North Central London
Joint Formulary Committee

Summary of Antiplatelet Options in Cardiovascular Disease

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NCL JFC is funded by and provides advice to Acute Trusts and NCL Clinical Commissioning Group.

Document control

Date	Version	Amendments
15Mar18	1	New document
26Nov18	1.1	Formatting amendments to Dual Antiplatelet Therapy (DAPT) table
12Aug2022	2.0	Addition of rivaroxaban and aspirin as per NICE TA Guideline amended following publication of NICE NG185

Document management

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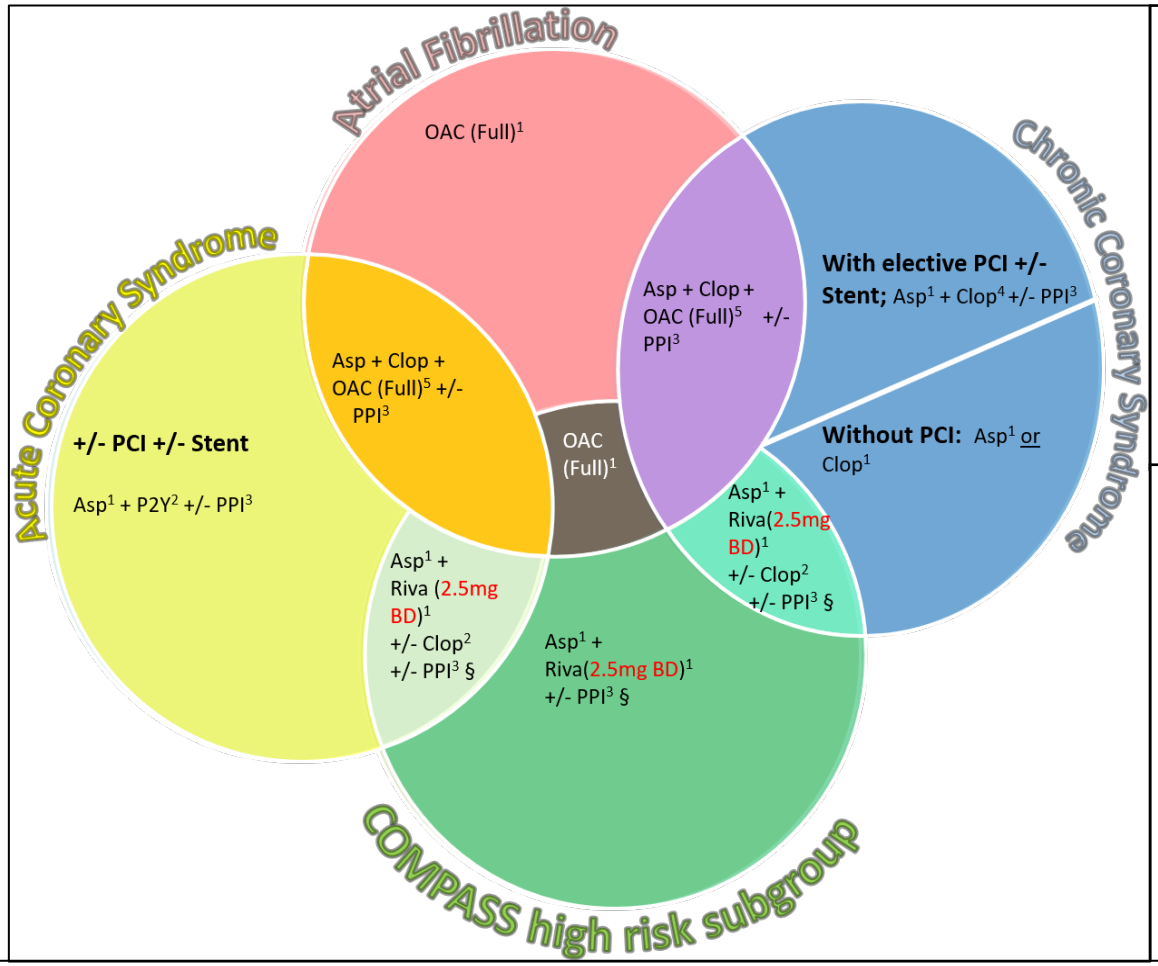
Groups which were consulted and have given approval:	NCL Specialists, Formulary Pharmacists and Commissioners NCL Joint Formulary Committee
File name:	Summary of Antiplatelet Options in CVD
Version number:	2.0
Available on:	www.ncl-mon.nhs.uk
Disseminated to:	NCL Formulary Pharmacists and Commissioners
Equality impact assessment:	Low
NCL Joint Formulary Committee Approval date:	12 Aug 2022
Review date:	12 Aug 2025

