NHS Grampian Staff Guidelines For The In-Hospital Management Of Unstable Angina And Non-ST-Segment-Elevation Myocardial Infarction Patients (17 Years And Older)

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Signature:
This document highlights the new recommendations for the initial treatment of in-hospital patients with a suspected ACS diagnosis across NHS Grampian.

Purpose/description:
This document highlights the new recommendations for the initial treatment of in-hospital patients with a suspected ACS diagnosis across NHS Grampian.

Group/Individual responsible for this document: Consultant cardiologists

Responsibility:
Responsibility for the effective management of the Acute Sector’s policy, protocol, procedure and process documentation ultimately lies with the General Manager for the Acute Sector. Delegation for formulating, disseminating and controlling these documents falls to either a named individual or a working group.
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Responsibilities for review of this document:
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1. Introduction
This document details the suggested in-hospital pharmacological management of patients within NHS Grampian who present with a working diagnosis of unstable angina (UA) or non-ST-segment-elevation myocardial infarction (NSTEMI).

1.1 Objectives
To ensure the uniform pharmacological management of patients with a working diagnosis UA/NSTEMI across the Health Board and maximise patient safety.

1.2 Clinical Situations
Patients presenting with symptoms suggestive of UA/NSTEMI, or presenting with a raised troponin result in keeping with a potential diagnosis of UA/NSTEMI.

1.3 Patient Groups To Which This Document Applies
This document applies to all patients in NHS Grampian who are 17 years of age or above and have a current working diagnosis of an UA/NSTEMI, unless any treatment is contra-indicated. See relevant Summary of Product Characteristics (SmPC) (3.2).

1.4 Patient Groups To Which This Document Does Not Apply
This document does not apply to children or those who have a contra-indication to the suggested treatments, e.g., Cr Cl < 20mL/min. See relevant SmPC (3.2).

2. In-Hospital Management Of Unstable Angina And Non-ST-Segment-Elevation Myocardial Infarction
This guideline has been developed to clarify pharmacological management of UA and NSTEMI, with particular focus on the role of ticagrelor and fondaparinux, and it is applicable to all medical and surgical wards across NHS Grampian.

If a diagnosis of UA/NSTEMI is suspected standard in-hospital treatment is immediate administration of dual antiplatelet therapy (aspirin plus ticagrelor) and anticoagulant therapy (low molecular weight heparin or fondaparinux).

Fondaparinux$^a$ is recommended in the current SIGN (3.3), NICE (3.4) and European Society of Cardiology (3.5) guidelines, and is associated with a lower risk of bleeding than low molecular weight heparins (3.6). It also has a simpler dosing regimen, 2.5mg given once daily regardless of the patient’s weight.

It is now recommended that after a coronary event (i.e. NSTEMI/STEMI) patients should receive 12 months of dual antiplatelet therapy (3.3), although there may be clinical reasons why a shorter duration is recommended (on the advice of a consultant cardiologist).

STEMI patients are not covered by this guideline and should be referred to the Coronary Care Unit (CCU) Decision Support or the cardiac cath lab for consideration of primary percutaneous coronary intervention (PCI). If thrombolysis is appropriate to be

$^a$ See Appendix 1 for more information about fondaparinux.
administered (after discussion with a cardiologist) then dalteparin (NOT fondaparinux) should be used in these patients (please contact CCU for thrombolysis and dalteparin administration guidance).

The European Society of Cardiology Guideline for Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation (Management of) 2011 recommends that ticagrelor be used in preference to clopidogrel (3.5).

Ticagrelor belongs to a novel chemical class, cyclopentyltriazolopyrimidine, and is an oral, reversibly binding P2Y₁₂ adenosine diphosphate receptor antagonist with a plasma half-life of 12 hours. Ticagrelor has a more rapid and consistent onset of action compared with clopidogrel, but additionally it has a quicker offset of action so that recovery of platelet function is faster (3.5).

Further information on antiplatelet agents may be found in the NHS Grampian Guidance on the use of Antiplatelets.

2.1 Pharmacological management of UA/NSTEMI patients not suitable for urgent PCI (PCI < 120 mins) or CABG within 24hours

Day 1 - At initial presentation (unless contraindicated*):
Aspirin 300mg once only (do NOT give if already administered in community) and ticagrelor 180mg once only loading dose, followed by ticagrelor 90mg twice daily. The second dose of ticagrelor (90mg) should be administered 6 to 18 hours after the loading dose.
and IF PATIENT NOT FOR URGENT PCI (PCI < 120mins) OR CABG within 24hours:
Fondaparinux 2.5mg subcutaneously (s/c) single dose**.

From Day 2 (unless contraindicated*):
Aspirin 75mg once daily to be continued indefinitely
Ticagrelor 90mg twice daily to continue for 1 year
Fondaparinux 2.5mg s/c once daily** at 6pm should be continued for up to a maximum of 8 days. Please note: fondaparinux should usually be stopped after successful revascularisation (PCI) unless otherwise directed by cardiology consultant.

*If a patient has a true hypersensitivity to aspirin, ticagrelor or fondaparinux, they should be discussed with the cardiologist on call. Other treatment should be administered as above.
**Note patients with body weight < 50kg are at increased risk of bleeding.

