VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

PLAVIX® (clopidogrel)

Effective Date: 10/27/05
Date Developed: 9/9/05 by C. Wilhelmy MD
Last Approval Date: 1/26/16, 1/24/17, 1/22/19, 2/18/20, 2/2/21, 2/1/22, 1/31/23
(Archive Date: 1/1/18)
Unarchived Date: 1/22/19 (Formulary Exclusion – For Exception Review)

Clopidogrel is an antiplatelet agent. It blocks the ADP receptors, which prevents fibrinogen binding at that site and thereby reduce the possibility of platelet adhesion and aggregation due to inactivation of the GPIIB/IIIa receptor complex. It thereby reduces atherosclerotic events (myocardial infarction, stroke, vascular deaths) in patients with atherosclerosis documented by recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease.

Pre-Authorization Criteria

Acute coronary syndrome:

ST-segment elevation myocardial infarction: To reduce the rate of myocardial infarction (MI) and stroke in conjunction with aspirin in patients who are to be managed medically.

Non-ST-segment elevation acute coronary syndromes(unstable angina/non-ST-elevation MI): To decrease the rate of MI and stroke in conjunction with aspirin in patients who are to be managed medically or with coronary revascularization.

Recent myocardial infarction, Recent ischemic stroke, or established peripheral atherosclerotic disease: To reduce the rate of MI and stroke in patients with a history of recent MI, recent stroke, or established peripheral atherosclerotic disease.

Off-Label Use:

Symptomatic carotid artery atherosclerosis; Carotid artery stenting; Coronary artery bypass graft surgery; Percutaneous coronary intervention for stable ischemic heart disease; Stable ischemic heart disease; Thromboprophylaxis (Transcatheter aortic valve replacement; Transcatheter mitral valve repair with MitraClip device)

DOSING: ADULTS

Recent MI, recent stroke, or established arterial disease: Oral: 75 mg once daily.

Acute coronary syndrome:

Unstable angina, non-ST-segment elevation myocardial infarction (UA/NSTEMI): Initial: 300 or 600 mg loading dose, followed by 75 mg once daily for at least 1 month and ideally up to 12 months (in combination with aspirin 75-162 mg once daily indefinitely) (Wright, 2011)

ST-segment elevation myocardial infarction (STEMI): 75 mg once daily (in combination with aspirin 162-325 mg initially followed by 81-162 mg/day). ~~**Note:**~~

NOTE*:*—If using fibrinolytic therapy for reperfusion: initiate therapy with a 300 mg loading dose

NOTE:**—**If using percutaneous coronary intervention for reperfusion (alternative agent) (off-label use): : initiate therapy with a 600 mg loading dose

Prevention of coronary artery bypass graft closure (saphenous vein): Aspirin-allergic patients (unlabeled use) [*Chest* guidelines, 2008]: Loading dose: 300 mg administered 6 hours following procedure; maintenance: 75 mg/day

Duration of therapy*:* Clopidogrel plus aspirin (dual antiplatelet therapy [DAPT]) should be continued for ≥12 months unless bleeding is a concern. If there have been no major bleeding complications after 12 months, continuation of DAPT may be considered.

MONITORING PARAMETERS — Signs of bleeding; hemoglobin and hematocrit periodically.

DRUG INTERACTIONS — Substrate (minor) of CYP1A2, 3A4; Inhibits CYP2C8/9 (weak). ,

PATIENT EDUCATION — Report any unusual or prolonged bleeding or fever; inform your prescriber before starting any new medications, changing your diet, or undergoing any procedures that may be associated with a risk of bleeding.

Although unlikely, serious bleeding in the stomach, gut, eyes, or brain may occur. Also, clopidogrel can rarely cause a very serious blood disorder (thrombotic thrombocytopenic purpura-TTP). Symptoms may appear any time after starting this medication. Get medical help right away if any of these symptoms occur: severe stomach/abdominal pain, uncontrolled bleeding from gums or nose, bloody/black stools, confusion, fever, extreme skin paleness, purple skin patches, fainting, fast heartbeat, sudden severe headache, unusual weakness/tiredness, vomit with blood or that looks like coffee grounds, slurred speech, vision changes, seizures, yellowing eyes/skin, bloody/red/pink/dark urine, change in amount of urine.

