

Sheffield guidelines for the use of antiplatelets in the prevention and treatment of cardiovascular disease (September 2020)

Approved by Sheffield Area Prescribing Group and Sheffield Teaching Hospitals Medicines Management and Therapeutics Committee

Table of Contents

Indications for antiplatelet use and corresponding advice	2
Primary prevention including diabetes (long term treatment)	2
Atrial fibrillation (long term treatment).....	2
Ischaemic stroke, secondary prevention (long term treatment) and Transient ischaemic attack (TIA) (long term treatment).....	2
Carotid stenosis with stent insert.....	2
Carotid endarterectomy patients (long term treatment)	2
Peripheral Vascular Disease (PVD) (long term treatment)	2
Superficial femoral, popliteal and tibial artery stents.....	2
Stable angina (long term treatment)	2
Stable angina with elective coronary stenting (PCI).....	3
Elective coronary artery bypass graft (CABG), including saphenous vein grafts	3
Urgent non-elective CABG	3
Patients with coronary heart disease (CAD) or symptomatic peripheral artery disease (PAD) at a high risk of ischaemic events.....	3
Acute coronary syndrome (ACS), loading doses.....	4
Patients with unstable angina	4
Patients with ST-segment-elevation myocardial infarction (STEMI) – defined as ST elevation or new left bundle branch block on electrocardiogram –	5
Patients with non-ST-segment-elevation myocardial infarction (NSTEMI).....	5
Extended treatment with ticagrelor 60mg after MI (STEMI or NSTEMI) for patients at high risk.....	5
Clopidogrel interaction with omeprazole and esomeprazole.....	6
Antiplatelet use in patients with hypersensitivity to aspirin.....	6
Rivaroxaban 2.5mg as an option for the prevention of atherothrombotic events	6
References.....	6

Indications for antiplatelet use and corresponding advice

The recommended treatment in Sheffield is given for the indications below.

Indication	Advice
Primary prevention including diabetes (long term treatment)	No antiplatelet is generally recommended. Where a secondary care clinician has assessed an individual patient and considers the balance of risk vs benefit favours treatment with antiplatelet then aspirin 75mg daily is the first line treatment Note: no antiplatelet is licensed for primary prevention
Atrial fibrillation (long term treatment)	Do not offer aspirin 75mg monotherapy solely for stroke prevention to people with atrial fibrillation. Please see the Anticoagulation for Stroke Prevention in Atrial Fibrillation guidelines.
Ischaemic stroke, secondary prevention (long term treatment) and Transient ischaemic attack (TIA) (long term treatment)	Clopidogrel 75mg daily (first line)- licensed post stroke; unlicensed post-TIA (see Sheffield primary care guidelines for Stroke and Transient Ischaemic Attack) or Aspirin 75mg daily + dipyridamole MR 200mg twice daily where clopidogrel is C/I or not tolerated (Either may be used as monotherapy if the other is not tolerated)
Carotid stenosis with stent insert	Clopidogrel 75mg daily long term plus aspirin 75mg daily for 1 month (unlicensed indication)
Carotid endarterectomy patients (long term treatment)	Clopidogrel 75mg daily, any other treatment combinations should be confirmed in writing by the Stroke Specialists or Neurologists (unlicensed indication)
Peripheral Vascular Disease (PVD) (long term treatment)	Clopidogrel 75mg daily (first line treatment) or Aspirin 75mg daily
Superficial femoral, popliteal and tibial artery stents	Clopidogrel 75mg daily (long term) (unlicensed indication) + aspirin 75mg daily (2-12 months, depending on stent used; duration to be specified on discharge)
Stable angina (long term treatment)	Aspirin 75mg daily. Consider clopidogrel 75mg daily if aspirin not tolerated (unlicensed)

