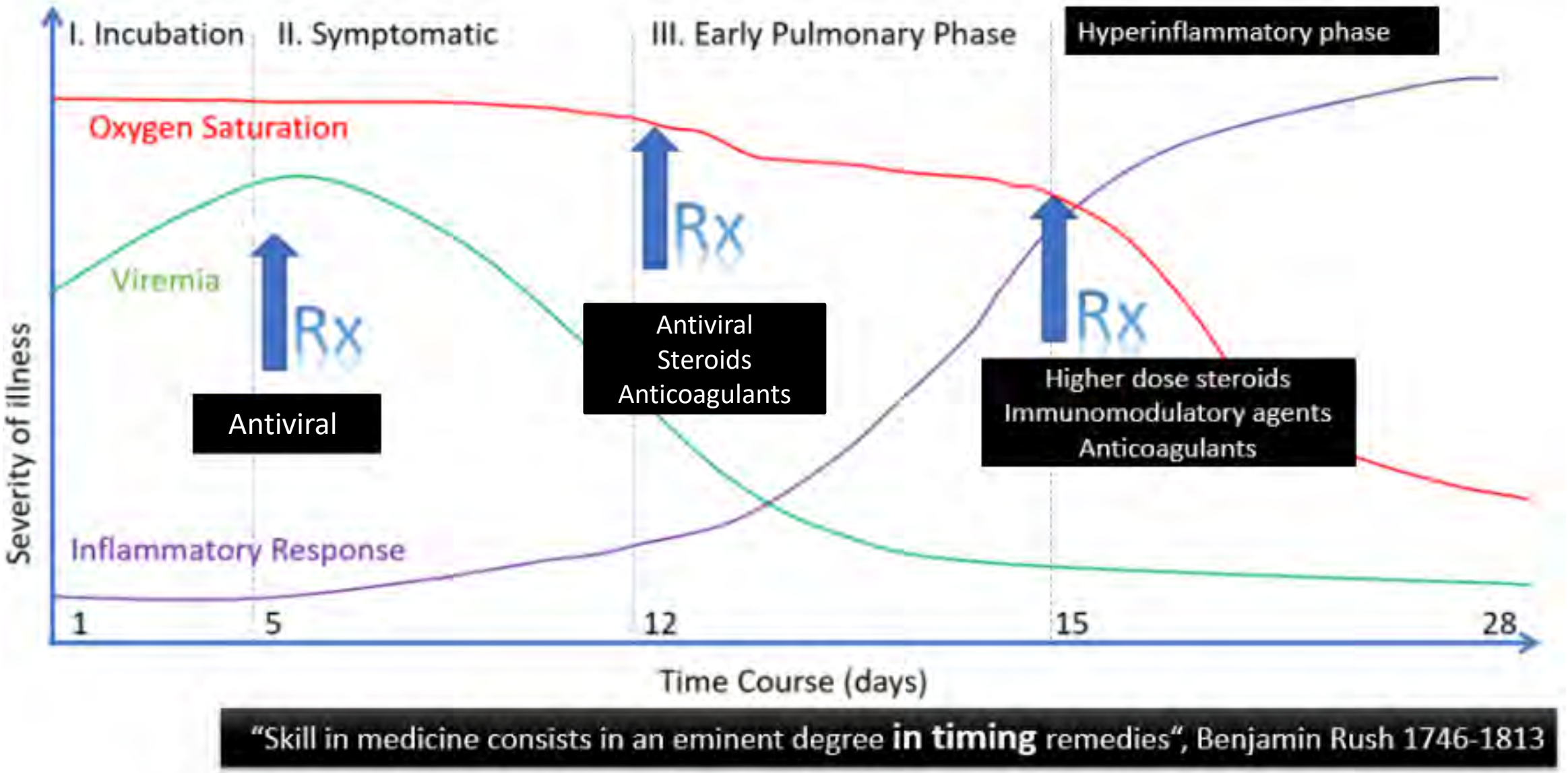
Adverse reaction: Haemorrhage

Monitoring: CBC, serum creatinine, LFT, bleeding symptoms (eg. weakness, dizziness, unexplained edema; unexplained decrease in hemoglobin or BP warrants prompt clinical evaluation for bleeding)

Drug interactions:
Strong inhibitors of CYP3A4 & P-glycoprotein:
- ↑ Rivaroxaban
- eg. Azoles & HIV protease inhibitors

Strong inducers of CYP3A4 & P-glycoprotein:
- ↓ Rivaroxaban
- eg. Rifampicin, Phenytoin, Carbamazepine, Phenobarbital or St. John's Wort

CLINICAL MANAGEMENT OF CONFIRMED COVID-19 CASE IN ADULT



"Skill in medicine consists in an eminent degree **in timing** remedies", Benjamin Rush 1746-1813

Clinical Staging of Syndrome Associated with COVID-19

Clinical Stage	Description
1	**Asymptomatic**
2	**Symptomatic, No Pneumonia**
3	**Symptomatic, Pneumonia**
4	**Symptomatic, Pneumonia, Requiring supplemental oxygen*** *(*Eg: Requiring nasal prong (NP) or face mask (FM) or high flow mask (HFM))*
5	**Critically ill with multi-organ involvement** *(*Eg: Requiring Non-invasive ventilation (NIV), including HFNC or Mechanical ventilation with or without other organ failures)*

