Guidance for prescribing Ticagrelor to treat Acute Coronary Syndromes (ACS)

1. BACKGROUND

Ticagrelor is a potent antiplatelet agent licensed for use in combination with aspirin to reduce the risk of further cardiovascular events in patients presenting with acute coronary syndrome (ACS).
NICE clinical guideline 172 (November 2013) recommends ticagrelor in combination with low-dose aspirin for up to 12 months as a treatment option in adults with acute coronary syndrome (ACS).

2. INDICATIONS

Ticagrelor should be considered for patients with:

- A new STEMI treated with primary PCI or thrombolytic therapy
- A confirmed diagnosis of NSTEMI irrespective of any revascularisation strategy.

3. DOSE

- STEMI: loading dose of ticagrelor 180mg STAT followed by **-**
  Ticagrelor 90mg TWICE a DAY for up to 12 months in combination with **aspirin 75mg once a day lifelong**
- ACS (except STEMI): load with clopidogrel 300mg STAT followed by 75mg once a day, plus aspirin 75mg once a day.
  When diagnosis of NSTEMI has been confirmed with a positive troponin result, load with ticagrelor 180mg STAT followed by
  Ticagrelor 90mg TWICE a DAY for up to 12 months in combination with **aspirin 75mg once a day lifelong**

  Ticagrelor 90mg twice a day should be stopped when clinically indicated or at 12 months.

  (Ticagrelor 90mg orodispersible tablets are now available)

4. DRUG INTERACTIONS

Ticagrelor is primarily a CYP3A4 substrate and a mild inhibitor of CYP4A4, also a P-glycoprotein (P-gp) substrate and a weak P-glycoprotein inhibitor and may increase the exposure of P-glycoprotein substrates.

Selected drug interactions (See BNF/SPC for a full up to date list)

Drug Interactions	
Strong CYP3A4 inhibitors: Ketoconazole, clarithromycin, nefazodone, ritonavir and atazanavir	Contra-indicated – significant increase in ticagrelor levels
Moderate CYP3A4 inhibitors: Erythromycin, fluconazole, diltiazem	Caution – increase or possible increase in ticagrelor levels
NSAID's and SSRI's	Caution - may increase the risk of bleeding
CYP3A inducers: Rifampicin, phenytoin, carbamazepine and phenytoin	Discourage – may lead to a decrease in exposure and efficacy of ticagrelor
P-glycoprotein and CYP3A inhibitors: Cyclosporin, verapamil and quinidine	May increase ticagrelor exposure
P-glycoprotein substrates: Digoxin	Levels maybe increased – monitor plasma levels advised
CYP3A4 substrates with narrow therapeutic index: i.e. ergot alkaloids	Not recommended – ticagrelor may increase the levels of ergot alkaloids
Drugs metabolised by CYP3A4: Simvastatin	Greater than 40mg is not recommended
Warfarin and new oral anticoagulant agents	Co-prescribing with ticagrelor increases the risk of bleeding – use with caution or avoid

5. CONTRAINDICATIONS AND CAUTIONS

Contra-indications: Ticagrelor is contra-indicated in the following situations:

- Active pathological bleeding
- History of intracranial haemorrhage
- Moderate to severe hepatic impairment
- Co-administration of ticagrelor with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir), as co-administration may lead to a substantial increase in exposure to ticagrelor.
- Hypersensitivity to the active substance or to any of the excipients

Cautions: Ticagrelor should be used with caution in the following patient groups: -

- Increased risk of bleeding
- Patients with a tendency to bleed (e.g. due to trauma, recent surgery, coagulation disorders, active or recent GI bleeding)
- Patients on concomitant administration of medications that may increase the risk of bleeding (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants,
- Antifibrinolytic therapy (tranexamic acid) and/or recombinant factor VIIa therapy may increase haemostasis. Ticagrelor may be resumed after the cause of bleeding has been identified and controlled.
- Elective surgery – discontinue ticagrelor 7 days prior to surgery
- Prior ischaemic stroke – ACS patients can be treated for up to 12 months (can use clopidogrel monotherapy after 12 months rather than aspirin monotherapy)
- Patients at risk of bradycardia
- Asthma/COPD: If a patient, particularly those with pre-existing asthma/COPD reports new, prolonged or worsened dyspnoea this should be investigated fully and if not tolerated, treatment with ticagrelor should be stopped and replaced with an alternative agent (clopidogrel, prasugrel).
- Renal impairment: Creatinine levels may increase during treatment with ticagrelor. Renal function should be checked at baseline, after one month and then as clinically indicated, paying special attention to patients ≥75 years, patients with moderate/severe renal impairment and those receiving concomitant treatment with an ACEI or ARB
- Ticagrelor may increase the risk of hyperuricaemia. Caution is advised in patients with history of hyperuricaemia or gouty arthritis. Ticagrelor is not recommended in patients with uric acid nephropathy.
- Co-administration of ticagrelor with high maintenance dose aspirin >300mg is not recommended
- Premature discontinuation should be avoided could result in an increased risk of cardiovascular death or MI
- Pregnancy and breastfeeding

6. ADVERSE EFFECTS

The most commonly reported adverse reactions (≥ 1/10) are blood disorder bleedings, hyperuricaemia, and dyspnoea

7. INFORMATION TO PATIENT

Patients should be advised on common side-effects

- Bruising
- Dyspnoea

All patients should be counselled on the duration of treatment: Avoid NSAIDs as increased bleeding risk
Patients should be advised to inform physician and dentists that they are taking ticagrelor before any surgery is scheduled and before any new medications is taken
Ticagrelor has no specific storage requirements and is suitable for compliance aids

