

## **Clopidogrel bisulfate (Plavix ®) (Thienopyridine) Therapy Guidelines**

### **Drug Effect**

A standard dose of 75 mg/day results in 50% to 60% platelet inhibition, which reaches a steady state 4 to 7 days after initiation. Platelet function returns to normal 5 to 7 days after the last dose (Lip, 2005; VAMC, 2001).

### **Mechanism of Action**

Clopidogrel bisulfate inhibits platelet aggregation by selectively and irreversibly inhibiting the binding of adenosine diphosphate (ADP) to its platelet receptor and by the subsequent inactivation of ADP-mediated glycoprotein GPIIb/IIIa complex. Since this action is irreversible, platelets are affected for the remainder of their lifespan. The average platelet's lifespan is 7 to 10 days with about 10% of circulating platelets being replaced every 24 hours. The plasma half-life of clopidogrel is 2–50 hours. These times are 2-3 times longer in the older patient.

### **Indications – (Usually in conjunction with aspirin)**

- Unstable angina
- Acute coronary syndrome (NSTEMI/STEMI)
- Post PCI/Stent placement
- Documented aspirin intolerance/allergy in patient requiring antiplatelet therapy
- Intracranial/carotid stent
- Brachytherapy
- Peripheral stent (renal, iliac, femoral etc.)
- Cerebrovascular disease with recurrent symptoms in patients refractory to Aspirin/Dipyridamol

*Note: Use of Clopidogrel in patients with prior stroke carries a higher risk of bleeding. For patients with prior strokes, Aspirin alone or Aspirin and Dipyridamol should be considered as first line.*

### **Contraindications**

- Active bleeding
- Hypersensitivity to clopidogrel or any component of the product

### **Variability of response to Clopidogrel**

- “Resistance” may occur in up to 10% of cases. The prevalence and clinical relevance are unknown.

### **Combined Therapy (Clopidogrel + Aspirin) Compared to Monotherapy (Clopidogrel)**

- No substantial clinical benefit in reduction of ischemic stroke demonstrated
- Increase in major bleeding complications

### **Clopidogrel and risk of perioperative bleeding**

- At present, there is no standard laboratory method available to predict the risk of perioperative bleeding in patients taking Clopidogrel. A rapid assessment system is presently being evaluated.
- All members of the medical staff, nursing staff and allied health professionals who perform invasive or surgical procedures or care for patients taking these medications must be aware of the potentially catastrophic risks of premature discontinuation of thienopyridine therapy as well as the possibility of periprocedural bleeding. Professionals who perform these procedures should contact the patient's cardiologist if issues regarding the patient's antiplatelet therapy are unclear, to discuss optimal patient management therapy.

*Note: Routine coagulation parameters will not identify patients at higher risk of bleeding peri-operatively.*

### **ELECTIVE Surgery - Preoperative management of patients on Clopidogrel**

- Elective surgery, with an expected high risk of bleeding should be delayed at least **six weeks** in patients after implantation of a bare metal stent and **twelve months** after implantation of a drug eluting stent to allow uninterrupted Plavix therapy. Low bleeding risk surgeries can be safely performed on Plavix.
- Clopidogrel should be held at least 5 days prior to planned surgery.
- For patients with drug eluting stents who are to undergo subsequent procedures that mandate discontinuation of thienopyridine therapy, aspirin should be continued if at all possible and the thienopyridine restarted as soon as possible after the procedure because of concerns about peri-operative stent thrombosis beyond the recommended twelve months.
- For selected high-risk patients, “bridging” therapy with a short – acting anti-platelet agent may be indicated, although no data to support its use is available.
- Contact the patient’s cardiologist if issues regarding the patient’s antiplatelet therapy are unclear, to discuss optimal patient management strategy.

**Any patient with a coronary stent who develops chest pain or ST segment elevation in the peri-operative setting should be suspected of having acute stent thrombosis and treated as a “Code White”. Immediate cardiac catheterization with percutaneous intervention is essential to prevent a large myocardial infarction or death.**

### **EMERGENT Surgery or Acute bleeding management of patients on Clopidogrel**

- If an emergent surgery or invasive procedure is required in patients with a drug eluting stent within the first year of implantation or within the first 6 weeks of implantation of a bare metal stent the risk of stent thrombosis is elevated if dual anti platelet therapy is withheld for any duration.
- If emergent surgery must be performed on dual antiplatelet therapy, anticipate more bleeding.
- In the event of uncontrollable bleeding, obtain a STAT Transfusion Medicine consult.
- Involve a cardiologist/interventionalist early.
- Watch for cardiovascular complications peri-procedurally – Risk of stent thrombosis is the highest intra and post –operative/post procedural period.

### **Postoperative management of patients on Clopidogrel**

- Restart Clopidogrel (dual antiplatelet therapy) after the first postoperative day or as soon as clinically possible, if held preoperatively
- A loading dose of 300 to 600 mg may be considered for rapid inhibition of platelet function.
- Surveillance for bleeding and stent thrombosis should continue in early post-operative period.
- Telemetry monitoring is suggested.