<p>Stable angina with elective coronary stenting (PCI)</p>	<p>Aspirin 75mg daily (long term) in combination with clopidogrel 75mg daily (unlicensed indication) for the following duration depending on type of stent- Bare metal stents: clopidogrel 75mg od for 1 month. Drug-eluting stents: clopidogrel 75mg od for 6 months but a reduced duration may be considered for management of serious bleeding or long term administration may be considered for high ischaemic risk patients; the specialist will clearly communicate the recommended duration to primary care prescribers.</p>
<p>Elective coronary artery bypass graft (CABG), including saphenous vein grafts</p>	<p>Aspirin 300mg daily for 12 months and then reduce to 75mg (long term) thereafter.</p>
<p>Urgent non-elective CABG</p>	<p>For loading doses, please see ACS section below.</p> <p>Maintenance dose- Aspirin 75mg daily (long term) in combination with ticagrelor 90mg twice daily for 12 months post CABG. Extended treatment beyond twelve months with ticagrelor has not been reviewed in patients who have undergone coronary-artery bypass grafting.</p>
<p>Patients with coronary heart disease (CAD) or symptomatic peripheral artery disease (PAD) at a high risk of ischaemic events</p>	<p>For people with CAD, high risk of ischaemic events is defined as ONE of the following:-</p> <ul style="list-style-type: none"> i.) Aged 65 or over, or ii.) Atherosclerosis in at least 2 vascular territories (e.g. coronary, cerebrovascular or peripheral arteries) <p>OR TWO or more of the following:-</p> <ul style="list-style-type: none"> i.) Current smoking status ii.) Diabetes iii.) Kidney dysfunction with eGFR <60ml/min/1.73m² iv.) Heart failure v.) Previous non-lacunar stroke <p>Aspirin 75mg once daily in combination with rivaroxaban 2.5mg twice daily</p>

<p>Acute coronary syndrome (ACS), loading doses</p>	<p>Treatment will usually be initiated by a specialist and the length of treatment clearly communicated to primary care prescribers.</p> <p>Note for ACS where an antiplatelet is indicated the following loading doses are usually appropriate. <i>Aspirin 300mg</i> <i>Clopidogrel 300mg (or 600mg if used prior to PCI) (Omit initial loading dose in patients over 75 years with STEMI managed with fibrinolysis)</i> <i>Ticagrelor 180mg</i> <i>Prasugrel 60mg</i></p>
<p>Patients with unstable angina</p>	<p>Aspirin 75mg daily (long term) and clopidogrel 75mg daily for one year regardless of management strategy (conservative or invasive), or For patients with moderate-to-high risk unstable angina – defined as ST or T wave changes on electrocardiogram suggestive of ischaemia plus one of the characteristics defined below- Age 60 years or older; previous myocardial infarction or previous coronary artery bypass grafting (CABG); coronary artery disease with stenosis of 50% or more in at least two vessels; previous ischaemic stroke; previous transient ischaemic attack, carotid stenosis of at least 50%, or cerebral revascularization; diabetes mellitus; peripheral arterial disease; or chronic renal dysfunction, defined as a creatinine clearance of less than 60ml per minute per 1.73m² of body-surface area- Aspirin 75mg daily (long term) and ticagrelor 90mg twice daily for one year regardless of management strategy (conservative or invasive) Note. Before ticagrelor is continued beyond the initial treatment, the diagnosis of unstable angina should first be confirmed, ideally by a cardiologist or For patients treated with PCI, aspirin 75mg daily (long term) and prasugrel 10mg daily for one year or 5mg daily for one year if body weight less than 60kg. (The use of prasugrel in patients ≥ 75 years of age is generally not recommended. Please see the SPC for more details on this patient group)</p>

<p>Patients with ST-segment-elevation myocardial infarction (STEMI) – defined as ST elevation or new left bundle branch block on electrocardiogram –</p>	<p>Treated with primary percutaneous coronary intervention (PCI) Aspirin 75mg daily (long term) and ticagrelor 90mg twice daily for one year or Aspirin 75mg daily (long term) and prasugrel 10mg daily for one year or 5mg daily for one year if body weight less than 60kg. (The use of prasugrel in patients ≥ 75 years of age is generally not recommended. Please see the SPC for more details on this patient group) or Aspirin 75mg daily (long term) and clopidogrel 75mg daily for one year and/or rivaroxaban 2.5mg twice daily (a decision on continuation of treatment should be taken no later than 12 months after starting treatment)</p> <p>Treated with fibrinolytic therapy Aspirin 75mg daily (long term) and clopidogrel 75mg daily for one year and/or rivaroxaban 2.5mg twice daily (a decision on continuation of treatment should be taken no later than 12 months after starting treatment)</p>
<p>Patients with non-ST-segment-elevation myocardial infarction (NSTEMI)</p>	<p>Aspirin 75mg daily (long term) and ticagrelor 90mg twice daily for one year regardless of management strategy (conservative or invasive), or For patients treated with PCI, aspirin 75mg daily (long term) and prasugrel 10mg daily for one year or 5mg daily for one year if body weight less than 60kg. (The use of prasugrel in patients ≥ 75 years of age is generally not recommended. Please see the SPC for more details on this patient group) or Aspirin 75mg daily (long term) and clopidogrel 75mg daily for one year and/or rivaroxaban 2.5mg twice daily regardless of management strategy (a decision on continuation of treatment should be taken no later than 12 months after starting treatment)</p>
<p>Extended treatment with ticagrelor 60mg after MI (STEMI or NSTEMI) for patients at high risk</p>	<p>Extended treatment with ticagrelor 60mg twice daily may be indicated for patients who have had an MI and are assessed as being at high risk of further coronary events. These patients would usually have received dual antiplatelet treatment with a combination of ticagrelor 90mg twice daily and aspirin 75mg daily for one year and require down-titration to ticagrelor 60mg twice daily in combination with aspirin 75mg daily. Treatment with this combination is for a maximum of a further 3 years (maximum up to 4 years post index MI). Identification of patients requiring down-titration and the duration of treatment will be made by the cardiologist during hospital admission for the index MI.</p>