In patients who **present with hypoxia, it is **important to determine is the cause is due to COVID-19 pneumonia or other causes** (e.g. bronchial asthma, fluid overload and heart failure). Positive SST (sit-to-stand test) does not necessarily categorize the patients as category 4.*

Risk of Hospitalization & Treatment for People with COVID-19

Risk Category for people with NON-SEVERE COVID-19		Treatments for people with NON-SEVERE COVID-19
High-risk for hospital admission (estimated hospitalization rate of 6%)	• People who are immunosuppressed: o solid organ transplant recipient on immunosuppressants o autoimmune illness on immunosuppressants	• **Paxlovid** 3 tabs BD x 5 days, given within 5 days from symptom onset • Alternative: ~~Molnupiravir~~ or **Remdesivir** 200 mg IV on Day 1, then 100 mg IV OD on Days 2 & 3
Moderate-risk for hospital admission (estimated hospitalization rate of 3%)	• People > 65 years old • Those with conditions such as: o Obesity o Diabetes o COPD o Kidney or liver disease o Cancer o People with disabilities o Comorbidities of chronic disease	• **Paxlovid** 3 tabs BD x 5 days, given within 5 days from symptom onset • Molnupiravir or Remdesivir is NOT recommended
Low-risk for hospital admission (estimated hospitalization rate of 0.5%)	• Those who are not in the categories above	• **For symptomatic treatment** only. Eg: Paracetamol. • Anti-viral therapy is NOT recommended.

Treatments for people with SEVERE or CRITICAL COVID-19

- **SEVERE:** Oxygen <90% on Room Air, Sign of pneumonia, Signs of respiratory distress
- **CRITICAL:** Intubated/on NIV, on Vasopressor, ARDS, Sepsis or Septic shock

Strong recommendation for:

1. **Systemic corticosteroid**
   - Choice: Dexamethasone 6 mg IV/PO OD
   - Timing: ≥ 7 days after symptoms onset
   - Duration: Up to 10 days, discontinue at hosp discharge

2. **Tocilizumab**
   - Dose: 8mg/kg (ABW)x 1 dose (Max: 800 mg)
   - Timing: At the same time as systemic corticosteroid
   - Duration: Single dose, over 1 hr. (Optional 2nd dose 12-48 hrs after 1st dose).

3. **Baricitinib**
   - Dose: 4 mg PO once daily (eGFR ≥ 60)
   - Timing: At the same time as systemic corticosteroid
   - Duration: 14 days or until hospital discharge
   - May be combined with corticosteroids and Tocilizumab.
   - Risk-benefit may be less advantageous, particularly in pts with HIV/TB/Fungal infections or at risk of OI.

Conditional recommendation for:

1. **Remdesivir**
   - Dose: 200 mg IV on Day 1, then 100 mg IV OD on Days 2 onwards
   - Timing: As early as possible in the time course of the disease
   - Duration: 5-10 days

Source: *WHO Therapeutics and COVID-19: living guideline, Nov 2023*

Prepared by: Izyana Munirah Idham (AMS Pharmacist). Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126/4114. Revised 22 Dec 2023.

Specific Treatment of COVID-19 Disease

<table>
<tr><th>Category</th><th>Recommended</th><th>Alternative</th><th>Remarks</th></tr>
<tr><td>Category 1</td><td>No treatment required
Monitor for warning sign</td><td></td><td></td></tr>
<tr><td rowspan="3">Category 2

OR

Category 3</td><td>For high risk patients
(Eligibility scoring for initiation of antiviral ≥3 link)
AND within 5 days of illness:

Nirmatrelvir 300mg with Ritonavir 100 mg (taken together) BD for 5 days1
(Preferred)

OR

Molnupiravir 800mg BD for 5 days
(If contraindicated to Nirmatrelvir or Ritonavir)</td><td>For high risk patients
(Eligibility scoring for initiation of antiviral ≥3 link)
AND within 5 days of illness:

IV Remdesivir 200mg loading (D1), then 100mg daily (D2-D3)
(Only if Nirmatrelvir /Ritonavir and Molnupiravir are not available)

OR

Casirivimab 600mg/ Imdevimab 600mg
(Ronapreve)
▪ Not for Omicron variant
▪ IV or SC single dose</td><td rowspan="3">Nirmatrelvir/Ritonavir (Paxlovid)
▪ Renal adjustment: eGFR 30-60mL/min: Nirmatrelvir 150mg with Ritonavir 100mg BD, <30mL/min: not recommended
▪ No data in pregnancy and breastfeeding mother
▪ Review concomitant medications to avoid drug-drug interaction due to Ritonavir (potent CYP3A4 inhibitor). Please refer to the list of common drug interactions (link), or visit https://www.covid19-druginteractions.org/checker

Molnupiravir
▪ Not recommended in pregnancy and breastfeeding mother
▪ Females of childbearing potential should use reliable contraception during treatment and for 4 days after the last dose

Remdesivir
▪ Not recommended for eGFR <30 ml/min [refer to remdesivir slide link]
▪ Liver function testing before and during therapy
▪ No data in pregnancy and breastfeeding mother</td></tr>
<tr><td colspan="2">Anticoagulation therapy:
In category 3, standard dose prophylaxis of heparin:
▪ In-hospitalised patient
▪ LMWH or UFH (LMWH is preferred)
▪ Check contraindication</td></tr>
<tr><td colspan="2">Corticosteroid is not recommended in non-hypoxic cases unless for other indications.</td></tr>
<tr><td rowspan="2">Category 4a
(requiring nasal prong or face mask#)</td><td>IV Dexamethasone phosphate6 8mg od (12mg if BMI >30) for up to 10 days or until discharge</td><td>IV Dexamethasone phosphate 8mg od (12mg if BMI >30) for up to 10 days or until discharge
AND
IV Remdesivir 200 mg loading (D1), then 100 mg daily (D2- D5)

