

Shared Care Guidance

Ticagrelor for the Treatment of Acute Coronary Syndromes and Prevention of Atherothrombotic Events post-Myocardial Infarction

This shared care agreement outlines the way in which the responsibilities for managing the prescribing of ticagrelor tablets can be shared between the Secondary Care Specialist and the General Practitioner.

The National Institute for Health and Care Excellence (NICE) recommends:

- ticagrelor combined with low-dose aspirin for up to a year as a possible treatment for some people with acute coronary syndromes⁽¹⁾
- ticagrelor, combined with low-dose aspirin, for preventing atherothrombotic events after myocardial infarction for a period of up to three years⁽²⁾

Indication:

Ticagrelor, co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with:

- acute coronary syndromes (ACS) or
- a history of myocardial infarction (MI) and a high risk of developing an atherothrombotic event⁽³⁾

Dose & Administration:

Acute coronary syndromes

Ticagrelor treatment should be initiated with a single 180 mg loading dose (two tablets of 90 mg) and then continued at 90 mg twice daily; for up to 12 months therapy.⁽³⁾

History of myocardial infarction

Ticagrelor 60 mg twice daily is the recommended dose when an extended treatment is required for patients with a history of myocardial infarction of at least one year and a high risk of an atherothrombotic event. Treatment may be started without interruption as continuation therapy after the initial one-year treatment with ticagrelor 90 mg or other adenosine diphosphate (ADP) receptor inhibitor therapy in ACS patients with a high risk of an atherothrombotic event. If a switch from a different treatment is needed, the first dose of ticagrelor should be administered 24 hours following the last dose of the other antiplatelet medication.

Adverse Effects:

The most commonly reported adverse effects are dyspnoea, haemorrhage and bruising; less commonly nausea, vomiting, diarrhoea, abdominal pain, dyspepsia, gastritis, dizziness, headache, rash and pruritus; rarely constipation, paraesthesia, confusion, hyperuricaemia, raised serum creatinine and vertigo.

Ticagrelor can commonly cause dyspnoea. In clinical trials most reported symptoms of dyspnoea were mild to moderate in intensity, and most were reported as a single episode early after starting treatment. About 1 in 3 episodes of dyspnoea resolved within 7 days. Patients more likely to report dyspnoea are those with congestive heart failure, COPD, asthma and the elderly. It should be noted that these patients were not excluded from the clinical trial. Ticagrelor does not affect lung function tests. Dyspnoea includes the terms dyspnoea exertional, dyspnoea at rest, and nocturnal dyspnoea. If there are concerns about dyspnoea with ticagrelor that persists beyond 10 days after starting treatment with no identifiable cause GPs should consider discussing this with the patient's consultant.

Contraindications:

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- Hypersensitivity to ticagrelor or to any of the excipients included within the medicinal form.
- Active pathological bleeding.
- History of intracranial haemorrhage.

Version: 2

Author: Paul Mills (Principal Pharmacist-CHUFT)

Reviewed by: Dr Kare Tang (Consultant Cardiologist), Sheila Baldwin (Head of Medicines Management, NHS North East Essex Clinical Commissioning Group)

Approved by: NEEMMC, April 2017

Next review date: April 2019

- Moderate to severe hepatic impairment.
- Co-administration of ticagrelor with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir) is contraindicated, as co-administration may lead to a substantial increase in exposure to ticagrelor.

Special warnings/precautions:

- Ticagrelor is not recommended during pregnancy. Women of childbearing potential should use appropriate contraceptive measures to avoid pregnancy during ticagrelor therapy.
- Ticagrelor is excreted into breast milk. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from ticagrelor therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.
- The use of ticagrelor in patients at known increased risk for bleeding should be balanced against the benefit in terms of prevention of atherothrombotic events. If clinically indicated, ticagrelor should be used with caution in the following patient groups:
 - Patients with a propensity to bleed (e.g. due to recent trauma, recent surgery, coagulation disorders, active or recent gastrointestinal bleeding). But see contraindications above
 - Patients with 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) within 24 hours of ticagrelor dosing.
- If a patient is to undergo elective surgery and antiplatelet effect is not desired, ticagrelor should be discontinued 7 days prior to surgery.
- Ticagrelor should be used with caution in patients with history of asthma and/or COPD. If a patient reports new, prolonged or worsened dyspnoea this should be investigated fully and if not tolerated, treatment with ticagrelor should be stopped.
- Creatinine levels may increase during treatment with ticagrelor. Renal function should be checked 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.
- The use of ticagrelor in patients with uric acid nephropathy is discouraged.

Drug Interactions:

The ticagrelor Summary of Product Characteristics gives full details of the drug interactions associated with the treatment.⁽³⁾

Ticagrelor is primarily a CYP3A4 substrate and a mild inhibitor of CYP3A4. It is also a P-gp substrate and a weak P-gp inhibitor and may increase the exposure of P-gp substrates.