Clopidogrel interaction with omeprazole and esomeprazole

Co-administration of clopidogrel with omeprazole or esomeprazole should be avoided. Other PPIs may weakly interact with clopidogrel and therefore potential risk of reduction in the efficacy of clopidogrel should be weighed against the GI benefit of PPI. PPIs are however recommended in patients on aspirin and/or clopidogrel who are at high risk of GI bleeding.

If a PPI is indicated, lansoprazole is first line for patients requiring or likely to require clopidogrel. Prasugrel and ticagrelor have no negative interaction with PPIs.

Antiplatelet use in patients with hypersensitivity to aspirin

Patients admitted to hospital following an acute coronary syndrome will require dual antiplatelet treatment, usually with aspirin on discharge. These patients are most likely to have undergone aspirin de-sensitization in hospital prior to discharge. The following is therefore the recommendation managing patients with aspirin allergy who have had aspirin de-sensitization-

“Continue aspirin 75 mg daily thereafter without any break in treatment. Advise patient that they will need further de-sensitization in the future if they stop or miss any doses of aspirin and then need to restart aspirin for any reason¹.”

Rivaroxaban 2.5mg as an option for the prevention of atherothrombotic events

Clinicians should regularly reassess the relative benefits and risks of continuing treatment with rivaroxaban 2.5mg and discuss them with the patient. Rivaroxaban is an anticoagulant rather than an antiplatelet drug. It is included for completeness as it is recommended in NICE TA335 for the management of ACS and NICE TA607 for the prevention of ischaemic events in patients with CAD or symptomatic PAD considered at very high risk.

References

2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* **124(23)**: 2610-2642

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). ESC Scientific Document Group, ESC Committee for Practice Guidelines (CPG), ESC National Cardiac Societies. *European Heart Journal*. **39(3):213-260**

2018 ESC/EACTS Guidelines on myocardial revascularization, ESC Scientific Document Group. *European Heart Journal* **40(2): 87-165**

National clinical guideline for stroke: Prepared by the Intercollegiate Stroke Working Party (2016). Royal College of Physicians. Fifth Edition

NICE GG126 July 2011- Management of stable angina (last modified December 2012).

¹ Taken from *Aspirin desensitisation protocol for patients undergoing percutaneous coronary intervention who have prior aspirin allergy. Version 2 by R.F.Storey 8 April 2016.*

NICE CG172 November 2013- Myocardial infarction- cardiac rehabilitation and prevention of further cardiovascular disease.

NICE CG180 June 2014- Atrial fibrillation: the management of atrial fibrillation (last modified in August 2014).

NICE NG28 December 2015- Type 2 diabetes in adults: management.

NICE TA210 December 2010- Clopidogrel and modified release dipyridamole for the prevention of occlusive vascular events.

NICE TA236 October 2011- Ticagrelor for the treatment of acute coronary syndromes.

NICE TA317 July 2014- Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of technology appraisal guidance 182).

NICE TA335 March 2015- Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome.

NICE TA420 December 2016- Ticagrelor for preventing atherothrombotic events after myocardial infarction.

NICE TA607 October 2019- Rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral artery disease.

Sheffield Primary Care Guidelines for Stroke and Transient Ischaemic Attacks: February 2019.

Summary of product characteristics for the agents mentioned are available at <http://www.medicines.org.uk/emc/>

Written by: Ebuloluwa Ojo (Lead Pharmacist for ACS, Hypertension & Lipids, NHS Sheffield CCG)

With thanks to:

Professor Rob Storey, Professor and Honorary Consultant in Cardiology, Department of Cardiovascular Science, University of Sheffield.

Mr Peter Braidley, Consultant in Cardiothoracic Surgery, Sheffield Teaching Hospitals NHS Foundation Trust.

Martin Brown, Advanced Clinical Pharmacist Cardiothoracic Services, Sheffield Teaching Hospitals NHS Foundation Trust

Version No. – v2

Approved by APG- September 2020

Approved by STH MMTC- October 2020

Review date- September 2025