Summary of antiplatelet options in cardiovascular disease



§	Combined AntiThrombotic & Mono AntiPlatelet +/-PPI
P2Y	P2Y12 Inhibitor (Clopidogrel, Prasugrel, Ticagrelor)
PCI	Percutaneous coronary intervention
DAPt	Dual Antiplatelet therapy (Aspirin with a $P2Y_{12}$ inhibitor)
OAC	Oral Anticoagulant (warfarin or direct oral anticoagulant (DOAC))
Asp	Aspirin
Clop	Clopidogrel
Riva	Rivaroxaban
PPI	Proton Pump Inhibitor
Full	Full licenced dose according to patient criteria characteristics (e.g. renal function)

1	Life-long
2	12 months
3	Lansoprazole preferred with clopidogrel. Duration of 12 months; consider long-term thereafter.
4	Duration depends on intervention: I. 12 months if drug-eluting stent used; II. At least 1 month if bare metal stent or drug-eluting balloon (up to 6 months depending on ischaemic + bleeding risk)
5	Triple therapy should be given for the shortest time feasible based on ischaemic and bleeding risk: I. Usually, 1 to 6 months as triple therapy; then II. Clopidogrel and OAC continued up to one year; III. Then OAC continued alone (unless strong indication for a concomitant antiplatelet)

Note: the benefit of anticoagulation is balanced with the individual patient's bleeding risk; therefore, there may be nuanced differences in the final dose decided by the specialist

The 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.

Antiplatelet therapies are used for a number of indications. This guidance summarises the recommended antiplatelet regimens for use across North Central and North East London. A graphical summary of these options can be seen in above.

Antiplatelet Monotherapy

The majority of patients will require antiplatelet monotherapy.

Indication	First-line treatment option	Alternative (especially in the event of C/I or intolerance to first-line options)
Stable coronary artery disease	Aspirin 75mg daily	Clopidogrel 75mg daily
Post-stroke or Transient Ischaemic Attack (TIA) (in the absence of atrial fibrillation)	Clopidogrel 75mg daily	Aspirin 75mg daily with dipyridamole MR 200mg twice daily
Peripheral arterial disease (PAD)	Clopidogrel 75mg daily	Aspirin 75mg daily
Multivascular disease (i.e. coronary artery disease and stroke / TIA or PAD)	Clopidogrel 75mg daily	Aspirin 75mg daily (with dipyridamole MR 200mg twice daily if prior stroke/TIA)

- Aspirin or clopidogrel as monotherapy is not indicated for stroke prevention in patients with Atrial Fibrillation (AF)
- Aspirin is not recommended for routine use in the primary prevention of cardiovascular disease.
- Prasugrel and ticagrelor are not licensed for use as monotherapy for the primary or secondary prevention of CV disease.
- Prasugrel, ticagrelor and clopidogrel have not been used in combinations together so are not recommended. All three are pharmacologically similar, and therefore a combination would not be appropriate.

Dual Antiplatelet Therapy (DAPT)

- **DAPT is only initiated in secondary care. All patients initiated on DAPT must leave hospital with a clearly documented plan that includes the indication and proposed duration of treatment or review date.**
- **Clear recommendation from the initiating team on when to stop DAPT or a review duration must be communicated to primary care – this is in keeping with NICE CKS recommendations (link here).**
- **It should be clear who to contact in the event of clinical queries or need for interruptions of DAPT**.
- For all patients on high intensity DAPT (i.e. aspirin with prasugrel or ticagrelor) or triple therapy, routine consideration of co-prescription with a PPI is encouraged to reduce the risk of GI bleeding. Please see more details on next page.

