Prescribing ticagrelor in acute coronary syndromes

This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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).

In South London, ticagrelor is recommended for use in:

- **Patients presenting with an ST-elevation MI (STEMI) undergoing primary percutaneous coronary intervention (PCI)**
- **Patients presenting with a non-ST-elevation MI (non-STEMI) who are considered at 'high risk'* and therefore need urgent PCI**

*'High risk' NSTEMI is defined as those patients with on-going or recurrent chest pain / discomfort believed to be of cardiac origin, together with at least one of the following:

- Persistent ECG changes of ST depression > 1mm, or transient ST elevation
- Pathological T wave inversion in V1-V4 suggesting an 'LAD syndrome'
- Dynamic T wave inversion >2mm in two or more contiguous leads
- Haemodynamic instability (hypotension, pulmonary oedema or heart failure) or electrical instability (sustained ventricular arrhythmias – VT/VF) which are thought to be due to cardiac ischaemia
- Troponin ≥0.1mcg/L

Ticagrelor should only be initiated in secondary care, usually by a consultant cardiologist.

Ticagrelor is not licensed for primary prevention or secondary prevention of stable cardiovascular (CV) disease and there is no evidence to support its use as monotherapy. Ticagrelor should not be initiated by primary care.

Contra-indications	Cautions
– Hypersensitivity to the active substance or to any of the excipients – 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) – Pregnancy and breast-feeding	– Patients with a propensity to bleed (e.g. due to recent trauma, recent surgery, coagulation disorders, active or recent gastrointestinal bleeding) – Concomitant administration of medicinal products that may increase the risk of bleeding (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants and/or fibrinolytics) – Patients with or at risk of bradycardia (see side effects) – Patients with asthma or COPD (see side effects) – Patients on renal dialysis – Use in patients with uric acid nephropathy is discouraged – Women of child-bearing age should use appropriate contraceptive measures whilst taking ticagrelor

Dosing

- **Initiation:** A loading dose of 180mg should be given as early as possible after ACS presentation
- **Maintenance dose:** Ticagrelor should be continued at a dose of 90mg twice daily for a period of 12 months. Patients prescribed ticagrelor should also be taking aspirin at a dose of 75mg daily which should continue lifelong (higher aspirin doses are not recommended due to increased risk of bleeding)

Ticagrelor should be initiated by the hospital team with on-going supplies to be obtained from the GP (a minimum 14 day supply should be provided at discharge to ensure continuity of supply into primary care).

Ticagrelor therapy should not be discontinued prematurely without cardiology advice

Monitoring

Renal Function: Creatinine levels may increase after initiation of ticagrelor. Secondary care must ensure a baseline eGFR is communicated on the discharge summary to facilitate on-going monitoring. Renal function should be checked by the patients own GP after one month and thereafter according to routine medical practice, paying special attention to patients ≥75 years, patients with moderate/severe renal impairment and those receiving concomitant treatment with an ARB (e.g. losartan, candesartan).

Side effects (for full details see the BNF or Summary of Product Characteristics (SPC))
The most commonly reported adverse reactions are dyspnoea, subcutaneous or dermal bleeding and epistaxis. Procedural site haemorrhage is also reported commonly. In the PLATO study the following bleeding episodes were seen uncommonly: intracranial haemorrhage, GI bleeding, haemoptysis and haematemesis, urinary and vaginal bleeding. GI side effects also included nausea, vomiting, diarrhoea and abdominal pain.

Dyspnoea: in the PLATO study, 11.8% of patients reported dyspnoea with ticagrelor, and approximately 1% withdrew from ticagrelor as a result. Most reported symptoms of dyspnoea were mild to moderate, and most were reported as a single episode early after starting treatment. Dyspnoea usually resolves within 7 days. Patients with asthma or COPD may be at increased risk.

Advice for GPs

1. Do not stop ticagrelor prematurely without discussion with a cardiologist (if urgent - via the on-call cardiology registrar). Premature discontinuation is associated with a very high risk of cardiovascular events. If the patient is experiencing significant adverse effects, seek advice from the initiating team to discuss suitable alternatives.
2. Check renal function one month after initiation – if there is a greater than 20% increase in serum creatinine (or 15% decline in eGFR) over pre-procedural baseline – seek advice from the initiating team (if urgent - via the on-call cardiology registrar).
3. When prescribing for patients on ticagrelor therapy, consider potential drug interactions (see BNF / SPC). The use of macrolide antibiotics, such as clarithromycin, erythromycin and azithromycin, should be avoided during ticagrelor treatment.
4. Concomitant use of NSAIDS and /or SSRIs will increase bleeding risk.
5. Mild to moderate dyspnoea can occur, particularly in the first 7 days of treatment. Dyspnoea is usually transient, but if it is persistent or severe, seek advice from the initiating team. Patients with asthma or COPD are at increased risk of dyspnoea.
6. Other side effects: see overleaf or BNF / SPC for more comprehensive details.
7. Ticagrelor is a black triangle drug and therefore all adverse effects should be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) using the yellow card system, even if well documented.
8. Please ensure that a 'stop date' at one year is entered onto the practice computer system (alerts). It is also recommended that the 'stop date' is added to the prescription dosing instructions (for inclusion on the dispensing label) and to the patient-held antiplatelet card.
9. Ensure aspirin is continued lifelong when the ticagrelor is discontinued at one year.

References

1. NICE guidance TA236 Acute Coronary Syndromes – Ticagrelor: guidance. Oct 2011
2. Brilique (ticagrelor) SPC 2011; Astra-Zeneca. Accessed at www.medicines.org.uk/emc/medicine/23935/SPC/brilique%2090%20mg%20film%20coated%20tablets/ 13th Feb 2012.
3. London Cardiovascular Project (LCVP) Defining High Risk NSTEACS, London Cardiac and Stroke Networks May 2011 www.slcsn.nhs.uk/lcv/card/nsteacs-high-risk-definition-0511.pdf
4. Wallentin L et al (2009) Ticagrelor versus Clopidogrel in Patients with Acute Coronary syndrome. NEJM 2009: 361:1045-1057