East Kent Hospitals University NHS Foundation Trust

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Cardiac Cath Labs IV Cangrelor use in PCI settings

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Ratified by:	Mr Qing Sun
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Name of originator/author:	**Dr Asrar Ahmed**
Director responsible for implementation:	EKHUFT Cardiology Governance Team
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Target audience:	All clinical staff (Cardiology)

Version Control Schedule

Version	Date	Author	Status	Comment
1	10/05/2024	Dr Asrar Ahmed	Consultant	Original author
1	10/05/2024	Shirley Wilson	Cath lab I/C Nurse	Reviewed
1	16/05/2024	Qing Sun	Pharmacist	Reviewed

Consultation and Ratification Schedule

Name and Title of Individual	**Date Consulted**
Dr Asrar Ahmed (Consultant Interventional Cardiologist)	April/2024
Shirley Wilson (East Kent Cardiac Catheter Suite Ward Manager)	April/2024
Dr Michael Jenkinson (DTAG Chair)	Feb/2024
Dr Michael Jackson (Deputy Clinical Service Pharmacist)	Feb/2024
Julie Featherstone (Medicines Value Programme Lead Pharmacist)	Feb/2024

Name of Committee	**Date Reviewed**
EKHUFT Cardiology Governance Team	Jan/2024
EHUFT Drugs and Therapeutic Advisory Group	Jan/2024
EKHUFT Medicine Value Team (Pharmacy Department)	Jan/2024

Contents

1. Introduction, Background and Purpose

Cangrelor is a potent, intravenous, fast-acting and reversible antiplatelet agent. When given by intravenous infusion it achieves a rapid onset on action with platelet inhibition achieved within two minutes and maintained for the duration of the infusion. Platelet reactivity returns to normal within one hour of the infusion being discontinued.

Approximately 6% of STEMI patients suffer VT/VF arrest. (JAMA. 2009 May 6;301(17):1779-89) whereas 1:10 would present in cardiogenic shock (J Am Heart Assoc.2014; 3: e000590). The majority of these patients end up intubated prior to being administered oral antiplatelets. As a result, these patients often undergo PCI with stent implantation with no antiplatelet inhibition on board. They are loaded either during the procedure or at a later stage when insertion of a nasogastric tube is feasible. Some operators opt for Glycoprotein IIb/IIIa inhibitors; however, their long offset time increases the risk for bleeding complications.

In arrested patients, the gastrointestinal tract is often affected by ischemia and stress ulcers, making it a potential bleeding source. Hence drugs with a short half-life such as Cangrelor would be preferable to Glycoprotein Ilb/IIIa inhibitors in this patient population.

Cangrelor would also be an attractive drug for patients presenting with electrocardiograms suggestive of left main stem ischemia (such as ST elevation in aVR and global ST depression). In these patient's, urgent surgical intervention is often the preferred strategy, however the administration of oral antiplatelets (such as clopidogrel or ticagrelor) would put off surgeons from operating in the acute setting.

There is good evidence that the use of an intravenous infusion of cangrelor during PCI can reduce ischemic complications and the incidence of stent thrombosis.

The data also supports a role for cangrelor in patients presenting with STEMI undergoing primary PCI who are unable to be loaded with oral antiplatelets in advance of PCI and in particular those patients who present following an OOHVFA when oral administration of

antiplatelet agents can be significantly delayed. Although we currently have tirofiban available for these patients, there are potential advantages of using a rapidly reversible antiplatelet agent in these high-risk cases and therefore cangrelor may be a safer alternative to tirofiban.

Place in therapy

1. STEMI patients presenting with out of hospital arrest requiring intubation
2. ACS patients in cardiogenic shock due to significant reduction in gastrointestinal absorption
3. High risk ACS patients presenting with ECGs suggestive of left main disease that could potentially end up requiring surgical revascularisation

Intravenous Cangrelor co-administered with acetylsalicylic acid (ASA), is indicated for the reduction of thrombotic cardiovascular events in adult patients with coronary artery disease undergoing percutaneous coronary intervention (PCI) who have not received an oral P2Y12 inhibitor prior to the PCI procedure and in whom oral therapy with P2Y12 inhibitors is not feasible or desirable.

Cangrelor may be considered as an alternative to tirofiban in patients who are unable to take an immediate oral dose of a P2Y12 inhibitor (ticagrelor, clopidogrel or prasugrel) and/or for whom the potential for very rapid reversal of the antiplatelet effect is desirable.

<u>Cangrelor may be considered in the following situations</u>:

• STEMI patients presenting with out of hospital arrest requiring intubation.

• ACS patients in cardiogenic shock who are expected to have a significant reduction in gastrointestinal absorption.

• High risk ACS patients presenting with an ECG suggestive of left main disease that could potentially require surgical revascularisation.