For patients on dexamethasone with increasing oxygen needs and systemic inflammation, consider
▪ IV Dexamethasone phosphate 24mg od
▪ Dexamethasone and Baricitinib
▪ IV Methylprednisolone 2mg/kg for 3-5 days</td><td rowspan="2">Remdesivir
▪ Maximum benefit if started ≤ 10 days of illness.
▪ Not recommended for eGFR < 30 ml/min [refer to remdesivir slide link]

Methylprednisolone
There is currently insufficient evidence to recommend for or against a short course of methylprednisolone as escalation treatment.

If corticosteroid is contraindicated, can use Remdesivir AND Baricitinib

Step-down to oral dexamethasone 6mg once improved

Note: IV dexamethasone phosphate 8mg = IV dexamethasone base 6mg = oral dexamethasone 6mg.</td></tr>
<tr><td colspan="2">Anticoagulation therapy:
▪ Therapeutic dose prophylaxis (preferably when D-dimer >ULN)
▪ Otherwise, for prophylactic dose heparin
▪ LMWH or UFH (LMWH is preferred)
▪ Check for bleeding risk and contraindication</td></tr>
</table>

#Note: In patients who present with hypoxia, it is important to determine if the cause is due to COVID-19 pneumonia or other causes (e.g. bronchial asthma, fluid overload and heart failure). Positive SST does not necessarily categorize the patients as category 4.

<table>
<tr>
<td rowspan="2">Category 4b
(requiring high flow mask)

OR

Category 5a
(noninvasive ventilation (NIV), including HFNC)</td>
<td>IV Dexamethasone phosphate 24mg od for 5 days, then 12mg od for 5 days</td>
<td>IV Dexamethasone phosphate 24mg od for 5 days, then 12mg od for 5 days
AND
IV Remdesivir 200 mg loading (D1) and 100 mg daily (D2- D5)

OR

IV Methylprednisolone 2mg/kg/day for 3-5 days, then step down to IV Dexamethasone phosphate 8-12mg od once improved</td>
<td rowspan="2">Remdesivir:
▪ Maximum benefit if started ≤ 10 days of illness.
▪ not recommended for eGFR < 30 ml/min [refer to remdesivir slide link]

Tocilizumab:
▪ IV 8mg/kg single dose (max: 800 mg/dose)
▪ Tocilizumab is preferred over Baricitinib in patients with poor gut absorption and eGFR

Baricitinib:
▪ 4mg OD oral x 14 days or until hospital discharge (whichever earlier)
▪ Avoid in patients with previous history of thrombosis
▪ Renal adjustment: eGFR ≥60: 4mg OD, 30-59: 2mg OD, 15-29: 1mg OD, <15: not recommended

Note:
IV Dexamethasone phosphate 24mg = IV Dexamethasone base 20mg</td>
</tr>
<tr>
<td colspan="2">Anticoagulation therapy:
Standard dose prophylaxis of heparin:
▪ LMWH or UFH (LMWH is preferred)
▪ Check contraindication
▪ If the patient is started on therapeutic dose earlier, switch to prophylactic dose</td>
</tr>
<tr>
<td rowspan="2">Category 5b
(mechanical ventilation with or without other organ failures)</td>
<td>IV Dexamethasone phosphate 24mg od for 5 days, then 12mg od for 5 days</td>
<td>IV Methylprednisolone 2mg/kg/day for 3-5 days, then step down to IV Dexamethasone phosphate 8-12mg od once improved

OR

Corticosteroid AND Tocilizumab

OR

Corticosteroid AND Baricitinib</td>
<td rowspan="2">Remdesivir is not recommended

Tocilizumab (as above)
Baricitinib (as above)</td>
</tr>
<tr>
<td colspan="2">Anticoagulation therapy:
Standard dose prophylaxis of heparin:
▪ LMWH or UFH (LMWH is preferred)
▪ Check contraindication
If the patient is started on therapeutic dose earlier, switch to prophylactic dose</td>
</tr>
</table>

Source: Clinical Management Of Confirmed Covid-19 Case In Adult And Paediatric (Annex 2E), released 30 March 2022

COVID 19 Treatment Guide in Pregnancy

By PRIC and AMS

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised **December 2023**.

Disclaimer: All information in this guide is merely for educational and informational purposes. It is not intended as a substitute for professional advice. Kindly seek consultation from your facility's physician for further management. We reserve the right to update this guide at any given time.

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SUNGAI BULOH

COVID-19 TREATMENT IN PREGNANCY & BREASTFEEDING

DRUG	PREGNANCY	LACTATING MOTHER
Baricitinib	**Recommended** in hospitalized patients, if indicated and to weigh potential risks and benefits	**Avoid** breastfeeding while taking baricitinib and for 4 days after the last dose.
Nirmatrelvir + Ritonavir	**Recommended**, if indicated.	**Continue** breastfeeding • Poor oral absorption if ingested by infant • Low levels of nirmatrelvir not expected to cause adverse effects
Remdesivir	**Recommended**, if indicated.	**Continue** breastfeeding • Low levels found in breast milk • Poor oral absorption if ingested by infant
Tocilizumab	**Recommended** in hospitalized patients, if indicated and to weigh potential risks and benefits	**Continue** breastfeeding

Reference: COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed 20 Dec 2023..