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

APPROVAL PROCESS

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Approved by:	**MMIG, HERPC Nov 2014**
Updated by:	**HERPC May 2018**
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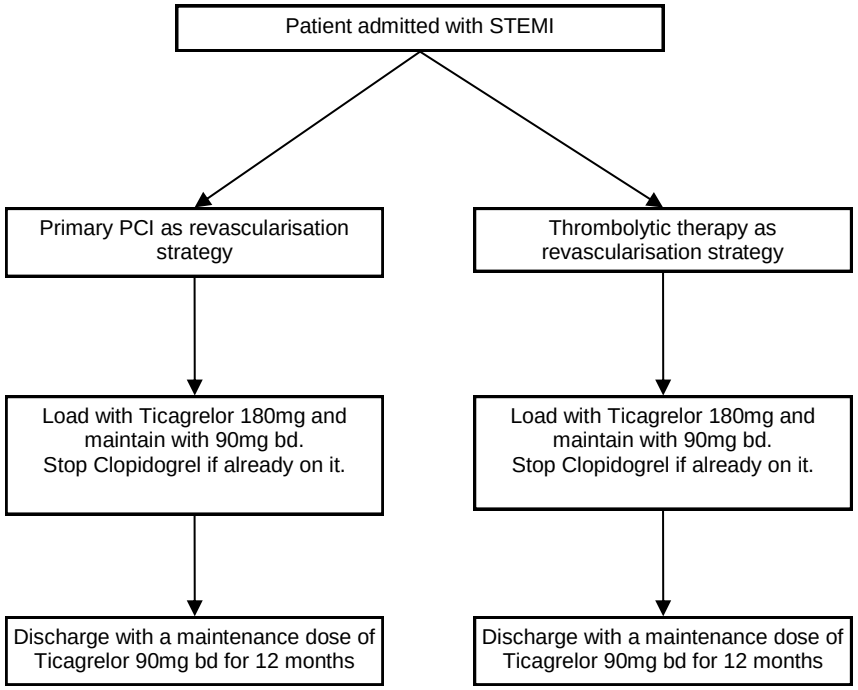
Use of Ticagrelor in patients with ST Elevation MI (STEMI)

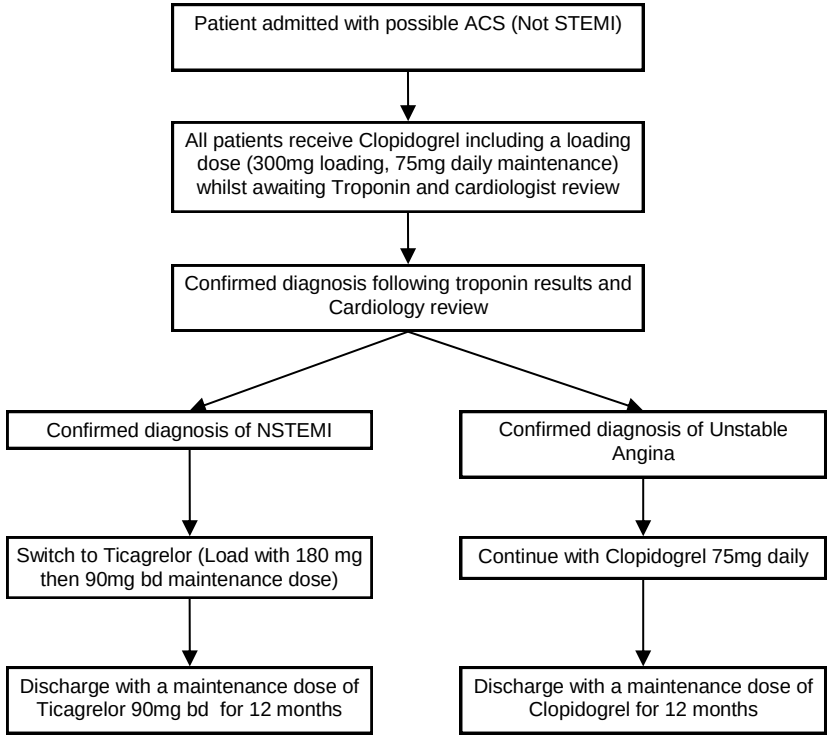


NB Ticagrelor should be given to this patient group regardless of any revascularisation strategy. The usual strategy of ceasing anti-platelet therapy 7 days prior to CABG still applies. Ticagrelor should be given for 12 months post CABG.

For patients who are intolerant of Ticagrelor,- clopidogrel or prasugrel should be considered.
Ticagrelor is available as an orodispersible preparation

This flowchart should be used alongside the product prescribing information.

Use of Ticagrelor in patients with possible Acute Coronary Syndrome (ACS)



NB

- All patients with a confirmed diagnosis of NSTEMI should receive Ticagrelor, unless contra-indicated.
- The initiation of Ticagrelor for NSTEMI patients should be restricted to Cardiologists therefore cardiologist review should be facilitated.
- Ticagrelor should be given to this patient group regardless of any revascularisation strategy. The usual strategy of ceasing anti-platelet therapy 7 days prior to CABG still applies.
- Ticagrelor should be given for 12 months post CABG.
- For patients who are intolerant of Ticagrelor, Clopidogrel should be considered.

This flowchart should be used alongside the product prescribing information.