BNSSG Shared Care Guidance

Section 1: Heading

Drug	Clopidogrel
Amber *one month*	
Indication	Anti-platelet in paediatric cardiology patients (PDA stents excluded)

Section 2: Treatment Schedule

Usual dose and frequency of administration *(Please indicate if this is licensed or unlicensed and any relevant dosing information)*	0.2mg/kg once daily (max 75mg) Greater or equal to 50kg 75mg od
Route and formulation	75mg tablets 25mg/5ml oral liquid (unlicensed special)-nationally recognised standardised strength[Local pharmacies can check brand used by BRHC] [only use the 5mg/5ml generally for PDA stents due to low weight of patients and measuring dose-those patients are excluded]. For the indication of PDA stents, this remains TLS Red.
Duration of treatment	As per cardiac specialist

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate

Liver function test
Full blood count, urea & electrolytes
Clotting factors

Subsequent tests - where appropriate *(Please indicate who takes responsibility for taking bloods and interpreting results)*

Test	Frequency	Who by	Action/management
Liver function tests	annually	Secondary Care	Avoid in severe hepatic impairment. Contact cardiac specialist for advice if abnormal.

FBC	annually	Secondary Care	Contact cardiac specialist for advice if results are abnormal
Urea and electrolytes	annually	Secondary Care	Contact cardiac specialist for advice if results are abnormal
Clotting factors	annually	Secondary Care	Contact cardiac specialist for advice if results are abnormal

Section 4: Side Effects

Please list only the most pertinent side effects and management. Please provide guidance on when the GP should refer back to the specialist. For everything else, please see BNF or SPC.

Side effects and management

Side effect	Frequency/severity	Action/management
Bleeding: haemorrhage (intracranial, GI), melaena, haematuria, hematemesis, haematochezia, epistaxis	Common Severe	For emergencies go to A&E and/or call 999. Cardiac team to review
GI disturbances: diarrhoea, constipation, nausea, dyspepsia, gastric ulcer	Common	Monitor, treat as appropriate and contact cardiac specialist if severe
Liver dysfunction: yellowing of eyes and/or skin	Severe Very rare	Go to A&E and/or call 999. Cardiac team to review
Bone marrow suppression	Uncommon Severe	Go to A&E and/or call 999. Cardiac team to review
Anaphylaxis	Severe	Go to A&E and/or call 999. Cardiac team to review

Referral back to specialist

See above

Section 5: Other Issues

(e.g. Drug Interactions, Contra-indications, Cautions, Special Recommendations)

Please list only the most pertinent action for GP to take (For full list please see BNF or SPC)

Issues

<u>Drug interactions</u>

- Medicines that also increase the risk of bleeding: NSAIDs, anticoagulants, SSRIs, glycoprotein IIb/IIIa inhibitors, Cox-2 inhibitors, thrombolytics
- Omeprazole and esomeprazole can reduce the efficacy of clopidogrel
- Inducers of CYP2C19 (rifampicin)
    - Clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicinal products that induce the activity of this enzyme would be expected to result in increased drug levels of the active metabolite of clopidogrel.
- Inhibitors of CYP2C19 (omeprazole, esomeprazole, fluvoxamine, fluoxetine, voriconazole, fluconazole, carbamazepine)
    - Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicinal products that inhibit the activity of this enzyme would be expected to result in reduced drug levels of the active metabolite of clopidogrel.

	• Montelukast – levels may be increase by clopidogrel
	• Opioids have the potential to delay gastric emptying which may reduce the absorption of clopidogrel
	
	Contra-indications
	• Active bleeding, e.g. peptic ulcer or intracranial haemorrhage
	• Hypersensitivity to the ingredients. Some formulations contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine
	• Severe hepatic impairment
	
	Cautions
	• Discontinue 7 days before elective surgery/cardiac catheter procedures
	• Renal impairment
	• Moderate hepatic impairment
	• Poor CYP2C19 metabolisers
	• Bleeding and haematological disorders:
	  ○ Recent ischaemic stroke
	  ○ Acquired haemophilia
	  ○ Thrombotic thrombocytopenic purpura (TTP)
	
	Special Recommendations
	Usually used in combination with aspirin. Consider gastro-protection for dual anti-platelets using lansoprazole. Omeprazole is not advised because it reduces the efficacy of clopidogrel

Reminder to ask patient about specific problems	See above

Section 6: Advice to the patient

Advice for prescribing clinician to inform patient

1. Note-we generally don't recommend crushing these but can do if liquid unavailable.
   For crushing and dispersing tablets: place the tablet in mortar and crush to a fine powder using the pestle. Add a few millilitres of water and mix to form a paste. Add up to 15ml of water and mix thoroughly ensuring that there are no large particles of tablet. Draw up the required volume into a syringe and administer to child either orally or via an enteral tube. For administering a whole tablet: Add another 15ml of water to the mortar and stir to ensure that any remaining drug is rinsed from the container. Draw this water into the syringe and also flush this via the feeding tube – this will rinse the mortar and syringe and ensure that the total dose is administered.
2. Discontinue clopidogrel 7 days prior to surgical or cardiac catheter procedures in discussion with surgical/interventional team
3. It might take longer than usual to stop bleeding and bruising more easily. Report unusual/excessive bleeding. Be careful when doing activities that might cause an injury or a cut. Always wear a helmet when cycling. Wear protective gloves when you use sharp objects like scissors, knives, and gardening tools. Use an electric razor instead of wet shaving, and use a soft toothbrush and waxed dental floss to clean your teeth. See a doctor if you're worried about any bleeding.
4. Indigestion or heartburn – take clopidogrel a few minutes before or after a meal. If the indigestion does not go away, it could be a sign that you have a stomach ulcer. Talk to your doctor, they may prescribe something to protect your stomach or switch you to a different medicine.
5. Diarrhoea – drink lots of fluids, such as water or squash, to avoid dehydration. Speak to a pharmacist if you have signs of dehydration, such as peeing less than usual or having dark, strong-smelling pee. Do not take any other medicines to treat diarrhoea without speaking to a pharmacist or doctor
6. Tell your pharmacist or doctor if you start giving other medicines, including herbal remedies, vitamins or supplements.

Section 7: Generic principles of shared care for SECONDARY CARE

Please do not amend.

Core responsibilities

1. Initiating treatment and prescribing for the length of time specified in **section 1.**
2. Undertaking the clinical assessment and monitoring for the length of time specified in **section 1** and thereafter undertaking any ongoing monitoring as detailed in **section 3.**
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. if blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of drug specified in **section 1.**
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see **section 5.**

Section 8: Generic principles of shared care for PRIMARY CARE

Please do not amend.

Core responsibilities

1. Responsible for taking over prescribing after the length of time specified in **section 1.**
2. Responsible for any clinical assessment and monitoring if detailed in **section 3** after the length of time specified in **section 1.**
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see **section 5.**

Section 9: Contact Details

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Section 10: Document Details

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Section 11: Collaboration

All shared care protocols should be BNSSG wide where possible. Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

Section 12: References

Please list references

1. Evelina Formulary
2. British National Formulary for Children
3. Clopidogrel SPC: https://www.medicines.org.uk/emc/product/5207/smpc#gref
4. Local UHBW guideline: Anticoagulation on PICU and Dolphin Ward for cardiac patients
5. NICE CKS: https://cks.nice.org.uk/topics/antiplatelet-treatment/prescribing-information/clopidogrel/#:~:text=Monitor%20blood%20glucose%20concentrations%20closely,The%20manufacturer%20discourages%20concurrent%20use.