



Information for Healthcare Professionals

Concomitant Use of Ibuprofen and Aspirin

New Information [9/2006] - Concomitant Use of Ibuprofen and Aspirin:

Ibuprofen can interfere with the anti-platelet effect of low dose aspirin (81 mg per day), potentially rendering aspirin less effective when used for cardioprotection and stroke prevention. Healthcare professionals should advise consumers and patients regarding the appropriate concomitant use of ibuprofen and aspirin.

This information reflects FDA's current analysis of data available to FDA concerning these drugs. FDA intends to update this sheet when additional information or analyses become available.

To report serious adverse events associated with the use of these drugs, please contact the FDA MedWatch program using the contact information at the bottom of this sheet.

Considerations

Health care professionals should consider:

- Counseling patients about the appropriate timing of ibuprofen dosing if they are also taking aspirin for cardioprotective effects.
- With occasional use of ibuprofen, there is likely to be minimal risk from any attenuation of the antiplatelet effect of low dose aspirin, because of the long-lasting effect of aspirin on platelets.
- Patients who use immediate release aspirin (not enteric coated) and take a single dose of ibuprofen 400 mg should dose the ibuprofen at least 30 minutes or longer after aspirin ingestion, or more than 8 hours before aspirin ingestion to avoid attenuation of aspirin's effect.
- Recommendations about the timing of concomitant use of ibuprofen and enteric-coated low dose aspirin cannot be made based upon available data.
- Other nonselective OTC NSAIDs should be viewed as having the potential to interfere with the antiplatelet effect of low-dose aspirin unless proven otherwise.
- Prescribing analgesics that do not interfere with the antiplatelet effect of low dose aspirin for high risk populations.

Data Summary

Aspirin is available over-the-counter as a tablet, buffered tablet, effervescent tablet, or caplet in immediate-release formulations and as a tablet in enteric-coated formulations. Individual aspirin doses range from 81 mg to 500 mg.

It has been demonstrated in published and unpublished human ex vivo studies, that ibuprofen interferes with the antiplatelet activity of low dose aspirin (81 mg, immediate release) when they



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are ingested concurrently. The mechanism by which this occurs may be through competitive inhibition of the acetylation site of cyclooxygenase (COX) in the platelet. Both ibuprofen (reversible inhibition) and aspirin (irreversible inhibition) occupy nearby sites on COX, such that the presence of ibuprofen interferes with aspirin binding. Once the ibuprofen releases from the binding site, COX will not be inhibited because some aspirin available to bind will have been excreted. This ibuprofen interference attenuates the expected aspirin-mediated irreversible inhibition of thromboxane B₂ (TXB₂) production and the expected inhibition of platelet aggregation.

There are no clinical endpoint studies conducted specifically to evaluate the interaction. Attenuation of 90% or more of the antiplatelet effect of aspirin has been defined as clinically significant by some investigators. Unpublished single dose trials with ibuprofen 400 mg indicate that interference with aspirin's antiplatelet activity, as measured by TXB₂ levels and platelet activation studies, occurs when ibuprofen is taken within 30 minutes after immediate release aspirin dosing. The interaction also occurs when a single dose of ibuprofen 400 mg is taken 8 hours or less prior to aspirin dosing. At least 8 hours should elapse after ibuprofen dosing, before giving aspirin, to avoid significant interference.

One study showed that the antiplatelet effect of enteric-coated low dose aspirin is attenuated when ibuprofen 400 mg is dosed 2, 7, and 12 hours after aspirin.⁶ FDA is unaware of studies that have looked at the same type of interference by ketoprofen with low dose aspirin, and there are no data looking at nonprescription doses of naproxen. There is at least one study that has suggested that naproxen at higher than nonprescription doses may interfere with aspirin's antiplatelet activity when they are co-administered. Acetaminophen appears to not interfere with the antiplatelet effect of low dose aspirin, and FDA is unaware of any interference by narcotic analgesics.

Implications

The clinical implication of the interference by ibuprofen on the anti-platelet effect of aspirin is unclear. However, it is potentially important because the cardioprotective effect of aspirin, when used for secondary prevention of myocardial infarction, could be decreased or negated.



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