2. Definitions

2.1. ACS - Acute coronary syndrome

2.2. ASA – Acetyl salicylic acid

2.3. CCU – Coronary Care Unit

2.4. ECG - Electrocardiogram

2.5. IV – Intravenous

2.6. OOHCA – Out-Of-Hospital Cardiac Arrest

2.7. OOHVFA - Out-Of-Hospital Ventricular Fibrillation Arrest

2.8. P2Y12 - Purinergic receptor P2Y, G-protein coupled, 12 protein

2.9. PCI - Percutaneous Coronary Intervention

2.10. TEMI – ST Elevation Myocardial Infarction

2.11. VF - Ventricular Fibrillation

2.12. VT - Ventricular Tachycardia

3. Scope

IV Cangrelor, co-administered with aspirin, will be initiated in cardiac cath lab at William Harvey Hospital, as an alternative P2Y12 inhibitor/antiplatelet agents when treatment with oral P2Y12 inhibitors is not feasible or desirable.

1.1. Cangrelor may be considered in the following situations:

- STEMI patients presenting with out of hospital arrest requiring intubation.
- ACS patients in cardiogenic shock who are expected to have a significant reduction in gastrointestinal absorption.
- High risk ACS patients presenting with an ECG suggestive of left main disease that could potentially require surgical revascularisation.

4. Procedure (also see appendix)

4.1. Cangrelor is provided as a 50mg vial of dry powder for reconstitution and further dilution.

4.2. Reconstitution: Reconstitute each 50mg vial with 5mL water for injection.

Swirl gently to dissolve, avoid vigorous mixing.

The resulting solution should be a clear colourless to pale yellow solution.

4.3. Dilution: Withdraw the contents from one reconstituted vial and add to 250mL of Sodium Chloride 0.9% to obtain a final concentration of 200micrograms/mL.

4.4. Standard dosage regimen for PPCI patients:

• Initial bolus dose - 30micrograms/kg given over a 1minute followed by:

• Continuous infusion at a rate of 4micrograms/kg/min for at least 2 hours or for the duration of the procedure, whichever is longer.

At the discretion of the consultant, the infusion may be continued for a total duration of 4 hours.

5. Consultation and Approval

5.1. Drugs and Therapeutic advisory group, M&M and Cardiology clinical governance meetings.

6. Review and Revision Arrangements

6.1. To be reviewed on a 2-yearly basis.

7. Training – *Industry supported training sessions* to start with and ongoing

7.1. Training provided with representative from industry on administration of IV Cangrelor and switching to oral P2Y12 inhibitors after the percutaneous coronary procedure. Staff in the cath lab, on CCU and ITU have been already trained and future ongoing training sessions will be organised.

8. Document Control including Archiving Arrangements

8.1. Cardiac cath lab at William Harvey Hospital (Shirley Wilson) and Pharmacy at William Harvey Hospital.

9. Monitoring – audit and training

9.1. Regular Audit will be set in place on appropriateness and safety of using IV Cangrelor. Ongoing training will be provided on initiating IV Cangrelor in the cath lab settings and switching to oral P2Y12 inhibitors.

10. References and Associated Documentation

10.1. Cost impact

	Total over 5 years	Average over 5 years
Patients eligible for treatment	202	40
Patients treated with cangrelor	101	20
Total costs in scenario without cangrelor	£417,771.78	£83,554.36
Total costs in scenario with cangrelor	£400,130.30	£80,026.06
Annual net budget impact (£)	-£17,641.49	-£3,528.30
Budget impact (%)	-4.22%	-4.22%

The table above is taken from the cangrelor budget impact report included with the application. This assumes uptake for suitable patients is modest in year 1 (10%) rising to 90% in year 5. It assumes current practice is to use tirofiban in patients not suitable for oral P2Y12 inhibitors in PCI procedures.

The budget impact takes into account drug acquisition costs (based on average weight patient 70kg) and the anticipated cost impact of complications and hospital activity based on comparative analysis from the literature.

The budget impact based solely on drug acquisition costs is estimated to be -£1775 (saving) per year for 40 patients treated with cangrelor vs tirofiban.

10.2. References

- Stone et al. Impact of lesion complexity on peri-procedural adverse events and the benefit of potent intravenous platelet adenosine diphosphate receptor inhibition after percutaneous coronary intervention: core laboratory analysis from10 854 patients from the CHAMPION PHOENIX trial European Heart Journal (2018) 0, 1–10 CLINICAL RESEARCH doi:10.1093/eurheartj/ehy562.
- Cavender et al. Ischemic Events Occur Early in Patients Undergoing Percutaneous Coronary Intervention and Are Reduced with Cangrelor: Findings from CHAMPION PHOENIX. Circulation Cardiovascular interventions. 2022;15(1): e010390.
- Centore et al. Intravenous antiplatelet therapy with cangrelor vs. tirofiban in patients with ST-elevation myocardial. Intravenous antiplatelet therapy with cangrelor vs. tirofiban in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention, European Heart Journal, Volume 43, Issue Supplement_2, October 2022, ehac544.2721 https://academic.oup.com/eurheartj/article/43/Supplement_2/ehac544.2721/6745580

- Yerasi et al. Cangrelor vs. glycoprotein IIb/IIIa inhibitors during percutaneous coronary intervention. American heart journal. 2021; 238:59-65.