STEROIDS

In pregnant / lactating patients requiring supplemental oxygen or mechanical ventilation

Usual duration of steroids: **10 days***

**May be longer if under Medical / ID and require dose tapering*

If indicated for FETAL LUNG MATURITY

IM Dexamethasone 6 mg 12 hourly for 4 doses **THEN** PO Prednisolone 40 mg OD or IV Hydrocortisone 80 mg BD

If indicated NOT for fetal lung maturity

PO Prednisolone 40 mg OD or IV Hydrocortisone 80 mg BD

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VTE PROPHYLAXIS IN PREGNANCY

VTE PROPHYLAXIS:

- Should be prescribed with LMWH unless contraindicated.
- Dose of thromboprophylaxis as per Management of Covid-19 in Obstetrics (Addendum to 1st revision) 9 Sept 2021
- **High prophylactic dose NOT routinely used**
- Enoxaparin (Clexane) is preferred over Fondaparinux (Arixtra) & unfractionated heparin (UFH) in pregnancy.

LMWH DOSE IN PREGNANCY:

Thromboprophylaxis for Pregnant Women:

- <50kg: SC Enoxaparin 20mg OD
- 50-90kg: SC Enoxaparin 40mg OD
- 91-130kg: SC Enoxaparin 60mg OD
- 131-170kg: SC Enoxaparin 80mg OD
- >170kg: SC Enoxaparin 0.6mg/kg/day (given in 1-2 divided dose)

Reference: RCOG & Annex 23a

DURATION:

- **Pregnant women (Antenatal):**
  To continue **until 10 days** post-discharge.
  May consider longer duration if needed (based on O&G assessment)
- **0-6 weeks Postpartum (Postnatal):**
  To continue **until 10 days** after discharge.
  May go up to 6 weeks postpartum if needed.
- **Post C-sec**:
  May continue **up to 6 weeks**. *Duration based on VTE scoring (decided by O&G specialist)*

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised 13 March 2022.

JABATAN FARMASI HOSPITAL SUNGAI BULOH
HOSPITAL SUNGAI BULOH

COVID 19 Treatment Guide in Paediatrics

By PRIC and AMS

Disclaimer: All information in this guide is merely for educational and informational purposes. It is not intended as a substitute for professional advice. Kindly seek consultation from your facility's physician for further management. We reserve the right to update this guide at any given time.

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GENERAL CARE

ANTIPYRETIC

Paracetamol (Syrup) Dosing

- **Neonate**
  10 mg/kg/dose TDS / QID / PRN
  (max 30 mg/kg/day- preterm , 40mg/kg/day- term)
- **Infant – Child**
  10-15 mg/kg/dose QID / PRN
  (max 75 mg/kg/day OR 4 g/day)

OTHERS

- Avoid use of nebulisation of **ß2 agonists**.
- To use **metered-dose inhaler (MDI) with spacer**.
  Refer *Alternatives for Nebulising Solutions Chart*.

ANTIBIOTICS

INDICATION	ANTIBIOTIC	IV DOSING	PO DOSING
Pneumonia	Amoxycillin	-	25-30 mg/kg/dose q8h for 5-7 days (Max 1 g/dose)
	Amoxicillin/ clavulanate (Dose is in Augmentin)	**Child 1-2 months old:** 30 mg/kg/dose q12h **Child ≥3 months old:** 30 mg/kg/dose q8h (Max 1.2 g/dose)	**Syrup (7:1)** **Mild- moderate**: 15-20 mg/kg/dose q12h **Moderate-severe**: 20-25 mg/kg/dose q12h (Max 570 mg q12h) **Tablet (4:1)** 625 mg BD (in severe cases with BW ≥40kg, can give 625 mg TDS)
	Cefuroxime	25-50 mg/kg/dose q8h (Max 1.5 g/dose)	10-15 mg/kg/dose q12h (Max 500 mg/dose)
Atypical pneumonia	Azithromycin	10 mg/kg/dose q24h (Max 500 mg/dose) for 1-2 days then oralise	**Preferred:** 10 mg/kg/dose q24h D1 (Max 500 mg) THEN 5 mg/kg/dose q24h D2-5 (Max 250 mg) **OR** *Alternative:* *15 mg/kg/dose q24h D1 (Max 500 mg),* *THEN 7.5 mg/kg/dose q24h D2-5 (Max 250 mg)*
Sepsis	Cefotaxime	50 mg/kg/dose q8-6h (Max 2 g/dose or 8 g/day)	-
	Ceftriaxone	50 mg/kg/dose q12-24h (Max 2 g/dose)	-