Table 1 – Antiplatelet options in NCL for ACS indications

<table>
<tr><th>Indication</th><th colspan="2">First line option</th><th>Alternatives (especially in the event of C/I or intolerance to first-line options)</th></tr>
<tr><td>ST elevation (STEMI)
OR
Non-ST elevated MI (NSTEMI) or unstable angina (troponin negative) WITH stent insertion</td><td>• Prasugrel 5mg or 10mg (based on license) daily plus aspirin 75mg daily for one year (may be shorter if the patient has a high bleeding risk) [3]

OR

• Ticagrelor 90mg twice daily plus aspirin 75mg daily for one year (may be shorter if the patient has a high bleeding risk)</td><td rowspan="2"><u>then continue:</u>

a) Aspirin monotherapy long-term [1]
OR
b) In patients who are at high risk of atherothrombotic event [2]: Aspirin 75mg daily plus ticagrelor 60mg twice daily after year 1, for a maximum of 3 years; followed by aspirin 75mg monotherapy long-term [1]. The decision to extend treatment beyond the first year should be made by cardiologist team during the MI event admission. Extended ticagrelor therapy is not recommended for patients on anticoagulation or at increased risk of major bleeding.</td><td>• Patients at high risk of bleeding events with DAPT (using scores such as CRUSADE) or on anticoagulation, consider clopidogrel 75mg daily with aspirin 75mg daily for one year then continue aspirin monotherapy long-term

For patients with ACS and in atrial fibrillation (AF), please see further information in “triple therapy” paragraph.</td></tr>
<tr><td>ST elevation (STEMI)
OR
Non-ST elevated MI (NSTEMI) or unstable angina (troponin negative) WITHOUT stent insertion</td><td>• Ticagrelor 90mg twice daily plus aspirin 75mg daily for one year (may be shorter if the patient has a high bleeding risk)</td><td>Patients at high risk of bleeding events with DAPT (using scores such as CRUSADE) or on anticoagulation, consider clopidogrel 75mg daily with aspirin 75mg daily for one year then continue aspirin monotherapy long-term

For patients with ACS and in atrial fibrillation (AF), please see further information in “triple therapy” paragraph.</td></tr>
<tr><td>STEMI OR NSTEMI or unstable angina (troponin negative) WITH OR WITHOUT stent insertion with high clot burden and low bleeding risk as per NICE TA335</td><td><u>Alternative first line option:</u>

• Rivaroxaban <u>2.5mg twice a day</u> in combination with aspirin 75mg daily plus clopidogrel 75mg daily or aspirin alone for one year as an alternative to ticagrelor/prasugrel and aspirin for certain ACS patients with high clot burden.</td><td>• Consider if eligible for extended DAPT beyond 1 year</td><td></td></tr>
</table>

Table 2 – Antiplatelet options in NCL for non-ACS indications

Indication	First line option	Alternatives (especially in the event of C/I or intolerance to first-line options)
Elective Percutaneous Coronary Intervention (PCI) with drug eluting stent insertion (*Not* ACS)	• Aspirin 75mg daily plus clopidogrel 75mg daily for one year (may be shorter if the patient has a high risk of bleeding); then continue aspirin monotherapy long term [1]	• Discuss with cardiology before changing drug therapy
Elective percutaneous coronary intervention (PCI) with bare metal or biofreedom stenting (*Not* ACS)	• Aspirin 75mg daily plus clopidogrel 75mg daily for at least one month but up to six months (depending on ischaemic and bleeding risk) then continue aspirin monotherapy long-term [1]	• Discuss with cardiology before changing drug therapy
Elective percutaneous coronary intervention (PCI) with drug eluting balloons (*Not* ACS)	• Aspirin 75mg daily plus clopidogrel 75mg daily for at least one month but up to six months (depending on ischaemic and bleeding risk) then continue aspirin monotherapy long-term [1]	• Discuss with cardiology before changing drug therapy
Post-Coronary Artery Bypass Graft (CABG) surgery (if initiated prior to hospital discharge)	• **In the context of ACS**: Aspirin 75mg daily plus clopidogrel 75mg daily for up to 12 months; then continue aspirin monotherapy long-term [1] • **In the context of elective CABG without ACS**: Aspirin 75mg daily monotherapy long-term	• **In the context of ACS**: Aspirin 75mg daily or clopidogrel 75mg daily as monotherapy • **In the context of elective CABG without ACS**: clopidogrel 75mg daily as monotherapy (if allergic to aspirin)
Post-Patent Foramen Ovale (PFO) device closure	• Aspirin 75mg daily and clopidogrel 75mg daily for up to three months then consider aspirin monotherapy long-term [1]	• Discuss with cardiology before changing drug therapy
Following Transcatheter Aortic Valve Insertion (TAVI)	• In line with local guideline. This is usually aspirin 75mg daily or clopidogrel 75mg daily long-term. Unless patient has an indication for anticoagulation, in which case continue anticoagulation alone.	• Switch to alternative agent. If this is not tolerated discuss with initiating team

