INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Aspirin (Primary & Secondary Prevention)***
-August 2024-

Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) conducted a comprehensive review of clinical practice guidelines concerning the use of aspirin in primary and secondary prevention during its Summer meeting in August 2024. Medication(s) currently listed on the National Core Formulary (NCF) relevant to these conditions include aspirin and clopidogrel. Following review, **no modifications** were made to the NCF.

Discussion:
Cardiovascular diseases (CVD) remain the leading cause of death among American Indians and Alaska Natives (AI/AN), and colorectal cancer (CRC) is the third leading cause of cancer-related deaths. The disproportionate burden of CVD and cancer in the AI/AN population underscores the importance of preventive measures, including pharmacologic interventions such as aspirin.

Aspirin has been investigated for its role in primary prevention, particularly in reducing the risk of a first cardiovascular event. However, results from key clinical trials have been mixed, demonstrating both potential benefits and risks. In a study of 12,546 participants at moderate risk for CVD, aspirin (100 mg daily) did not significantly reduce the rate of major cardiovascular events compared to placebo (4.29% vs. 4.48%, p=0.6038).[1] However, there was a notable increase in gastrointestinal bleeding in the aspirin group (0.97% vs. 0.46%, p=0.0007).[1] Another trial, involving 15,480 patients with diabetes but no evident CVD, aspirin use (100 mg daily) resulted in a 12% reduction in serious vascular events compared to placebo (8.5% vs. 9.6%; rate ratio [RR] 0.88; 95% CI 0.79-0.97; p=0.01).[2] Major bleeding events however were also more common in the aspirin group (4.1% vs. 3.2%; RR 1.29; 95% CI 1.09-1.52; p=0.003).[2]

One of the more foundational trials for aspirin use included 19,114 healthy elderly participants aged 70 and older (or 65+ for Black and Hispanic participants in the United States). Aspirin (100 mg daily) did not reduce the rate of CVD-related events compared to placebo (10.7 events per 1,000 person-years vs. 11.3 events per 1,000 person-years; HR 0.95; 95% CI 0.83-1.08).[3] Notably, aspirin increased the risk of major hemorrhage (8.6 events per 1,000 person-years vs. 6.2 events per 1,000 person-years; HR 1.38; 95% CI 1.18-1.62).[3]

Aspirin has shown potential in reducing cancer mortality, particularly colorectal cancer. For instance, in a large cohort study of 146,152 adults aged 55 to 74 years, aspirin use 1-3 times per month was associated with a reduction in all-cause mortality (HR 0.84; 95% CI 0.80-0.88) and colorectal cancer mortality (HR 0.71; 95% CI 0.61-0.84).[4] This protective effect was more pronounced in individuals with a body mass index of 20 or higher.

Given the mixed results, **aspirin is generally not recommended for primary prevention of CVD** due to the increased risk of bleeding, except in specific high-risk populations where the benefit may outweigh the risk. For cancer prevention, particularly colorectal cancer, aspirin use may be considered in select populations, particularly those at high risk, but must be carefully weighed against bleeding risks.

For individuals with a history of cardiovascular events, aspirin is strongly recommended for secondary prevention. Key trials highlight aspirin's efficacy in reducing recurrent events: A large meta-analysis of over 200,000 patients demonstrated a 25% relative reduction in recurrent cardiovascular events in patients with previous myocardial infarction, stroke, or other vascular disease (event rate reduced from 8.2% to 6.7% per year, p<0.0001).[5] In another trial involving 15,603 patients, the combination of aspirin and clopidogrel did not significantly reduce the risk of major cardiovascular events compared to aspirin alone (6.8% vs. 7.3%, p=0.22).[6] However, the combination therapy significantly increased the risk of moderate-to-severe bleeding (3.7% vs. 2.3%, p<0.001).[7]

Aspirin remains a cornerstone of therapy for secondary prevention in patients with a history of cardiovascular events. The recommended dosage typically ranges from 75 to 162 mg daily. Combination therapy with other antiplatelet agents, such as clopidogrel, should be considered based on individual patient risk factors and clinical judgment.

Findings:
While aspirin provides significant benefits in reducing cardiovascular and cancer-related mortality, particularly in secondary prevention, it also poses risks, especially regarding major bleeding events. These risks necessitate a

personalized approach when considering aspirin for primary prevention. For secondary prevention, aspirin's benefits are well-established, making it a critical component of long-term management for individuals with a history of cardiovascular events. Aspirin's role in prevention must be carefully balanced between its protective effects and associated risks. For primary prevention, careful patient selection is crucial, while for secondary prevention, aspirin remains a recommended therapy.

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.

References:

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