It should be noted that currently national advice requires that the ambulance paramedics administer 300mg of clopidogrel and 300mg of aspirin. These patients would then subsequently have to be loaded with ticagrelor on admission to hospital. The data from the PLATO study suggests that patients already loaded with clopidogrel are not at a higher risk of major and minor bleeding events if they then receive ticagrelor, compared to a patient who doesn't receive open label clopidogrel (3.8).

Consideration of secondary prevention:
Simvastatin 40mg at night.
Bisoprolol started at 2.5mg once daily and titrated as tolerated (see BNF) up to usual maximum dose of 10mg daily.
Ramipril started at 1.25mg twice daily and titrated as tolerated (see BNF) up to a maximum of 10mg daily (usually as 5mg twice daily).
For further information see References and Appendices.

3. References
3.1 Management of Patients in the Coronary Care Unit in Aberdeen Royal Infirmary [intranet].
3.2 SmPC for fondaparinux and ticagrelor – see http://www.medicines.org.uk
3.3 SIGN 93 (http://www.sign.ac.uk/pdf/sign93.pdf).
3.4 NICE CG 94 (http://www.nice.org.uk/nicemedia/live/12949/47921/47921.pdf)
3.7 Policies from NHS Lothian for the use of fondaparinux and the management of ACS.

4. Distribution list
All hospital consultants, nurse managers, clinical pharmacists, lead for non-medical prescribers, community hospital prescribers.
Appendix 1: Fondaparinux 2.5mg/0.5mL solution for injection.  
Also see SmPC - http://www.medicines.org.uk/emc/medicine/15123/SPC/  
Pre-filled syringe containing 2.5mg (0.5mL) of fondaparinux sodium.

Indication: Treatment of unstable angina or non-ST segment elevation myocardial infarction (NSTEMI) in patients for whom urgent (<120 mins) invasive management (PCI) is not indicated.

Recommended dosage for adults:  
2.5mg subcutaneously once daily at 6pm.  
This should be discontinued if 12-hour troponin comes back negative.

Contraindications:  
• Patient attending the cardiac catheterisation laboratory for urgent PCI.  
• Patients with CrCl < 20mL/min. In these patients intravenous heparin infusion (25,000units in 50mLs) should be used and adjusted according to the APTTr.  
• Hypersensitivity to fondaparinux or any excipients.  
• The needle shield of the pre-filled syringe may contain dry natural latex rubber that has the potential to cause allergic reactions in latex sensitive individuals.  
• NSTEMI patients to undergo CAGB within 24 hours.  
• Patients under the age of 17 years.  
• Active signs of bleeding.  
• Pregnancy.  
• Lactation.

Cautions:  
• Severe hepatic impairment.  
• Patients with body weight < 50kg are at increased risk of bleeding.  
• Patients with a history of heparin induced thrombocytopenia (HIT).  
• Elderly patients (increased bleeding risk).  
• Patients with an increased risk of haemorrhage.  
• Patients being treated concomitantly with any agents that may increase risk of haemorrhage (e.g. glycoprotein IIa/IIIb inhibitors or thrombolytics).

Administration:  
Do not expel the air bubble prior to administration. Administer subcutaneously and ensure that the whole length of the needle is inserted perpendicularly into a skin fold between the thumb and forefinger.

Length of treatment:  
Discontinue fondaparinux following successful revascularisation, at discharge or after 8 days whichever is sooner.

Side Effects:  
• Bleeding (patient should be monitored for signs of bleeding).  
• Increase in hepatic enzymes.  
• Rash.  
• Pruritis.  
• Hypokalaemia.  
• GI effects including nausea, vomiting, diarrhoea, constipation, abdominal pain.

Additional notes:  
Contains less than 1mmol sodium per dose.  
Not for intramuscular injection.
Appendix 2: Flowchart: In-hospital management of UA/NSTEMI

Day 1 - Patient with suspected UA/NSTEMI
(all medicines recommended assuming NO contraindications or hypersensitivities)

At initial presentation:
- Aspirin 300mg once only (do not give if already administered in community)
- Ticagrelor 180mg once only.

Suitable for urgent PCI?

- YES
  - Urgent PCI

- NO

Suitable for CABG within 24hours?

- YES
  - CABG

- NO

Day 2

- Aspirin 75mg once daily and continue indefinitely.
- Ticagrelor 90mg twice daily for 1 year. The second dose of ticagrelor (90mg) should be administered 6 to 18 hours after the loading dose
- Fondaparinux 2.5mg s/c once daily at 6pm** should be continued for up to a maximum of 8 days; discontinue at discharge, after PCI (unless otherwise directed) or after 8 days whichever is sooner.

Consideration of secondary prevention:
- Simvastatin 40mg at night.
- Bisoprolol started at 2.5mg once daily and titrated as tolerated (see BNF) up to usual maximum dose of 10mg daily.
- Ramipril started at 1.25mg twice daily and titrated as tolerated (see BNF) up to a maximum of 10mg daily (usually as 5mg twice daily).

** see SmPC – Patients with body weight < 50kg are at increased risk of bleeding.