ALTERNATIVES FOR NEBULISING SOLUTIONS
ACUTE EXACERBATION OF BRONCHIAL ASTHMA / COAD

Prepared by PRIC Hospital Sungai Buloh

No	Nebulizing solution	Dose	Alternatives available	Dose	
				Adult	Paed
1	Salbutamol 0.5% w/v (5mg/ml)	2.5mg (0.5ml) 5mg (1ml)	Salbutamol MDI 100mcg/puff	4-12puff (maximum: q20mins for 1 hour)[1],[2]	Children 6-11 years old: 8-12puff[3] Children < 6 years: 4-6puff[3] (maximum: q20mins for 1 hour)
2	Ipratropium bromide	250mcg 500mcg	Salbutamol MDI 100mcg/puff ***OR*** Ipratropium Bromide 20mcg & Fenoterol 50mcg MDI	Salbutamol MDI*(preferred)*: 4-12 puff (maximum: q20mins for 1 hour) [1],[2] ***OR*** Ipratropium Bromide 20mcg & Fenoterol 50mcg MDI: 6 puff (maximum q20mins for 3 hours)[4,5]	*Refer to Salbutamol MDI dosing*
3	Ipratropium bromide 0.5mg & Salbutamol 2.5mg	1vial			
4	Budesonide 1mg/ml	1mg	Fluticasone MDI (125mcg/puff)	4 puff (500mcg) q15-30mins for 90mins[2]	**Moderate & Severe croup**[3,6]**:** MDI Fluticasone 125mcg 8 puffs STAT then BD Note: 1. Usage is considered **OFF LABEL USE**. Kindly fill in excel sheet: ***Farmasi>Kuota>QUOTA BY DEPT>PAEDIATRIC>KPK Off Label Application*** 2. For more details on croup management, refer next section.
			Budesonide MDI (200mcg/puff)	4 puff (800mcg) q30mins for 90-120mins[2]	

References:

1. *Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2019. Available from: ginaasthma.org*
2. *Soo, H., Lau, L., Chew, P. and Hu, M., 2011. Sarawak Handbook Of Medical Emergencies. 3rd ed. C.E. Publishing, pp.2.2-2.11.*
3. *Muhammad Ismail, H., Mohd Ibrahim, H., Ng, H. and Thomas, T., 2019. Paediatric Protocols For Malaysian Hospitals. 4th ed. Putrajaya: Kementerian Kesihatan Malaysia, pp.182-192.*
4. *Ipratropium. In: Lexi-drugs online [database on theInternet]. Hudson (OH): Lexicomp, Inc; 2020 [updated 2020]. Available from http://online.lexi.com.*
5. *Fenoterol. In: Lexi-drugs online [database on theInternet]. Hudson (OH): Lexicomp, Inc; 2020 [updated 2020]. Available from http://online.lexi.com.*
6. *The Malaysian Thoracic Society Recommendations on Inhalational Therapy During the COVID-19 Pandemic (5 April 2020)*

JABATAN FARMASI HOSPITAL SUNGAI BULOH

HOSPITAL SUNGAI BULOH

Prepared by PRIC Hospital Sungai Buloh& Nur Amiirah Rosli

Management of Viral Croup in COVID-19 Paediatric Patients

Mild Croup

Stridor with excitement or at rest, with no respiratory distress[1]

- **Dexamethasone***(Preferred)* PO/IV 0.15mg/kg STAT, then repeat if needed at 12 & 24 hours[1]

OR

- **Prednisolone** PO 1-2mg/kg STAT[1]

Moderate Croup

Stridor at rest with intercostal, subcoastal or sternal recession[1]

- **Dexamethasone** PO/IV 0.3-0.6mg/kg STAT[1]

AND / OR (if poor response)

- **MDI Fluticasone 125mcg** 8 puffs STAT then BD[1, 2]

Severe Croup

Stridor at rest with intercostal, subcoastal or sternal recession[1]

- **Dexamethasone** PO/IV 0.6mg/kg STAT

AND

- **MDI Fluticasone 125mcg** 8 puffs STAT, then 8 puffs BD[1,2]

AND

- **Oxygen and escalating ventilation support**

Note:
- Equivalent dose conversion of Nebuliser Budesonide 1mg = MDI Fluticasone (125mcg) 8 puffs[2]
- Syrup Dexamethasone can be freshly prepared from tablet

References:
1. *Muhammad Ismail, H., Mohd Ibrahim, H., Ng, H. and Thomas, T., 2019. Paediatric Protocols For Malaysian Hospitals. 4th ed. Putrajaya: Kementerian Kesihatan Malaysia, pp.196-197.*
2. The Malaysian Thoracic Society Recommendations on InhalationalTherapy During the COVID-19 Pandemic (5 April 2020).

Disclaimer: All usage of MDI Fluticasone for viral croup is considered OFF LABEL USE.
Kindly fill in the excel sheet: : ***Farmasi>Kuota>QUOTA BY DEPT> PAEDIATRIC>KPK Off Label Application***

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STEROIDS

METHYLPREDNISOLONE (IV)

Dose:

- **COVID-19 Stage 4 / 5**
  0.8 mg/kg/dose OD (Max 32 mg)
- **MISC**
  Please refer to Steroids (MISC) *[click here]*.

DEXAMETHASONE (IV / PO)

Dose:

- **COVID-19 Stage 4 / 5**
  0.15 mg/kg/dose OD (Max 6 mg) up to 5 days
- **Croup**
  Please refer to Management of Viral Croup in COVID-19 Paediatric Patients *[click here]*.