[1] Clopidogrel monotherapy long-term may be indicated in some patients – refer to monotherapy antiplatelet table above

[2] Extended treatment with ticagrelor 60mg twice daily plus aspirin 75mg daily may be started without interruption (continuation therapy) after initial 1 year treatment with dual antiplatelet therapy. Treatment can also be initiated up to 2 years from the myocardial infarction, or within one year after stopping previous adenosine diphosphate (ADP) receptor inhibitor treatment.. The following risk factors are taken into account when assessing risk of future ischaemic events: diabetes mellitus requiring medication, previous myocardial infarction in addition to index event, multivessel coronary artery disease and CKD (GFR <60ml/min) not requiring dialysis

[3] If patient is over the age of 75 and/or of low bodyweight (under 60kg) a lower maintenance dose of prasugrel 5mg daily may be considered

Rivaroxaban 2.5mg twice daily with aspirin 75mg once daily for CAD/PAD

In October 2019, NICE published their technology appraisal guidance for using rivaroxaban with aspirin as an option for preventing atherothrombotic events in people with coronary or symptomatic peripheral artery disease who are at high risk of ischaemic events. In order to safely introduce this therapy across NCL, it will be initiated from Secondary care. Please see NICE TA607 for more information.

It should only be initiated following a review of the benefit versus risk of treatment. Patients who have either a suspected or confirmed diagnosis for one of the populations listed in the NICE TA made in any cardiology, heart failure, vascular or renal clinics should be reviewed in an MDT setting. After assessing the individual's risk and addressing risk factors, pharmacotherapy options are considered. If the patient is eligible for treatment and does not have a contraindication or significant caution to treatment, the MDT will make a recommendation for combination rivaroxaban and aspirin treatment. Please note, rivaroxaban is contraindicated in patients with creatinine clearance <15ml/min.

If a patient is reviewed in Primary care routinely (i.e. does not access hospital services regularly) but may be eligible for treatment based on their associated risks, the Primary care physician can refer them to their local cardiology, nephrology or vascular centre for consideration of treatment depending on their risk profile.

Triple Therapy (Dual antiplatelet therapy plus anticoagulant)

On occasion, patients may require dual antiplatelet therapy and oral anticoagulation (OAC) – for example, in a patient with AF, following an ACS event and/or PCI with a stent insertion. The decision to prescribe triple therapy should be made by a consultant cardiologist. This indication is separate to the DAPT plus low dose rivaroxaban (2.5 mg twice daily) use in non-AF patients.

The following needs to be taken into consideration if the patient is on triple therapy with anticoagulation:

