

The following points summarize our position regarding the approved dose range of aspirin in the professional labeling for the secondary prevention of cardiovascular and cerebrovascular events.

Safety and Efficacy

- While all doses of ASA confer some degree of GI bleeding risk, there is no demonstrable difference in the evidence from randomized controlled trials (RCT) and meta-analyses of RCTs among ASA regimens within the low dose range (75-325 mg).
- Different doses of ASA, within this low dose range, have shown variability in impacting thromboxane; thus a range of doses remains necessary to ensure physician's choice and appropriate patient care.
- Disease states such as smoking, diabetes, obesity and others which may modify platelet function and aggregation. Consequently higher doses of ASA may be needed.
- Variable platelet function and aggregation changes under ASA therapy have been observed. With higher doses of ASA, a more uniform inhibition of platelet function can be achieved in individual patients.
- There may be a dose related, non-antiplatelet dependent benefit related to anti-inflammatory and anti-oxidative effects of ASA.

Clinical Trial Evidence

- Few trials have compared ASA doses in a randomized, controlled fashion; in those few trials doses were often outside of the low dose range.
- Meta-analysis data shows there is no meaningful difference in GI safety between ASA regimens within the low dose range.
- Observational evidence may suggest a difference in safety among doses within the low dose range; however, observational evidence is subject to significant confounding. Also, the efficacy data in these same observational studies is inconsistent with one trial even suggesting greater efficacy for higher doses.
- Contemporary stroke trials have used higher doses (≥ 650 mg daily) of ASA and demonstrated safety and efficacy; thus supporting the acceptance of higher doses in certain secondary prevention populations.

Guidelines and Practice

- AHA/ACC guidelines support the entire dose range in both recurrent MI and stroke prevention.
- Guidelines support the higher end of the dose range in other CV indications such as acute MI and post procedure prophylaxis.
- Physician survey data demonstrate utilization and support for 325 mg regimen.