Note: Syrup Dexa can be freshly prepared from tablet

PREDNISOLONE (PO)

Dose:

- **COVID-19 Stage 4 / 5 or Asthma or Viral / Multitrigger wheeze**
  1-2 mg/kg OD (Max 40 mg) up to 5 days

STRESS ULCER PROPHYLAXIS

- Use in patients not tolerating orally while on steroids.
- Omeprazole: **IV** 1 mg/kg/dose OD / BD
  PO 0.4-0.8 mg/kg/dose OD / BD

DOSING ADJUSTMENT IN OBESE

- Methylprednisolone:
  Use **Ideal Body Weight** in kg
  Kindly reconfirm IBW with attending Dr
- Dexamethasone / Prednisolone / Omeprazole:
  Use **Actual Body Weight** in kg
  (patient's current measured weight)

Additional note:

- Use of steroids are **not routinely recommended**

Consider only when:

a) Underlying medical conditions where steroid is needed (e.g.: bronchial asthma, relapsed nephrotic syndrome etc.)

b) COVID Stage 5

c) COVID Stage 4: children who require increasing supplementary oxygen support or have risk factors for disease progression (e.g.: bronchitis, has history of ARDS)

d) Worsening lung function at least 7 days from beginning of symptoms in association with marked alteration or increasing levels of inflammatory markers

e) An additional diagnosis where steroid therapy is appropriate (e.g.: croup with COVID-19).

- Should not use in children who do not require oxygen or only low levels of oxygen (e.g. nasal cannula)

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised March 2022.

MIS-C

Multisystem Inflammatory Syndrome in Children

(Kindly refer to Annex 2e : Clinical Management Of Confirmed COVID-19 Case In Adult and Children for more information)

ANTIPLATELET / ANTICOAGULANT

Consider preventive therapy in children with:

- MIS-C
- Children with Kawasaki Disease (KD) like features or significant LV dysfunction

ENOXAPARIN S/C

VTE Prophylaxis

<2 months of age : 0.75 mg/kg BD

>2 months of age : 0.50 mg/kg BD

Adolescent (>40 kg): 40 mg OD

VTE Treatment

(in selected cases decided by specialist)

<2 months of age: 1.5 mg/kg BD

>2 months of age: 1 mg/kg BD

ASPIRIN PO

(Note: To round up dose for easy administration)

Low Dose

3 – 5 mg/kg OD

**Duration is usually based on advice from paediatric cardiologist from Hospital Serdang / IJN*

KD / KD-like features

30 – 50 mg/kg/day in divided doses

(until afebrile 2-3 days or 14 days of illness)

THEN switch to LOW DOSE

Contraindications

Active bleeding

Significant bleeding risk

Platelet count ≤ 80,000/µL

IVIG

Please refer to IVIG DRUG INFO GUIDE *[click here]*.

STEROIDS

Please refer to STEROIDS (MIS-C) *[click here]*.

STEROIDS (MIS-C)

METHYLPREDNISOLONE - Available as 500 mg Inj & 1000mg Inj

Dose & Indication

FOR IVIG REFRACTORY CONDITION

Not responding within 36 hours of IVIG completion

IV MTP 2 mg/kg/day followed by PO PREDNISOLONE (equivalent dose) and taper down over few weeks.

FOR LIFE-THREATENING / RAPID PROGRESSING MIS-C

IV MTP 10-30 mg/kg/day (Max 1000 mg/day) for 1-3 days then IV MTP 2 mg/kg/day and taper over 4-8 weeks (subject to case-to-case basis).

Note: To use IBW in obese children. Kindly reconfirm current IBW with attending Dr

Reconstitution:

500mg in 7.8 ml (*Solumedrol*) / 500mg in 8ml (*Medixon*) or 1000mg in 15.6 ml (*Solumedrol*) of benzyl alcohol in WFI (provided solvent)

Diluent: NS , D5

Dilution & Route of administration:

- **For low dose (1-2 mg/kg/dose)**
  - Dilute to concentration of 2.5-20 mg/mL
  - IV infusion over 15-30 minutes
- **For high dose (10-30 mg/kg/dose, Max 1000 mg)**
  - Dilute to concentration of 20 mg/mL
  - IV infusion over 4 hours

Note: Higher concentration and longer infusion time is to prevent overloading patients with fluid (i.e. not to exceed patient's fluid requirement / hour)

OTHER INDICATIONS (NOT FOR COVID / MISC)

Dose: 15-30 mg/kg/day (Max 1000 mg/dose) in 1-3 divided doses

Dilution & Route of administration:

- Dilute to concentration of 2.5-20 mg/mL
- IV infusion over 30 minutes to 3 hours
- For **doses ≥ 1000 mg**: infuse over **AT LEAST** 60 minutes

References for this page:
*Taketomo CK, Hodding, JH, Kraus DM. **Pediatric & Neonatal Dosage Handbook**, 22nd ed. USA: Lexi-Comp, Inc.; 2015.*
IBM Micromedex Pediatrics Ref version v72_2202031830 [accessed on 9 March 2022]
*Phelps SJ, Hagemann TM, Lee KR and Thompson AJ. **Pediatric Injectable Drugs (The Teddy Bear Book)**, 11th ed. American Society of Health-System Pharmacists, Inc.; 2018*
Solu-Medrol Product Insert (Pfizer, 29 Oct 2019)
Medixon Product Insert (PT Bernofarm, June 2016)

JABATAN FARMASI HOSPITAL SUNGAI BULOH

Ibuprofen

Available as Tablet 200mg & Syrup 20mg/mL

INDICATION

For use in Paediatric COVID patients with pericardial diseases (pericarditis / pericarditis associated with myocarditis)

DOSING RECOMMENDATIONS[1]

30-50 mg/kg/**DAY** in 3 divided doses
(max 2.4 g/**DAY**)
Start at lower end of dose range and to titrate upwards

