FDA links once-promising pain drugs to bone decay

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Some of the world's largest drugmakers will face an uphill battle next week in their bid to revive a class of experimental arthritis drugs that have been sidelined by safety concerns for nearly two years.

The Food and Drug Administration says there is a clear association between the nerve-blocking medications and incidences of joint failure that led the agency to halt studies of the drugs in 2010. However, the agency also notes that those side effects were less common when the drugs were used at lower doses, potentially leaving the door open for future use. The agency released its safety analysis ahead of a public meeting next week where outside experts will discuss the drugs' safety.

On Monday, Pfizer Inc., Johnson & Johnson and Regeneron Pharmaceuticals will make their case to continue studies of the drugs, with safety precautions to protect patients.

The request to restart testing is unusual, since drugmakers often abandon research on experimental drugs that appear to have safety issues. However, with more than 50 million U.S. adults diagnosed with arthritis - one in five - the potential multibillion dollar market opportunity may be too big to ignore.

If the drugs eventually win FDA approval though, they may be used for much narrower indications than initially envisioned. The FDA's proposed questions to its experts appear designed to limit any future testing of the drugs.

"Considering what is known thus far about the risks and benefit associated with this class of biologic agents, are there any populations for which further clinical development would be acceptable?" asks one agency discussion question.

Drugmakers once touted the drugs, known as nerve growth factor inhibitors, as a potential breakthrough for treating osteoarthritis, back pain and other chronic pain conditions. For more than a century doctors have treated pain with familiar painkillers like aspirin and Advil, or powerful opiate-based drugs. Both approaches can be problematic. Anti-inflammatory painkillers like Advil can cause stomach bleeding, while opiates carry a high risk of addiction

The injectable nerve-silencing drugs offered a new approach, by blocking proteins that control pain sensations throughout the body.

But problems with the drugs began to emerge in the summer of 2010. Beginning in June, Pfizer halted studies of its experimental injection tanezumab in patients with osteoarthritis, low back pain and diabetic nerve pain. The action was requested by the Food and Drug Administration, after researchers reported that osteoarthritis actually worsened in some patients, causing joint failure in some cases.

In December the FDA put a research hold on all drugs in the class after similar problems emerged, halting studies by Johnson & Johnson and Regeneron Pharmaceuticals Inc.

Regeneron was developing a compound called REGN475 in cooperation with Sanofi-Aventis. Johnson & Johnson was testing its drug fulranumab in several pain conditions. The FDA lifted its hold on a trial of the drug for cancer pain last summer, though studies for osteoarthritis remain on hold.

The drugmakers are expected to argue Monday that the joint deterioration was caused by a rare drug side effect caused by patients taking multiple painkillers simultaneously. According to briefing materials, Pfizer and J&J both found that the bone problems almost exclusively occurred in patients taking the experimental drugs along with traditional anti-inflammatory painkillers like aspirin and Advil.

The FDA's analysis published Thursday supports that theory, noting that the side effects were worst among patients taking both nerve-blocking drugs and older painkillers. However, the agency notes that Pfizer's tanezumab was associated with significant bone problems even when used alone. The FDA analyzed nearly 500 cases of bone damage reported by all three drugmakers studying the medications.

Pfizer executives are expected to argue for continued testing of the newer drugs, with restrictions on combining them with older painkillers. Additionally, if patients do not improve after taking a few doses, the drugs would be discontinued.