INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Antiplatelet Therapies***
-January 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a focused drug class review of oral antiplatelet agents. The IHS National Core Formulary (NCF) currently lists the antiplatelet agents, aspirin and clopidogrel. This marks the second review of antiplatelet agents, with the most recent completed in 2015. This evaluation provided updated literature findings from aspirin, cilostazol, clopidogrel, dipyridamole, dipyridamole/aspirin, prasugrel, and ticagrelor. Following the clinical review and analysis, the NPTC made **no modifications to the NCF.**

Cardiovascular disease (CVD) is the leading cause of death among American Indians and Alaska Natives.[1,2] Globally, CVD accounts for approximately 17.9 million deaths annually, with 85% resulting from heart attack or stroke. In the United States, CVD is responsible for 1 in every 5 deaths, with an occurrence of one death every 33 seconds and an annual economic burden of about $252.2 billion.[3,4] Among American Indians/Alaska Natives, CVD contributes to 15.5% of all deaths and demonstrates a 12% higher prevalence compared to other racial/ethnic groups - with underreporting estimated at up to 20%, alongside risk factors such as a 20% higher smoking rate and 10% lower hypertension diagnosis.[1,2]

Discussion:

Recent literature reinforces the critical role of antiplatelet therapy in both primary and secondary prevention of CVD. Aspirin continues to be the cornerstone of therapy. Multiple studies have demonstrated that aspirin use is associated with a 10–15% reduction in recurrent cardiovascular events in secondary prevention [HR 0.76 (95% CI: 0.69–0.84; p<0.001)], clearly underscoring its statistically significant benefit.[5] In primary prevention, low-dose aspirin may offer modest benefits in carefully selected high-risk patients; however, these benefits must be balanced against an increased bleeding risk.[6]

In acute coronary syndrome (ACS) settings, P2Y12 inhibitors play a pivotal role. Although clopidogrel remains widely used due to its established efficacy, safety and lower cost, emerging evidence suggests that newer agents - ticagrelor and prasugrel - offer additional benefit.[7,8] Some studies have reported that ticagrelor may provide up to a 20% relative reduction in composite ischemic endpoints compared with clopidogrel, although with a 15–25% increased risk of significant bleeding. This enhanced efficacy makes these agents particularly attractive in patients at lower bleeding risk.

A key aspect of antiplatelet management is the appropriate duration of therapy. Recent studies have explored abbreviated dual antiplatelet therapy (DAPT) regimens, particularly for patients undergoing percutaneous coronary intervention (PCI) who require concomitant oral anticoagulant (OAC) therapy or who are at elevated bleeding risk.[9] Evidence indicates that a shortened DAPT duration (≤6 weeks) may reduce bleeding complications by up to 30% without a significant compromise in major adverse cardiovascular event (MACE) outcomes. This approach is especially appropriate for patients with a high bleeding risk profile or where prolonged DAPT could lead to adverse events.

Populations with chronic kidney disease (CKD) are especially vulnerable to both thrombotic and bleeding complications.[8] In CKD cohorts, antiplatelet therapy has been associated with a 12–15% reduction in myocardial infarction risk; however, this benefit is offset by an observed 35% increase in major bleeding events (RR 1.35; 95% CI: 1.10–1.65) which underscores the need for individualized therapy decisions in this high-risk group.

Additional agents such as cilostazol and dipyridamole retain niche roles. Cilostazol has been shown to improve walking distance in patients with intermittent claudication by an average of 26–40 meters.[11] However, a higher incidence of headaches and other side effects often limits its use. This emphasizes the importance of patient-specific risk–benefit assessments when considering alternative antiplatelet agents.

Overall, the cumulative evidence indicates that while aspirin and clopidogrel remain the mainstay of antiplatelet therapy for most patients, there is a distinct role for newer agents and for tailoring therapy duration in selected populations. Individual patient factors - including ACS status, CKD, bleeding risk, and the need for concomitant anticoagulation - should guide both the choice of antiplatelet agent and the duration of therapy to optimize overall cardiovascular outcomes.

Guideline	Key Points
2023 NICE – CVD Risk Assessment/Reduction	• Emphasizes lifestyle modifications and hypercholesterolemia treatments. • Do not recommend routine aspirin use for primary prevention due to increased bleeding. • Recommendations are based on ARRIVE, ASCEND, and ASPREE trial data.
US Preventive Services Task Force – Aspirin Use to Prevent CVD	• Recommend aspirin for adults 40–59 years with >10% 10-year CVD risk (individualized). • Do not recommend routine aspirin for primary prevention in adults ≥60 years. • Emphasis on weighing cardiovascular benefits against bleeding risk.
2024 ACC/AHA/et. al – Guideline for Lower Extremity PAD	• Recommend antiplatelet therapy for symptomatic PAD (Class I, Level A). • Suggest single antiplatelet therapy (SAPT) with ASA or clopidogrel for stable PAD. • Post-revascularization, combination therapy (aspirin + rivaroxaban) may be considered.
Canadian Cardiovascular Society – Guidelines for PAD	• Strong recommendation for antiplatelet therapy in symptomatic lower extremity PAD. • For high-risk patients, recommend aspirin plus rivaroxaban; for lower-risk patients, single antiplatelet therapy is advised.
NICE – Heart Valve Disease	• Recommend aspirin as first-line; if not tolerated, consider clopidogrel. • Does not recommend dual antiplatelet therapy (DAPT) due to elevated bleeding risk.
AHA/ACC/et. al. – Chronic Coronary Disease	• Emphasizes the use of aspirin in all patients without contraindications. • Combination antiplatelet therapy may be indicated in acute coronary syndrome (ACS).
ACC/AHA/et. al. – Coronary Artery Revascularization	• Aspirin is recommended for all patients without contraindications. • Dual antiplatelet therapy is indicated for patients undergoing percutaneous coronary intervention (PCI) with defined duration guidelines.
AHA/ASA – Stroke Prevention	• Recommend antiplatelet therapy (aspirin, clopidogrel, or their combination) to reduce stroke recurrence. • Avoid prolonged DAPT or triple therapy to minimize bleeding risk.
US Preventive Services Task Force – Aspirin Use to Prevent Preeclampsia	• Recommend 81 mg daily aspirin for high-risk pregnant women starting after 12 weeks gestation. • Shown to reduce risk of preeclampsia and lower perinatal mortality.
2021 ESC – CVD Prevention	• Recommend ASA 81 mg daily for secondary prevention; clopidogrel as an alternative in select cases. • Stresses individualized risk assessment to guide therapy choice.
2023 ESC – Acute Coronary Syndromes	• Advocate pretreatment with P2Y12 inhibitors for patients undergoing primary PCI. • Provides specific recommendations on DAPT duration and resumption post-CABG.
2024 ESC – Atrial Fibrillation	• For atrial fibrillation patients undergoing PCI, recommend short-term triple therapy followed by dual therapy. • Advise consideration of reduced DOAC dosing when used in combination with antiplatelet therapy in high-bleeding risk patients.

Findings:

Based on the current body of evidence and guideline recommendations, the NPTC recommended no changes to the NCF at this time. However, individual sites may consider selective use of ticagrelor or prasugrel in specific patient populations where enhanced platelet inhibition is indicated. Overall, the benefit–risk profiles support the continued reliance on aspirin and clopidogrel as first-line therapies, with the flexibility to tailor antiplatelet therapy based on individual patient risk factors and clinical context.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

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