Duration: 1-4 weeks (depending on patient's clinical progress and ECG changes)

Case is usually referred to Paediatric Cardiologist Hospital Serdang / IJN

[1]ESC Guidelines for the diagnosis and management of pericardial diseases (2015)

DOSING ADJUSTMENT IN OBESE:

Use Adjusted BW (correction factor 0.4)

AdjBW = IBW + 0.4 (TBW-IBW)

TBW : Total / measured body weight

IBW : Ideal body weight

Kindly reconfirm current TBW & IBW with attending Dr

For Pharmacists only:
Usage is considered **OFF LABEL USE**.
Kindly fill in excel sheet: ***Farmasi> Kuota> QUOTA BY DEPT> PAEDIATRIC> KPK Off Label Application***

ADDITIONAL NOTES

- **Syrup Ibuprofen 20 mg/mL**
  - Use is for dose **LESS THAN 200 MG**
- **Tablet Ibuprofen 200 mg**
  - Use for dose ≥ 200 mg
  - Can be crushed and freshly prepare as syrup (for patients who are unable to swallow tablet)
  - Adjust dose for easier administration (ensure dose is within recommended range)
    - Eg: 36 kg patient

    Dose prescribed: 360 mg TDS (30 mg/kg/DAY) → round dose to 400 mg TDS (33 mg/kg/DAY)

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised 13 March 2022.

IVIG Paediatric Dose Based on Specific Indications

HOSPITAL SUNGAI BULOH

UPDATED: DECEMBER 2022

IVIG (Intravenous Immunoglobulin)

Available as 3 g/50mL

DOSING RECOMMENDATIONS

KD-like features

2 g/kg over 8-12 hours as a single infusion

MIS-C / SEPSIS (in newborn <1 month old)

2 g/kg over 8-12 hours as a single infusion

OR

1 g/kg over 8-12 hours for 2 days

(if concerned about fluid overload)

PATIENTS WITH SIGNIFICANT LV DYSFUNCTION

(caution for fluid overload)

1 g/kg over 8-12 hours (DAY 1)

0.5 g/kg over 8-12 hours (DAY 2-3)

DOSING ADJUSTMENT IN OBESE:

Use Ideal Body Weight (IBW)

Kindly reconfirm current IBW with attending Dr

CAUTION!

Please be aware that there are different strength of IVIG available in HSgB *[click here]*.

**Number of vials needed depends on the brand to be supplied.

INFUSION RATE OF ADMINISTRATION

Please refer to Human Normal Globulin (IVIG) Paediatrics Administration Guide HSgB *[click here]*.

ADDITIONAL NOTES

- Use Ideal Body Weight (IBW) in obese paediatrics patients.
- Round up to the nearest vial strength to reduce wastage

  e.g. if using 3g/50mL for 20g dose = 6.67 vials (round up to 7 vials) if using 2.5g/50mL for 20g dose = 8 vials

Please refer to IVIG Dose Calculation *[click here]*.

For Pharmacists only:
Usage is considered **OFF LABEL USE**.
Kindly fill in excel sheet: ***Farmasi> Kuota> QUOTA BY DEPT> PAEDIATRIC> KPK Off Label Application***

Only for internal circulation (HSgB). For further enquires, kindly contact ext 03-6145 4126. Revised 15 Sept 2021.

Prepared By Pharmacy Resource Information Centre (PRIC) & Ms. Nur Amiirah Rosli
For Internal circulation only
Revised October 2021

JABATAN FARMASI HOSPITAL SUNGAI BULOH

Comparison between Human Normal Globulin (IVIG) products available in HSgB

Brand		Intragam P	Flebogamma 5% DIF	I.V. Globulin SN Inj.
Strength		6%	5%	5%
Pack size		3g/50ml	2.5g/50ml	2.5g/50ml
Content per 100ml	**IgG_1**	61%	66.6%	≥ 95% of total protein 90 – 110 % of labelled content
	IgG_2	36%	28.5%	
	IgG_3	3%	2.7%	
	IgG_4	1%	2.2%	
	IgA	<0.025mg/mL	<0.05mg/mL	< 100mcg/mL
	Excipient	10g maltose	5g D-sorbitol	10g maltose
Source		Malaysian donor	US donor	US donor
Storage Conditions		2 to 8 °C	Room temperature / 2 – 25 °C	2 to 8 °C
Stability		Once removed from refrigeration, store below 25 °C and use within 3 months	Use immediately once opened	Unopened: Stable up to 6 months at RT Once opened: Stable for 1 hour
Presentation				