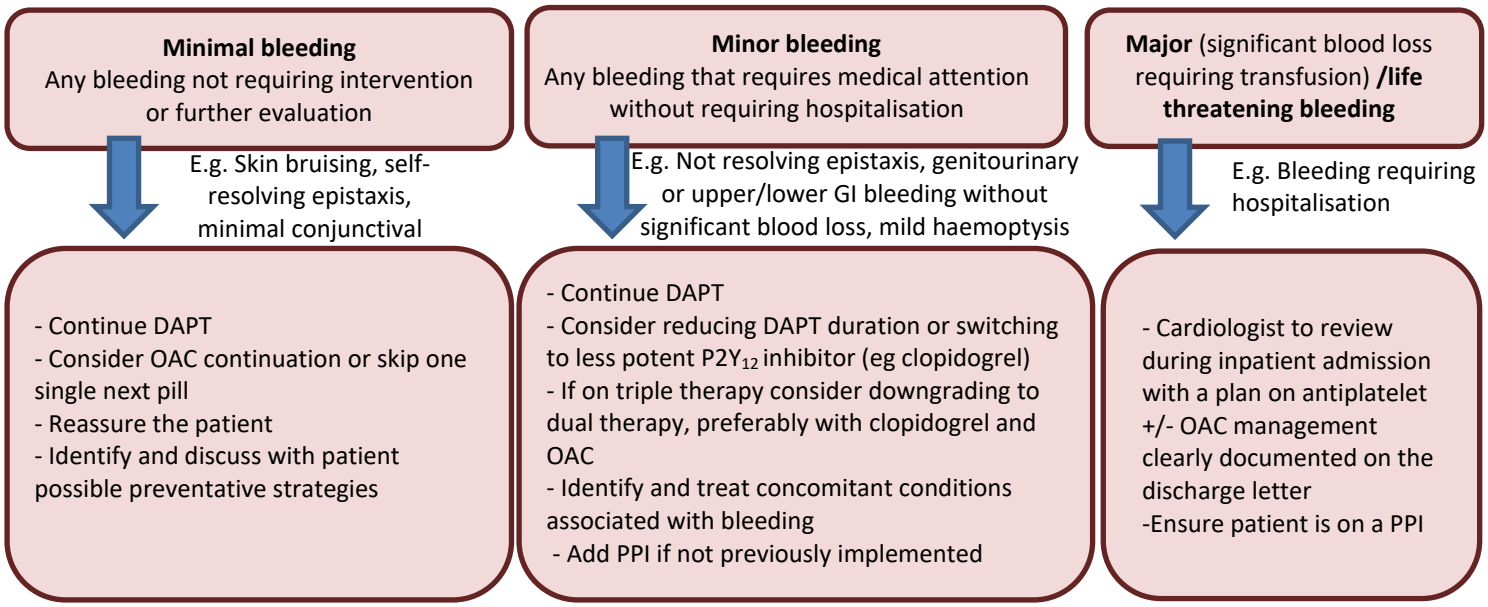
- The duration of triple therapy should be as short as possible. Triple therapy may continue for one to three months, then anticoagulation and clopidogrel to one-year post ACS event and/or PCI then anticoagulation alone is used long term, unless there is a strong indication to continue clopidogrel or aspirin in addition to the anticoagulant. Duration and indications for triple therapy must be clearly documented in the hospital discharge summary.
- The anti-platelets of choice for patients on full dose anticoagulation are clopidogrel and aspirin. The use of ticagrelor or prasugrel is not recommended as part of triple therapy plan with full dose anticoagulation due to excessive bleeding risk. Evidence of other combinations is emerging from trials of patients undergoing PCI with non-valvular atrial fibrillation.
- Recent ESC guidance suggests that, when using dual antiplatelets also, using one of the direct oral anticoagulants at the lowest dose effective for prevention of AF-related stroke as part of the triple therapy regimen may be appropriate. Detailed guidance from the ESC can be found at: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management.
- Ensure the patient has been prescribed a PPI for gastro protection.

Co-prescription of a PPI with clopidogrel

Following an analysis of new data, the European Medicines Agency (EMA) has recommended that concomitant use of clopidogrel and omeprazole or esomeprazole should now be discouraged. https://www.gov.uk/drug-safety-update/clopidogrel-and-proton-pump-inhibitors-interaction-updated-advice. Omeprazole has been shown to inhibit the isoenzyme (CYP2C19) that metabolises clopidogrel to its active metabolite, thereby reducing the ability of clopidogrel to inhibit platelet aggregation. Prescribers are advised that where co-prescription of a PPI with clopidogrel is necessary, lansoprazole is preferred to omeprazole. For other PPIs, concomitant use can be considered if specifically indicated.

Patients who develop bleeding whilst on treatment

Patients who develop bleeding complications while on DAPT represent a challenging patient population for whom no guidance from randomised controlled trials is available. The decision to withhold or continue DAPT in this setting largely depends on ischaemic (e.g. indication for DAPT and time from last stent insertion, if any, to bleeding) vs. recurrent or prolonged bleeding risks. A practical flow chart in order to aid management of this challenging population is provided on the next page.



Continuation and documentation in primary care

- To ensure patients do not continue antiplatelet therapy for longer than necessary, please make sure the patient's records and prescriptions in primary care have a stop date (or review date for potential extended DAPT therapy) documented.
- If a high-risk patient needs to continue on extended treatment with ticagrelor 60mg twice a day with aspirin 75mg once daily, please add to patient's records a maximum duration of three years followed by aspirin monotherapy.
- Consider cardiology review if new AF occurs needing triple therapy or for interruptions of DAPT for any type of surgery or if there's no documented stop date. For further information on antiplatelet duration, please see the relevant NICE guidance (e.g., NICE CKS for 'antiplatelet treatment of secondary prevention of CVD').
- If a patient develops AF and has stable coronary artery disease but without an ACS and/or coronary intervention in the previous 12 months, OAC monotherapy, and not combination with antiplatelets, is recommended.

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