Alerts and Recalls

Generic Name (Trade Nameâ€”Company)	**Uses**/Notes
July 9, 2018	
Celecoxib	FDA approved a labeling supplement for celecoxib, a COX-2 selective NSAID, to include results from a postmarketing cardiovascular outcomes trial that found that at the lowest dose, cardiovascular safety of celecoxib was similar to that of moderate doses of naproxen and ibuprofen. Concerns about the cardiovascular thrombotic risk of COX-2 selective NSAIDs emerged in the early 2000s. Following an FDA Advisory Committee meeting held in 2005, which considered data from large clinical outcome trials in a wide range of indications and epidemiology studies of several individual NSAIDs, FDA concluded that the risk for cardiovascular thrombotic events was present for both COX-2 selective NSAIDs and nonselective NSAIDs. The Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen (PRECISION) trial was conducted to address the remaining concerns about the relative cardiovascular safety of COX-2 selective NSAIDS and nonselective NSAIDs. PRECISION was a large, randomized, double-blind controlled trial that began in 2006. Ninety percent of the patients enrolled in the trial had osteoarthritis, and the remaining 10% had rheumatoid arthritis. Results of the PRECISION trial demonstrated that celecoxib at the lowest approved dose of 100 mg twice daily is noninferior to (or no worse than) ibuprofen dosed in the range of 600 mg to 800 mg three times daily or naproxen dosed in the range of 375 mg to 500 mg twice daily on a composite cardiovascular endpoint consisting of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke. In an ambulatory blood pressure monitoring study that was part of the larger PRECISION trial, celecoxib dosed at 100 mg twice daily showed little effect on average 24-hour systolic blood pressure (SBP), whereas ibuprofen dosed in the range of 600 mg to 800 mg three times daily and naproxen dosed in the range of 375 mg

(Celebrex—Pfizer)

At lowest dose, CV safety similar to moderate doses of naproxen, ibuprofen

to 500 mg twice daily increased average 24-hour SBP by 3.7 mmHg and 1.6 mmHg, respectively.

Too few patients received higher doses of celecoxib to evaluate the risk of cardiovascular events or the effect on blood pressure for doses greater than 100 mg twice daily. The cardiovascular risks of the NSAID class are dose dependent; therefore, the results for celecoxib 100 mg twice daily on the composite cardiovascular endpoint and the lack of effect on SBP cannot be extrapolated to dosing regimens using the higher strengths of celecoxib (200 mg or 400 mg).

Patients with recent cardiovascular events such as acute MI, coronary revascularization, or coronary stent placement were not studied in the PRECISION trial. NSAID class labeling warns against use of NSAIDs in such patients.

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