IVIG DOSE BASED ON SPECIFIC INDICATIONS

INDICATION	DOSE	REMARKS
Immune Thrombocytopenic Purpura (ITP)	**General management of ITP:** 0.8g/kg as a **SINGLE** dose **Emergency Treatment of ITP:** 0.8 – 1g/kg as a SINGLE dose; in combination with IV Methylprednisolone in severe life-threatening ITP[4,6]	• One repeat dose at 24 to 48 hours may be given if response is inadequate and symptomatic thrombocytopenia recurs, provided a total dose of 2g/kg is not exceeded.[4]
Kawasaki Disease	2 g/kg over 10-12 hours as a **single infusion**[6] OR 1 g/kg over 10-12 hours for 2 days (if concerned about fluid overload)	• Consider repeat dose of IVIG in Kawasaki Disease not responding to primary treatment whereby patient has persistent fever ≥ 36hrs after completion of initial dose of IVIG.[6]
Guillain-Barré syndrome (GBS)	To be started within first 2 weeks of illness **:**[3,6] 2 g/kg total divided over 2 - 5 days[6] **(To consult Paediatric Neuromedical Specialist)**	• Second dose of IVIG can be given to those who may suffer a relapse of symptoms in the first weeks after improvement from IVIG.[6]
Autoimmune Encephalitis	2 gm/kg total divided over 2 - 5 days[6] **(To consult Paediatric Neuromedical Specialist)**	• In adjunct with IV Methylprednisolone 10mg/kg/dose 8 hourly (up to 1 g daily) for 5 days with IV/Oral Omeprazole[6]
Multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19	2 g/kg over 8-12 hours as a **single infusion**[1,2] OR 1 g/kg over 8-12 hours for **2 days** (if concerned about fluid overload) **PATIENTS WITH SIGNIFICANT LV DYSFUNCTION**[1,2] (caution for fluid overload) 1 g/kg over 8-12 hours **(DAY 1)** 0.5 g/kg over 8-12 hours **(DAY 2-3)**	
**** Dosing Adjustment in obese paediatric patients : Use Ideal Body Weight (IBW)*** **** Use with caution in patients with renal impairment***		

References

1. Annex 2e: Clinical Management of Confirmed COVID-19 Case in Adult and Children (updated August 2021). Retrieved from https//covid-19.moh.gov.my/garis-panduan/garis-panduan-kkm
2. Children's Minnesota Clinical Guideline for MIS-C Rev-6/21. Retrieved from https://www.childrensmn.org/Departments/Infectioncontrol/pdf/mis-c-clinical-guideline.pdf
3. Gullain-Barre syndrome including variants (GBS). Criteria for Clinical Use of Immunoglobulin in Australia, 30 March 2020. Retrieved from: https://www.criteria.blood.gov.au/MedicalCondition/View/2614
4. Immune thrombocytopenia (ITP) in children 15 Years and Younger. Criteria for Clinical Use of Immunoglobulin in Australia, 20 October 2018. Retrieved from: https://www.criteria.blood.gov.au/MedicalCondition/View/2574
5. Intragam P 6% Information Leaflet. Retrieved from https://www.medsafe.govt.nz/profs/Datasheet/i/IntragamPinj.pdf
6. Paediatric Protocols for Malaysian Hospitals. MOH Malaysia. 4th Edition. 2018.

Prepared By Pharmacy Resource Information Centre (PRIC) & Ms. Nur Amiirah Rosli
For Internal circulation only
Revised October 2021

Human Normal Globulin (IVIG) Paediatrics Administration Guide HSgB

IVIG DOSE CALCULATION

Step 1: Patient's dose of IVIG (g) = Planned dose (g/kg) X Weight (kg)

Step 2: Number of Vials = $\frac{Patient's\ Dose\ (g)}{Strength\ (g/50mL)}$ **(Available strength: 2.5g or 3g)**

Step 3: Total Dose of IVIG (mL) = Number of vials x 50mL

Note:
- Use Ideal Body Weight (IBW) in obese paediatrics patients.[1]
- Round up to the nearest vial strength to reduce wastage
  e.g. if using **3g/50mL** for 20g dose = 6.67 vials (round up to 7 vials)
  if using **2.5g/50mL** for 20g dose = 8 vials

ADMINISTRATION

IVIG is given **UNDILUTED.**
The rate of administration of IVIG has been standardised for **all brands**.

Step (1) Start with **0.5 mL/kg/hour**
= 0.5 mL X (patient's weight) kg/hour
= ***A*** mL/hour run over 15 minutes

Step (2) Start with **1 mL/kg/hour**
= 1 mL X (patient's weight) kg/hour
= ***B*** mL/hour run over 15 minutes

Step (3) Start with **2 mL/kg/hour**
= 2 mL X (patient's weight) kg/hour
= ***C*** mL/hour run over 15 minutes

Step (4) Start with **3 mL/kg/hour**
= 3 mL X (patient's weight) kg/hour
= ***D*** mL/hour run over 15 minutes

Step (5) If no adverse reaction, continue administration for *up to 11 hours* **<u>without exceeding maximum rate:</u>**

Balance dose (mL) = Total dose (mL) – [$\frac{A+B+C+D}{4}$ **] (mL)**

Calculate based on **MAXIMUM rate of infusion (Brand specific):**
- I.V.-Globulin SN 5% : 3.6mL/kg/hour[5]
- Intragam P 6% : 5mL/kg/hour[2,3]
- Flebogamma 5% : 6mL/kg/hour[4]

Note:
1. Ensure product is brought to room temperature or body temperature before use.

2. **Monitor vital signs** for any **allergic / adverse reactions.**

   a) In response to a **minor allergic reaction (flushes, nausea, back or abdominal pain, dizziness, headache)**, withhold IVIG infusion and treat symptomatically.
   Once patient is stable, consider IVIG administration at the previous tolerable infusion rate.[2]

   b) In response to **severe allergic reaction (anaphylaxis) with respiratory or cardiac compromise),** stop IVIG infusion immediately and implement emergency procedures for treatment of acute anaphylaxis.[2]

   c) Adverse reactions are usually dependent on the infusion rate and most commonly occur in the first hour of infusion.[2]

   All adverse reactions must be reported to <u>Pharmacy Resource Information Centre.</u>

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