11. Appendices

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IV Cangrelor:

Cangrelor co-administered with acetylsalicylic acid (ASA), is indicated for the reduction of thrombotic cardiovascular events in adult patients with coronary artery disease undergoing percutaneous coronary intervention (PCI) who have not received an oral P2Y12 inhibitor prior to the PCI procedure and in whom oral therapy with P2Y12 inhibitors is not feasible or desirable.

Cangrelor may be considered as an alternative to tirofiban in patients who are unable to take an immediate oral dose of a P2Y12 inhibitor (ticagrelor, clopidogrel or prasugrel) and/or for whom the potential for very rapid reversal of the antiplatelet effect is desirable.

Cangrelor may be considered in the following situations:

- **STEMI patients presenting with out of hospital arrest requiring intubation.**
- **ACS patients in cardiogenic shock who are expected to have a significant reduction in gastrointestinal absorption.**
- **High risk ACS patients presenting with an ECG suggestive of left main disease that could potentially require surgical revascularisation.**

Dose:

- Initial bolus dose – 30 micrograms/kg given over 1 minute followed immediately by:
- Continuous infusion at a rate of 4 micrograms/kg/min
- The bolus and infusion should be initiated prior to the procedure and continued for at least two hours or for the duration of the procedure, whichever is longer
- At the discretion of the consultant, the infusion may be continued for a total duration of 4 hours. Please refer to the posters in the cath lab and appendix 1 below for further dosing and administration details.

Contraindications:

Cangrelor is contraindicated in patients with:

- Active bleeding or increased risk of bleeding, because of impaired haemostasis and/or irreversible coagulation disorders or due to recent major surgery/trauma or uncontrolled severe hypertension.
- Any history of stroke or transient ischaemic attack (TIA).
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the Kengrexal SPC.

Conversion from IV Cangrelor to oral P2Y12 inhibitors (ticagrelor, clopidogrel or prasugrel):

Cangrelor has a half-life of 3-6 minutes. Platelet function is restored within 60 minutes of stopping the infusion.

- Ticagrelor – Cangrelor and ticagrelor can be administered concomitantly. Ideally a ticagrelor loading dose of 180mg should be administered one hour prior to stopping the Cangrelor infusion. If this is not feasible, ticagrelor should be administered immediately after discontinuation of the infusion.
- Clopidogrel – ***Clopidogrel should not be administered during the infusion of cangrelor as expected inhibition of clopidogrel on platelets will not be achieved.*** A clopidogrel loading dose of 600mg should be administered immediately after discontinuation of the infusion to achieve full pharmacodynamic effect.
- Prasugrel – Cangrelor and prasugrel can be administered concomitantly. Ideally a prasugrel loading dose of 60mg should be administered one hour prior to stopping the Cangrelor infusion. If this is not feasible, prasugrel should be administered immediately after discontinuation of the infusion.

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Appendix 1: Cangrelor (Kengrexal®) – Dosage and administration

Cangrelor is provided as a 50mg vial of dry powder for reconstitution and further dilution.

Reconstitution: Reconstitute each 50mg vial with 5mL water for injection. **Swirl gently to dissolve, avoid vigorous mixing**. The resulting solution should be a clear colourless to pale yellow solution.

Dilution: Withdraw the contents from one reconstituted vial and add to 250mL of Sodium Chloride 0.9% to obtain a final concentration of 200micrograms/mL.

Standard dosage regimen for PPCI patients:

- Initial bolus dose - 30micrograms/kg given over a 1minute followed by:
- Continuous infusion at a rate of 4micrograms/kg/min for at least 2 hours or for the duration of the procedure, whichever is longer. At the discretion of the consultant, the infusion may be continued for a total duration of 4 hours.

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Cangrelor (Kengrexal®) Dosing table:

Patient Weight (Kg)	Bolus Dose 30 mcg/kg for 1 minute			Maintenance Infusion Rate 4 mcg/kg/min
	Bolus (ml)		1-minute Infusion Rate (ml/hour)	Maintenance Infusion Rate (ml/hour)
38-42	6	→	360	48
43-47	7	→	420	54
48-52	7.5	→	450	60
53-57	8	→	480	66
58-62	9	→	540	72
63-67	10	→	600	78
68-72	10.5	→	630	84
73-77	11	→	660	90
78-82	12	→	720	96
83-87	13	→	780	102
88-92	13.5	→	810	108
93-97	14	→	840	114
98-102	15	→	900	120
103-107	16	→	960	126
108-112	16.5	→	990	132
113-117	17	→	1020	138
118-122	18	→	1080	144
123-127	19	→	1140	150
128-132	19.5	→	1170	156
133-137	20	→	1200	162
138-142	21	→	1260	168
143-147	22	→	1320	174
148-152	22.5	→	1350	180

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