REFERENCES

1. A Randomized, Blinded, Trial of Clopidogrel Versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE). CAPRIE Steering Committee. Lancet 1996; 348:1329.
2. Antman, EM, Anbe, SC, Alpert, JS, et al. ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction - Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). Circulation 2004; 110:588-636. Available at: http://www.circulationaha.org/cgi/content/full/110/5/588. Last accessed August 26, 2004.
3. Bal dit Sollier, C, Mahe, I, Berge, N, et al. Reduced Thrombus Cohesion in an ex vivo Human Model of Arterial Thrombosis Induced by Clopidogrel Treatment: Kinetics of the Effect and Influence of Single and Double Loading-Dose Regimens. Thromb Res 2003; 111:19.
4. Berger, PB, Bell, MR, Rihal, CS, et al. Clopidogrel Versus Ticlopidine After Intracoronary Stent Placement. J Am Coll Cardiol 1999; 34:1891.
5. Bertrand, ME, Rupprecht, HJ, Urban, P, et al. Double-Blind Study of the Safety of Clopidogrel With and Without a Loading Dose in Combination With Aspirin Compared With Ticlopidine in Combination With Aspirin After Coronary Stenting. Circulation 2000; 102:624.
6. Braunwald, E, Antman, EM, Beasley, JW, et al. ACC/AHA 2002 Guideline Update for the Management of Patients With Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction - Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol 2002; 40(7):1366-74. Available at: http://www.acc.org/clinical/guidelines/unstable/incorporated/index.htm. Accessed May 20, 2003. 7. Kastrati, A, Mehilli, J, Schuhlen, H, et al. A Clinical Trial of Abciximab in Elective Percutaneous Coronary Intervention After Pretreatment With Clopidogrel. N Engl J Med 2004; 350:232.
8. Lange, RA, Hillis, LD. Antiplatelet Therapy for Ischemic Heart Disease. N Engl J Med 2004; 350:277.
9. Lidell, C, Svedberg, LE, Lindell, P, et al. Clopidogrel and Warfarin: Absence of Interaction in Patients Receiving Long-Term Anticoagulant Therapy for Non-Valvular Atrial

Fibrillation. Thromb Haemost 2003; 89:842.
10. Mehta, SR, Yusuf, S, Peters, RJ, et al. Effects of Pretreatment With Clopidogrel and Aspirin Followed by Long-Term Therapy in Patients Undergoing Percutaneous Coronary Intervention: The PCI-CURE Study. Lancet 2001; 358:527.
11. Mishkel, GJ, Aguirre, FV, Ligon, RW, et al. Clopidogrel as Adjunctive Antiplatelet Therapy During Coronary Stenting. J Am Coll Cardiol 1999; 34:1884.
12. Moussa, I, Oetgen, M, Roubin, G, et al. Effectiveness of Clopidogrel and Aspirin Versus Ticlopidine and Aspirin in Preventing Stent Thrombosis After Coronary Stent Implantation. Circulation 1999; 99:2364.
13. Seventh ACCP Consensus Conference on Antithrombotic and Thrombolytic Therapy. Chest
2004; 126(3 Suppl):172.
14. Steinhubl, SR, Berber, PB, Mann, JT, et al. Early and Sustained Dual Oral Antiplatelet Therapy Following Percutaneous Coronary Intervention. A Randomized Controlled Trial. JAMA 2002; 288:2411.
15. Yusef, S, Zhao, F, Mehta, SR, et al. Effects of Clopidogrel in Addition to Aspirin in Patients With Acute Coronary Syndromes Without ST-Segment Elevation. N Engl J Med 2001; 345:494.
16. Frontera JA, Lewin JJ 3rd, Rabinstein AA, et al; Guideline for reversal of antithrombotics in intracranial hemorrhage: a statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. Neurocrit Care. 2016;24(1):6-46.
17. Brouwer J, Nijenhuis VJ, Delewi R, et al. Aspirin with or without clopidogrel after transcatheter aortic-valve implantation. N Engl J Med. 2020;383(15):1447-1457. doi:10.1056/NEJMoa2017815
18. Basra SS, Tsai P, and Lakkis NM. Safety and Efficacy of antiplatelet and antithrombotic therapy in acute coronary syndrome patients with chronic kidney disease. J Am Coll Cardiol. 2011;58(22):2263-2269.
19. Adams DH, Popma JJ, Reardon MJ, et al; US CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014;370(19):1790-1798. doi: 10.1056/NEJMoa1400590
20. Alonso-Coello P, Bellmunt S, McGorrian C, et al. Antithrombotic therapy in peripheral artery disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2)(suppl):e669S-e690S. doi: 10.1378/chest.11-2307
21. Amsterdam EA, Wenger NK, Brindis RG, et al; ACC/AHA Task Force Members. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Revision History:

Date Revised: 10/17/11 by A. Reeves MD
Date Reviewed/No Updates: 4/2/12; 1/16/13 by A. Reeves, MD
Date Approved by P&T Committee: 10/27/05; 10/25/11; 4/24/12; 1/29/13
Date Reviewed/No Updates: 1/28/14 by C. Sanders MD
Date Approved by P&T Committee: 1/28/14
Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD
Date Approved by P&T Committee: 1/27/15
Date Reviewed/No Updates: 1/26/16 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/26/16
Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/24/17
Date Reviewed/Archived: 1/1/18 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/23/18
Date Reviewed/No Updates/Unarchived: 1/22/19 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/22/19
Date Reviewed/No Updates: 2/18/20 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 2/18/20
Date Reviewed/No Updates: 2/2/21 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 2/2/21
Date Reviewed/Updated: 8/3/21 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 8/3/21
Date Reviewed/No Updates: 2/1/22 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 2/1/22
Date Reviewed/No Updates: 1/31/23 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/31/23

Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/1/18	No	Catherine Sanders, MD; Robert Sterling, MD	Archived – excluded from the Formulary effective 1/1/18
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Unarchived – Formulary Exclusion – For Exception Review Use Only Annual Review
2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/2/21	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
8/3/21	Yes	Howard Taekman, MD; Robert Sterling, MD	Updated preauthorization criteria, duration of therapy and references. Formatting changes
2/1/22	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
1/31/23	No	Howard Taekman, MD; Robert Sterling, MD	Annual review