NHS
South London Cardiac and Stroke Networks

SLCSN Guidance on Prescribing Clopidogrel for Cardiac Patients

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.

- The routine maintenance dose of clopidogrel is 75mg daily for all indications
- **Clopidogrel Monotherapy:** The main indication for long-term clopidogrel monotherapy for secondary prevention of cardiovascular disease (CVD) is established hypersensitivity to aspirin (anaphylaxis or acute bronchospasm). There is no evidence to support clopidogrel in primary prevention of CVD and it is not licensed for this indication.

  The risk of gastro-intestinal adverse effects with clopidogrel is similar to that of aspirin. Therefore, for patients who develop gastro-intestinal side effects when taking aspirin (i.e. dyspepsia) or are at high risk of gastro-intestinal bleeding, consider prescribing aspirin with a proton pump inhibitor (PPI) (for example, generic lansoprazole), rather than initiating clopidogrel as an alternative
- **Clopidogrel and Aspirin Dual Therapy:** clopidogrel may be used in combination with aspirin for a number of indications. For indications and recommended durations of clopidogrel - see table below. **Clopidogrel should not be stopped earlier than recommended without discussion with the initiating clinician.**

Recommended Clopidogrel Indications and Durations

Duration	Indications	Suggested Primary Care Read Codes
One month	• Elective percutaneous coronary intervention (PCI) with bare metal stenting (BMS)	793G
	• Post-Coronary Artery Bypass Graft (CABG) surgery (if initiated prior to hospital discharge)	792-1
	• ST-elevation Myocardial Infarction (STEMI)*	G30X0
Six months	• Post-Patent Foramen Ovale (PFO) closure • Post Transcatheter Aortic Valve Insertion (TAVI)	790C4
One year	• Acute Coronary Syndromes (ACS / Non-STEMI) with PCI (except STEMI)	G3115 + 793G
	• Acute Coronary Syndromes (ACS / Non-STEMI) without PCI (except STEMI)	G3115
	• Any PCI with Drug-Eluting Stent insertion (DES)**	#79295
Lifelong	• Established hypersensitivity to aspirin (secondary prevention only)	8I70

***STEMI** – should be given for at least one month but the optimal duration has not been established, many local consultants now recommend continuing for one year, as for other ACS. If patients undergo PCI with drug-eluting stent insertion post-STEMI, clopidogrel must be continued for one year.
****Drug-eluting stents** – durations of more than one year are being recommended in individual high-risk patients by some consultants due to concerns regarding late stent thrombosis on cessation of clopidogrel therapy.

- In most cases, clopidogrel will be initiated in secondary care. For courses of one month, the patient should be discharged with the full supply. Patient-held clopidogrel cards should be issued from secondary care
- A clear indication and duration for clopidogrel should be communicated to primary care at discharge. If prescribed for a longer duration than indicated above or the intended indication and/or the duration is unclear, please contact the initiating clinician for clarification
- After clopidogrel has been stopped, aspirin should be continued indefinitely at a dose of 75mg daily (except following PFO closure, when advice should be sought from the consultant cardiologist)
- Recent advice from the MHRA recommends that omeprazole and esomeprazole should be avoided in patients taking clopidogrel. For patients requiring a PPI whilst taking clopidogrel use an alternative PPI in line with local guidelines. See overleaf for more information.

References

- *SPC Plavix. Sanofi Pharma Bristol-Myers Squibb SNC. Sept 2006.*
- *NICE Clinical Guideline CG94: Unstable Angina and NSTEMI. March 2010.*
- *Chan FK, Ching JY, Hung LC, Wong VW, Leung VK, Kung NN, Hui AJ, Wu JC, Leung WK, Lee VW, Lee KK, Lee YT, Lau JY, To KF, Chan HL, Chung SC, Sung JJ. Clopidogrel versus aspirin and esomeprazole to prevent recurrent ulcer bleeding. N Engl J Med. 2005 Jan 20;352(3):238-44*
- *MHRA Drug Safety Update 2010;3 (9) 4-5*

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Clopidogrel and Proton Pump Inhibitors

The MHRA issued amended guidance on the use of clopidogrel and PPIs in April 2010.

- The concomitant use of clopidogrel with omeprazole or esomeprazole should be discouraged and alternative PPIs (such as generic lansoprazole or pantoprazole) used.

- The current evidence base does not support the extension of this recommendation to other PPIs, however, because it is not possible to completely exclude a possible interaction with other PPIs on the basis of the available data, the potential risk of a slight reduction in the efficacy of clopidogrel should be balanced against the potential GI benefit of the PPIs. Prescribers may consider the use of a H_2 antagonist, such as ranitidine, as an alternative to PPI therapy. Ranitidine is endorsed by NICE at a dose of 300mg twice daily (unlicensed) for gastroprotection; dose reduction may be required in renal dysfunction.

Table 2: SLCSN Guidance on Prescribing Gastroprotection for Patients on Clopidogrel

Indication for Acid Suppression	Recommendation	Comments
• **Patients at low GI risk**	**No acid suppression**	
• **Prophylaxis of ulceration in those at risk** (for example, over 65 years old or on other gastric irritant medication)	**Ranitidine 300mg twice daily**	No known interaction with clopidogrel metabolism. This dose is unlicensed but is approved by NICE for the prophylaxis of NSAID induced ulceration
• **Recently healed (<6 months) gastric or duodenal ulcer** • **Treatment of gastric disease** (for example, active ulceration or during ulcer healing phase, Barretts Oesophagus, Zollinger-Ellison Syndrome)	**Consider a PPI at a dose appropriate to the indication** Generic lansoprazole or pantoprazole are the preferred PPIs within the sector.	**Where in the clinical judgement of the physician the risk of a recurrent gastric event is greater than the risk of a cardiac event.**

For patients that experience an acute cardiac event (ie stent thrombosis) whilst on clopidogrel and any PPI: Check compliance with clopidogrel, consider stopping PPI and substituting ranitidine 300mg twice a day. Secondary care may consider testing the patient for platelet reactivity

- Remember to check whether patients prescribed clopidogrel are purchasing over-the-counter omeprazole. If so, consider whether an alternative gastrointestinal therapy should be prescribed.

- Other CYP2C19 inhibiting medicines are expected to have a similar effect to omeprazole and esomeprazole on the efficacy of clopidogrel. Avoid the concomitant use of clopidogrel and fluvoxamine, fluoxetine, moclobemide, voriconazole, fluconazole, ticlopidine, ciprofloxacin, cimetidine, carbamazepine, oxcarbazepine, and chloramphenicol.

References

- *Public statement on possible interaction between clopidogrel and proton pump inhibitors. EMEA/328956/2009. London 2009#*
- *Clopidogrel and Proton Pump Inhibitors: Possible Interaction. MHRA: Drug Safety 2009: 11(2). 11*
- *Clopidogrel and Proton Pump Inhibitors: Interaction> Drug Safety 2009; 12 (2) 2.*
- *NICE CG17 Dyspepsia Clinical Guideline (2004 at www.nice.org.uk*
- *MHRA Drug Safety Update 2010;3 (9) 4-5*