AMBER GUIDANCE FOR TICAGRELOR 90MG 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. Indication

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/Duration

- 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 earlier when clinically indicated or at 12 months.

  (Ticagrelor 90mg orodispersible tablets are now available)

  For information on 60mg dosing please refer to separate guidance.

4. Contraindications

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 (consider gastro protection in groups at increased risk)
- 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

5. Adverse effects

Adverse effects (≥ 1/10)	Action for GP
Hyperuricaemia	No specific guidance, encourage patients to maintain adequate hydration. Consider monitoring uric acid levels if indicated.
Dyspnoea	Normally mild to moderate in intensity and resolves without treatment discontinuation. If not resolving seek advice from cardiology.

6. Drug interactions

The following drugs are known or suspected interactions:	
Interacting Drug	Advice
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
CYP3A4 inducers: Rifampicin, phenytoin, carbamazepine and phenytoin	Discourage – may lead to a decrease in exposure and efficacy of ticagrelor
P-glycoprotein and CYP3A4 inhibitors: Ciclosporin, 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. Ticagrelor increases plasma concentration of dabigatran

7. Pregnancy and Lactation

Manufacturer advises to avoid use in pregnancy and lactation.

8. Information for 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

Document and version control	**This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.**		
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1	Yvonne Holloway	Principal pharmacist	Adapted from HERPC guidance