JPP November 2021

7 days of clopidogrel

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Day 1: While searching for novel anti-inflammatory drugs in the 1980s, the pro-drug [#clopidogrel](https://twitter.com/search?q=%23clopidogrel) was discovered and launched worldwide as an oral anti-platelet agent in 1998

Day 2: Indications include prevention of atherothrombotic events e.g acute & post-MI; AF & percutaneous coronary interventions (PCIs), & as an alternative to aspirin for TIA/ischaemic stroke. Used as an adjunct with aspirin in non-ST segment elevation acute coronary syndrome & PCIs. Prevention maintenance dose is 75mg once daily. Loading doses 300-600mg e.g for percutaneous coronary interventions

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Day 3: Kinetics; Rapid oral absorption cmax 45-60mins. [#clopidogrel](https://twitter.com/search?q=%23clopidogrel) is a prodrug & extensive liver metabolism leads to release of the active metabolite. Many enzymes can do 1st step (1A2,2B6,2C19); 2nd step oxidation by enzymes CYP3A4 & 2C19 is required. Excretion 50:50 faecal/renal. T½ of active metabolite 8 hours

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Day 3(cont) If someone has a CYP2C19 poor metaboliser genotype, then there is a reduced effect/increased risk major CV event when taking [#clopidogrel](https://twitter.com/search?q=%23clopidogrel); CYP2C19 polymorphism affects around 2% of Caucasians, 4% of Black populations & 14% of Chinese people; genetic tests are available to guide decisions

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Day 4: MOA: [#clopidogrel](https://twitter.com/search?q=%23clopidogrel) is a strong inhibitor of ADP-induced platelet aggregation, via irreversible inactivation of the ADP P2Y12 receptor. This impairs platelet reactivity & amplification of the platelet response. Effect lasts for the lifetime of exposed platelets, approximately 10 days

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Day 5: [#clopidogrel](https://twitter.com/search?q=%23clopidogrel) common ADEs include nose bleeds, bruising, GI haemorrhage, diarrhoea, dyspepsia; uncommon/serious include; arthritis, fever, eye bleeding, agranulocytosis, vertigo, DRESS, SJS (not exhaustive). Caution for elderly where there is increased bleeding risk

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Day 6 Drug-drug interactions. Increased risk of bleeding for all anti-coagulants/platelets, NSAIDs, SSRIs. The metabolism process means issues of liver enzyme variations by inducers (increased production of metabolite, so more effect) e.g rifampicin, as well as inhibitors (reduced drug levels) e.g some PPIs, fluconazole, carbamazepine (not exhaustive)

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Day 7: [#clopidogrel](https://twitter.com/search?q=%23clopidogrel) is the preferred agent post TIA/ischaemic stroke as monotherapy, or combined with dipyridamole or aspirin. The irreversible effect impacts for platelet lifespan, hence drug is usually stopped 7 days pre-surgery, where appropriate, re CVS condition & procedure

CPD: in addition to the tweets, read the BNF treatment summary on Antiplatelet drugs, as well as the monograph on clopidogrel. The SPC for clopidogrel contains useful information about undesirable effects and drug interactions, as well as genetic variations and their relevance.

<https://bnf.nice.org.uk/treatment-summary/antiplatelet-drugs.html>

<https://bnf.nice.org.uk/drug/clopidogrel.html>

<https://www.medicines.org.uk/emc/product/5207/smpc#gref>

1. Clopidogrel is a prodrug

TRUE or FALSE

1. The effect of clopidogrel on platelets is reversible, once the drug concentration drops

TRUE or FALSE

1. Which of the following is true?
2. Clopidogrel cannot be combined with other antiplatelet agents because of the risk of bleeding
3. It is possible to be allergic to clopidogrel
4. Clopidogrel is not used to manage atrial fibrillation
5. Mostly renal excretion means clopidogrel cannot be used in any stage of renal impairment
6. Which of the following is TRUE?
7. Clopidogrel is broken down in the liver by one major step to release the active metabolite
8. The clopidogrel metabolite has equal activity to the parent drug
9. Only one CYP450 family is involved in metabolism
10. The most important CYP450 family for clopidogrel breakdown is CYP2C19
11. Genetics are important for effective clopidogrel use because if you are a poor metaboliser, you will have higher drug levels and may develop a bleeding complication

TRUE or FALSE

1. Clopidogrel should be used with caution in people who are at increased risk of bleeding, as this drug prolongs bleeding time

TRUE or FALSE

1. Clopidogrel works on a different platelet communication system to aspirin, which means the drugs can work synergistically

TRUE or FALSE

1. Which of the following is a common side-effect of clopidogrel?
2. Bruising
3. Colitis
4. Rash
5. Thrombotic thrombocytopenic purpura

9.Fluconazole is an example of a drug which will inhibit liver enzyme conversion to the active metabolite of clopidogrel and result in reduced drug levels and loss of therapeutic effect

TRUE or FALSE

10.The best proton pump inhibitor to use with clopidogrel is omeprazole

TRUE or FALSE