Interactions with ticagrelor are listed below (those in red indicates the combinations that should be avoided)

Atazanavir	plasma concentration of ticagrelor possibly increased by atazanavir — manufacturer of ticagrelor advises avoid concomitant use
Carbamazepine	plasma concentration of ticagrelor possibly reduced by carbamazepine
Ciclosporin	plasma concentration of ticagrelor increased by ciclosporin
Citalopram	possible increased risk of bleeding when ticagrelor given with citalopram
Clarithromycin	plasma concentration of ticagrelor possibly increased by clarithromycin — manufacturer of ticagrelor advises avoid concomitant use
Dabigatran	ticagrelor increases plasma concentration of dabigatran
Digoxin	ticagrelor increases plasma concentration of digoxin
Diltiazem	plasma concentration of ticagrelor increased by diltiazem
Ergot alkaloids	ticagrelor possibly increases plasma concentration of ergot alkaloids

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Erythromycin	plasma concentration of ticagrelor possibly increased by erythromycin Note: Interactions do not apply to small amounts of erythromycin used topically
Fosphenytoin	plasma concentration of ticagrelor possibly reduced by fosphenytoin
Paroxetine	possible increased risk of bleeding when ticagrelor given with paroxetine
Phenobarbital	plasma concentration of ticagrelor possibly reduced by phenobarbital
Phenytoin	plasma concentration of ticagrelor possibly reduced by phenytoin
Primidone	plasma concentration of ticagrelor possibly reduced by primidone
Rifampicin	plasma concentration of ticagrelor reduced by rifampicin
Ritonavir	plasma concentration of ticagrelor possibly increased by ritonavir — manufacturer of ticagrelor advises avoid concomitant use
Sertraline	possible increased risk of bleeding when ticagrelor given with sertraline
Simvastatin	ticagrelor increases plasma concentration of simvastatin (increased risk of toxicity)

Monitoring Requirements:

Creatinine levels may increase during treatment with ticagrelor (the mechanism for this effect not being fully elucidated). Renal function should be checked after one month of treatment 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.

Parameters for Intervention:

Apart from the recommended renal function test at one month post-treatment, there are no specific parameters for intervention in terms of blood tests, therapeutic monitoring, etc. Any possible ticagrelor-related adverse effects must be reported back to the Secondary Care Specialist who will then make a decision as to the clinical appropriateness of continuing therapy.

Shared Care Responsibilities:

Secondary Care Specialist

1. Send a letter to the GP with Shared Care Guidelines requesting shared care for the patient.
2. Initiation of ticagrelor therapy with the correct dose prescribed; providing the patient with an initial 4 weeks supply of medicine.
3. Discuss the benefits and side effects of treatment with the patient.
4. Clearly state to the patient the intended length of treatment (dependent on the indication), highlighting any future need to reduce the dose to 60mg twice daily if clinically indicated.
5. Report adverse events to the Medicines and Healthcare Products Regulatory Agency (MHRA).
<https://yellowcard.mhra.gov.uk/>
6. Act promptly on any communication from GP colleagues requesting advice and support.
7. Communicate the decision to discontinue therapy prior to expected completion date; if on-going therapy is no longer thought to be beneficial.

Primary Care Practitioner

1. Submit letter of reply confirming acceptance.
2. Monitor patient's overall health and wellbeing.
3. Prescribe the drug treatment as described within this document.
4. Continue prescribing ticagrelor (usually after a minimum of 4 weeks therapy); stopping therapy after the indicated period of time.
5. If treatment is to continue for 3 years reduce the dose from 90mg twice daily to 60mg twice daily after the first 12 months of treatment

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6. To undertake any necessary monitoring of the patient, including checking renal function after one month of treatment. Future checks should be carried out in accordance with routine medical practice paying special attention to patients aged ≥ 75 years, patients with moderate/severe renal impairment and those requiring monitoring with regards to concomitant medication.
7. Report to and seek advice from the Secondary Care Specialist on any aspect of patient care that is of concern and may affect treatment.
8. Refer patient to the Specialist if patient's condition deteriorates.
9. Report any ticagrelor-related adverse events to the hospital specialist and MHRA.
10. Ensure that any new medication started is reviewed in terms of interactions with ticagrelor.
11. Stop treatment on the advice of the Secondary Care Specialist.
12. Consider adding "to be taken until" on future ticagrelor prescriptions (12 months duration for 90mg twice daily then 24 months for the 60mg twice daily continuation regime).

Patient (and if appropriate, the carer):

1. Report to the Secondary Care Specialist or GP if he or she does not have a clear understanding of the prescribed treatment.
2. Share any concerns in relation to treatment with ticagrelor.
3. Report any adverse effects to the Secondary Care Specialist or GP whilst taking ticagrelor therapy.

Contact Numbers for Advice and Support:

Colchester Hospital University NHS Foundation Trust (01206) 747474 (Switchboard)

Consultant Cardiologists:

Dr Kare Tang (01206) 742219
kare.tang@colchesterhospital.nhs.uk

Dr Allan Harkness (01206) 742626
allan.harkness@colchesterhospital.nhs.uk

CHUFT Pharmacy Department (01206) 742355

CHUFT Medicines Information Help Line: (01206) 742161

References

- (1) Ticagrelor for the treatment of Acute Coronary Syndromes, October 2011
<https://www.nice.org.uk/guidance/ta236>
- (2) Ticagrelor for preventing atherothrombotic events after myocardial infarction, December 2016
<https://www.nice.org.uk/guidance/ta420>
- (3) Summary of Product Characteristics – Brilique® (ticagrelor) 60mg and 90mg film-coated tablets. Astra Zeneca UK Limited.
<https://www.medicines.org.uk/emc/medicine/23935/SPC/Brilique+90+mg+film+coated+tablets/>

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Section A (to be completed by Secondary Care Specialist):

Hospital Number:	
NHS No:	
Date:	
GP Courier No:	
GP Name:	

Name of patient:	
Date of Birth:	
Address:	

Background:

Medications:

Dear GP,
See attached clinic letter. Please can you sign and return (using the above fax number) to indicate you are in agreement with the Shared Care Guidelines.

Yours sincerely,

Section B (to be completed by General Practitioner):

The above patient (with associated ticagrelor treatment) has been accepted into our monitoring service.

Accepting GP Name:	
Accepting GP Signature:	
Date:	

Practice Stamp: