Information Summary on Ticagrelor (Brilique®▼) Update 2019

Ticagrelor is an antiplatelet drug, which reversibly inhibits adenosine triphosphate mediated platelet activation and aggregation. The mechanism is similar to that of clopidogrel and prasugrel, although both of these drugs have in irreversible effect on platelet aggregation, and ticagrelor has a faster onset and shorter duration of action.

Ticagrelor is licensed for use in combination with low dose aspirin for the secondary prevention of ACS (STEMI, NSTEMI, unstable angina), including patients managed medically, with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).[1]

Ticagrelor for the treatment of acute coronary syndromes (NICE TA 236)[2]

NICE advises that ticagrelor 90mg bd, may be used in combination with aspirin for a duration of up to 12 months as a treatment option in adults with ACS. Ticagrelor is substantially more expensive than clopidogrel and therefore it would be advisable to have robust procedures in place to ensure that ticagrelor therapy is stopped following the 12 month treatment period.

The main evidence base for ticagrelor is the 12 month long PLATO study (n = 18,624). Ticagrelor consistently demonstrated a reduction in MI and cardiovascular death in addition to overall death when compared to clopidogrel, for the management of STEMI and NSTEMI patients, including those undergoing planned invasive management. In addition, there is a comparable bleeding rate overall with both treatments. Ticagrelor also demonstrated a higher response rate than clopidogrel, and may be useful in clopidogrel non-responders.

Ticagrelor for preventing atherothrombotic events after myocardial infarction (NICE TA420)[3]

NICE published a technology appraisal of ticagrelor post MI in December 2016. This guidance describes the place of ticagrelor post MI:

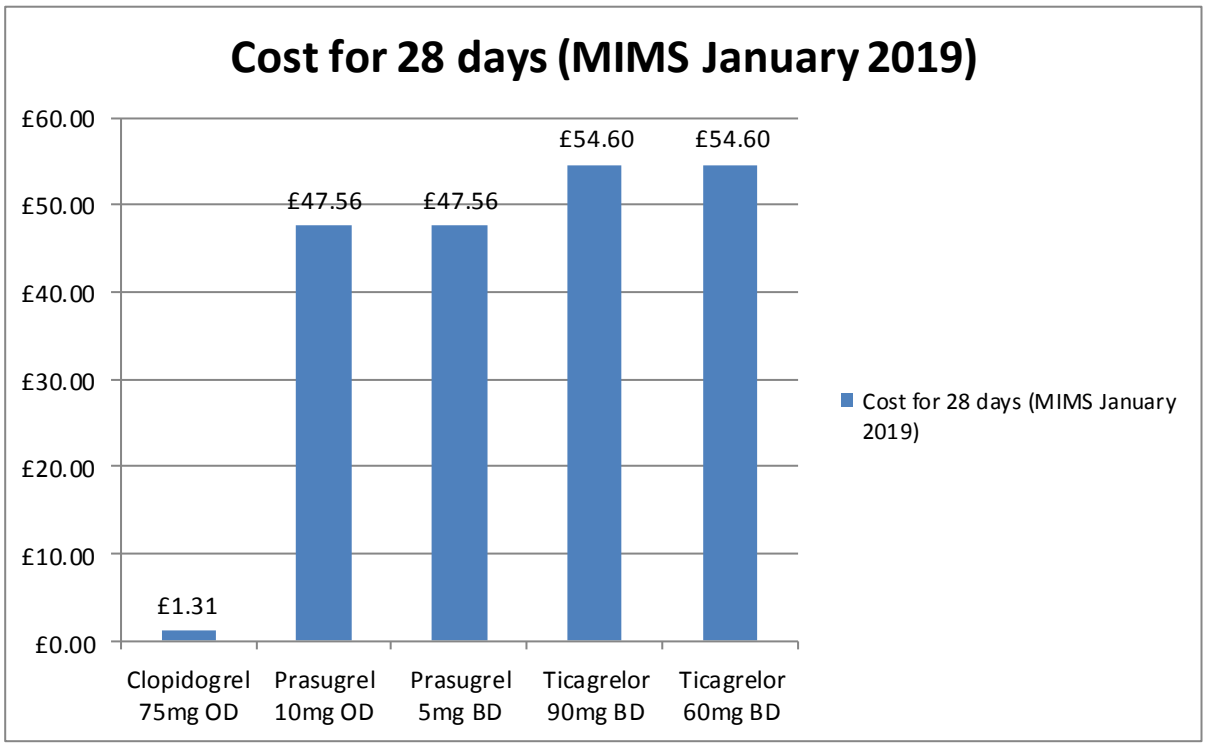
- A dose of 60mg bd is indicated in patients who are at high risk (see below) of atherothrombotic events and:
    - Have a history of an MI of at least 1 year (for the first 12 months post ACS ticagrelor 90mg bd should be prescribed)
    - Should be started straight after 1 year of ticagrelor 90mg bd **OR** up to 2 years from MI (i.e. within 1 year of stopping ticagrelor 90mg bd) **OR** in patients who had an MI more than 2 years ago and stopped taking antiplatelet therapy no more than 1 year ago
    - Should be given with aspirin 75mg-150mg od
    - Should be stopped when clinically indicated (in the event of bleeding complication or if ticagrelor is deemed to be contributing to dyspnoea or bradycardia), or at a maximum of 3 years of extended treatment

Ticagrelor is licensed to be given for 1 year post acute MI at 90mg BD **plus** up to an additional 3 years at 60mg BD (i.e. total duration of treatment = 4 years).

Risk of atherothrombotic events

The PEGASUS-TIMI 54 trial formed the basis of the submission to NICE. In this trial, patients had a history of MI (occurring between 12 and 36 months before entry) and had at least one of the following additional risk factors (also known as DRAMA criteria):

- Diabetes mellitus needing medication
- Renal dysfunction (Chronic non-end-stage; creatinine clearance<60ml/min)
- Age 65 or over
- Multi-vessel coronary artery disease
- Additional prior MI



Precautions for use

According to the manufacturer's information, Ticagrelor is contraindicated in the following:

- Patients with a history of intracranial bleeding
- Patients with moderate to severe hepatic impairment

Ticagrelor should also be used with caution in the following circumstances:

- Increased risk for major bleeding, such as GI bleed within the last 6 months, major surgery within the last 30 days, clinically significant thrombocytopenia or anaemia, previous intracranial bleed. Bleeding risk should be weighed against thrombosis risk on an individual patient basis.
- Patients undergoing surgery. If a patient is to undergo elective surgery, the manufacturer recommends stopping the ticagrelor 7 days before the surgery date.
- Patients at risk of bradycardia, or taking medications which may induce bradycardia.
- Patients at risk of dyspnoea, such as those with pre-existing asthma or COPD as they may be more susceptible to dyspnoea as a side effect of ticagrelor.
- Patients with moderate to severe renal impairment.

- Patients with pre-existing gout and hyperuricaemia

It is recommended that serum creatinine levels are checked after 1 month of treatment with ticagrelor.

The manufacturer's information states that ticagrelor is contraindicated when administered concomitantly with strong inhibitors of CYP3A4 (such as ketoconazole, clarithromycin, ritonavir and atazanavir), as such use may substantially increase exposure to ticagrelor.

Caution is also advised when used in combination with strong CYP3A4 inducers (such as rifampicin, phenytoin and Phenobarbital) as this may reduce exposure to ticagrelor leading to treatment failure, and with substrates of P-glycoprotein (such as verapamil) as the combination may be associated with increased incidence of side effects.
Further information can be found in the current BNF or in the manufacturer's information online at www.medicines.org.uk/EMC/medicine/23935/SPC/Brilique+90+mg+film+coated+tablets/

References:

1. Summary of product characteristics (SmPC) for Brilique, accessed online via
2. NICE TA 236 – Ticagrelor for the treatment of acute coronary syndromes (ACS) October 2011. Accessed online at www.nice.org.uk
3. NICE TA 420 - Ticagrelor for preventing atherothrombotic events after myocardial infarction. https://www.nice.org.uk/guidance/ta420
4. Scottish Medicines Consortium appraisal document on ticagrelor (Brilique) April 2011 (SMC 699/11). Accessed online at www.scottishmedicines.org.uk
5. MTRAC commissioning guidance for Ticagrelor May 2011. Accessed online at www.mtrac.co.uk
6. MIMS, accessed online at www.mims.co.uk
7. NICE Medicines Evidence Commentary: Non-ST-elevation acute coronary syndrome (NSTE-ACS): antiplatelets September 2015. Accessed online via www.evidence.nhs.uk

This document was originally approved by Barnsley Area Prescribing Committee 10th May 2017; the update was approved on 6th February 2019