Guidance for prescribing ticagrelor to treat acute coronary syndromes (ACS) in the West Yorkshire Cardiovascular Network (adopted by the Leeds Health Economy)

Background
Ticagrelor has been approved for the treatment of ACS by the NICE TA 236 (October 2011). The West Yorkshire Cardiovascular Network has developed pathways to implement the NICE guidance in patients diagnosed with STEMI or NSTEMI (see overleaf).

Selection of Patients
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.

Dose
- STEMI: loading dose of ticagrelor 180mg stat followed by 90mg bd for 12 months, plus aspirin 75mg od lifelong
- ACS (except STEMI): load with clopidogrel 300mg stat followed by 75mg od, plus aspirin 75mg od. When diagnosis of NSTEMI has been confirmed with a positive troponin result, load with ticagrelor 180mg stat followed by 90mg bd for 12 months, plus aspirin 75mg od lifelong.

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)
- Hypersensitivity to the active substance or to any of the excipients

Cautions
Ticagrelor should be used with caution in the following patient groups:-
- Increased bleeding risk, for example clinically important thrombocytopenia or anaemia, gastrointestinal bleed within the past 6 months or major surgery within the past 30 days. These groups were excluded from PLATO and so ticagrelor should be used with consideration of the balance of the risks and the expected benefit to the patient.
- Patients with concomitant administration of medicinal products that may increase the risk of bleeding (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants, or fibrinolytics) within 24 hours of ticagrelor dosing.
- 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 clopidogrel or prasugrel.
- Renal impairment: Creatinine levels may increase during treatment with ticagrelor. Renal function should be checked at baseline and after one month and six months, paying special attention to patients ≥75 years, patients with moderate/severe renal impairment and those receiving concomitant treatment with an ARB.

Commonly Used Interacting Drugs (See SPC for a full list of drug interactions)
- Clarithromycin - contra-indicated.
- Ketoconazole - contra-indicated.
- Nefazodone - contra-indicated
- Ritonavir and atazanavir - contra-indicated
- Dexamethasone, phenytoin, carbamazepine and phenobarbital can reduce the efficacy of ticagrelor. Consider clopidogrel or prasugrel as an alternative.
- Verapamil, quinidine, and cyclosporine may increase ticagrelor exposure. Consider clopidogrel or prasugrel as an alternative.

Written by: Andrew Whitehead, Lead Cardiology Pharmacist, Leeds Teaching Hospitals
Dr. Dan Blackman, Consultant Cardiologist, Leeds Teaching Hospitals
Dr. Stephen Wheatcroft, Consultant Cardiologist, Leeds Teaching Hospitals

Approval date: December 2011
Review date: December 2013
Patient admitted with STEMI

Use of Ticagrelor in patients with ST Elevation MI (STEMI)

Primary PCI as revascularisation strategy
- Load with Ticagrelor 180mg and maintain with 90mg bd. Stop Clopidogrel if already on it.
- Discharge with a maintenance dose of Ticagrelor 90mg bd for 12 months

Thrombolytic therapy as revascularisation strategy
- Load with Ticagrelor 180mg and maintain with 90mg bd. Stop Clopidogrel if already on it.
- Discharge with a maintenance dose of Ticagrelor 90mg bd for 12 months

Stop Clopidogrel if already on it.

Discharge with a maintenance dose of Ticagrelor 90mg bd for 12 months

NB  Ticagrelor should be given to this patient group regardless of any revascularisation strategy, 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, Prasugrel should be considered first, clopidogrel second in the STEMI patient group.

This flowchart should be used alongside the product prescribing information.

Patient admitted with possible ACS (Not STEMI)

All patients receive Clopidogrel including a loading dose (300mg loading, 75mg daily maintenance) whilst awaiting Troponin and cardiologist review

Confirmed diagnosis following troponin results and Cardiology review

Confirmed diagnosis of NSTEMI
- Switch to Ticagrelor (Load with 180 mg then 90mg bd maintenance dose)
- Discharge with a maintenance dose of Ticagrelor 90mg bd for 12 months

Confirmed diagnosis of Unstable Angina
- Continue with Clopidogrel 75mg daily
- Discharge with a maintenance dose of Clopidogrel for 12 months

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

This flowchart should be used alongside the product prescribing information.