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PLAIN LANGUAGE SUMMARY

Apremilast in osteoarthritis: exploring its therapeutic mechanisms

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Apremilast: mechanisms of its therapeutic effect in osteoarthritis

Osteoarthritis (OA) is often mistakenly viewed as simple 'wear-and-tear' disease. However, it is now recognized as a complex, chronic disease involving low-grade inflammation, oxidative stress, and damage to cartilage and the underlying bone. This destructive cycle is driven by pro-inflammatory signals, primarily proteins called cytokines (like IL-17 and TNF).

What is apremilast?

Apremilast is an oral drug currently approved for conditions like psoriasis and psoriatic arthritis. It is a selective phosphodiesterase 4 (PDE4) inhibitor. It works by increasing a natural messenger molecule inside cells called cAMP (cyclic adenosine monophosphate).
Raising cAMP levels activates anti-inflammatory pathways and, crucially, reduces the body's over-active immune signals, targeting the inflammation that fuels OA progression.

How might apremilast work in OA (preclinical potential)?

Scientific studies conducted in laboratory and animal models (preclinical data) suggest that apremilast could be highly effective by targeting multiple disease mechanisms:

1. **Fighting inflammation:** It directly suppresses the production of key destructive cytokines (IL-1β, TNF, IL-17 and IL-6) that accelerate joint damage.
2. **Protecting cartilage:** It guards living cells in cartilage (chondrocytes) from premature ageing and death (senescence) caused by inflammation and stress, helping to maintain cartilage structure.
3. **Regulating bone:** It helps stabilize the subchondral bone (the bone underneath the cartilage) by directly inhibiting the cells that break down bone (osteoclasts), which could slow structural changes.
4. **Reducing pain:** By dampening overall joint inflammation and influencing pain-related nerve pathways, apremilast may help reduce chronic OA pain.
5. **Acting as an antioxidant:** It counteracts excessive reactive oxygen species that contribute to tissue damage.

Clinical reality and future directions of apremilast

Despite this strong scientific foundation, the clinical evidence for apremilast in patients with OA is currently very limited and inconclusive. A key phase II trial testing the drug for erosive hand OA did not meet its primary goals, failing to show a significant benefit for pain or other measures of disease activity.
Therefore, while the drug has a strong mechanistic rationale, acting as an anti-inflammatory, antioxidant and cartilage-protecting agent, its role in OA treatment is still uncertain. Researchers believe future studies should explore whether apremilast could benefit specific sub-groups of patients with OA or if it needs to be used in combination with existing symptomatic treatments, such as non-steroidal anti-inflammatory drugs, to achieve a greater therapeutic effect.