Metacam | Previcox

OSTEOARTHRITIS...

MORE THAN CHRONIC PAIN

Treating inflammation is key to reducing disease progression and pain sensitisation

MECHANOFLAMMATION–
THE SCIENCE OF OSTEOARTHRITIS

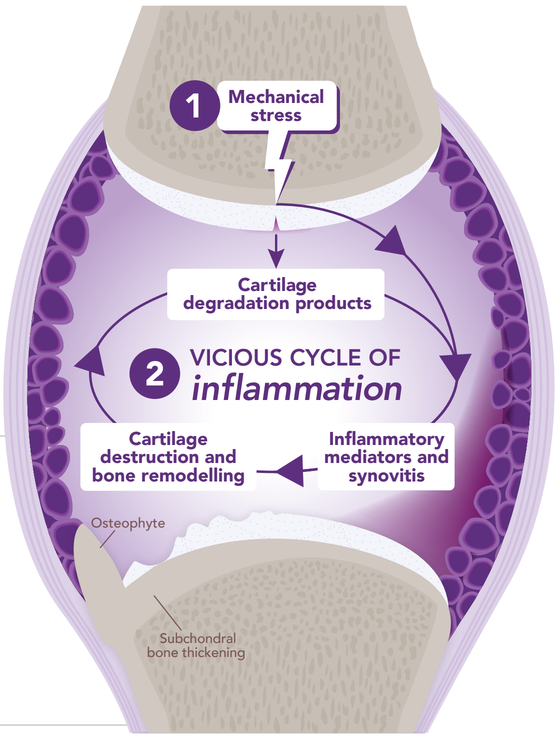
Mechanoflammation *(noun)*
The **inflammatory response to mechanical stress**, resulting in the development and progression of osteoarthritis.[1]

2 FACTORS

ARE CENTRAL TO THE PATHOGENESIS OF OSTEOARTHRITIS[2–4]:

1 Mechanical stress—joint injury, conformation issue or overuse

2 A perpetuating vicious cycle of inflammation resulting in progressive cartilage destruction and bone remodelling



(1) Mechanical stress results in (2) the release of inflammatory mediators from bone, cartilage and synovial cells. This induces synovitis and further amplification of the inflammatory response, resulting in progressive cartilage destruction and bone remodelling. Ongoing release of cartilage degradation products leads to a vicious cycle of inflammation.

WHY DOES MECHANOFLAMMATION MATTER?

Osteoarthritis is more than chronic pain, and managing osteoarthritis requires more than analgesia.

Reducing mechanical stress and inflammation are vital to prevent ongoing joint degeneration and pain sensitisation.

The anti-inflammatory and analgesic properties of non-steroidal anti-inflammatory drugs (NSAIDs) make them the ideal first-line treatment for osteoarthritic pain and inflammation.

NSAIDs are the foundation of osteoarthritis management.[5]

THE ROLE OF MECHANICAL STRESS IN OSTEOARTHRITIS

MECHANICAL STRESS—THE #1 RISK FACTOR[1]

Mechanicial stress is the result of either a normal load through an abnormal joint or an abnormal load through a normal joint.[1]

A normal load through an abnormal joint

Conformation—affected by breed and genetics, conformation and associated joint issues are an important risk factor in dogs[6]

Trauma—an important risk factor in cats, with outdoor cats at greater risk[7]

An abnormal load through a normal joint

Obesity—an important risk factor in both dogs and cats through increased mechanical load and the induction of a chronic pro-inflammatory state[7,8]

Overuse—repetitive stress causes repeated micro-traumas and is a risk factor in working and sporting dogs[9]

Table 1: Common joint issues that predispose to osteoarthritis and breeds at risk

Issue/ Species	Hip dysplasia[10,11]	Elbow dysplasia[12]	Cranial cruciate ligament disease[10]	Patellar luxation[11,13]
Dog	**Large-breed dogs** including: • Newfoundland • Saint Bernard • Rottweiler • German shepherd • Golden retriever • Labrador retriever	**Large-breed dogs** including: • Bernese mountain dog • Labrador retriever • Rottweiler • German shepherd	**Large-breed dogs** including: • Newfoundland • Rottweiler • Labrador retriever • Bulldog • Boxer • Chow chow	**Small-breed dogs** including: • Pomeranian • Chihuahua • Yorkshire terrier • French bulldog • Pug • Bichon frise
Cat	• Maine coon • Himalayan • Siamese • Abyssinian • Devon rex • Persian	The elbow is one of the most common sites for osteoarthritis in the cat but underlying disease processes have not been identified.[11]	No breed predisposition reported but trauma and obesity are risk factors.[11]	• Abyssinian • Devon rex

MECHANICAL STRESS CAUSES INFLAMMATION

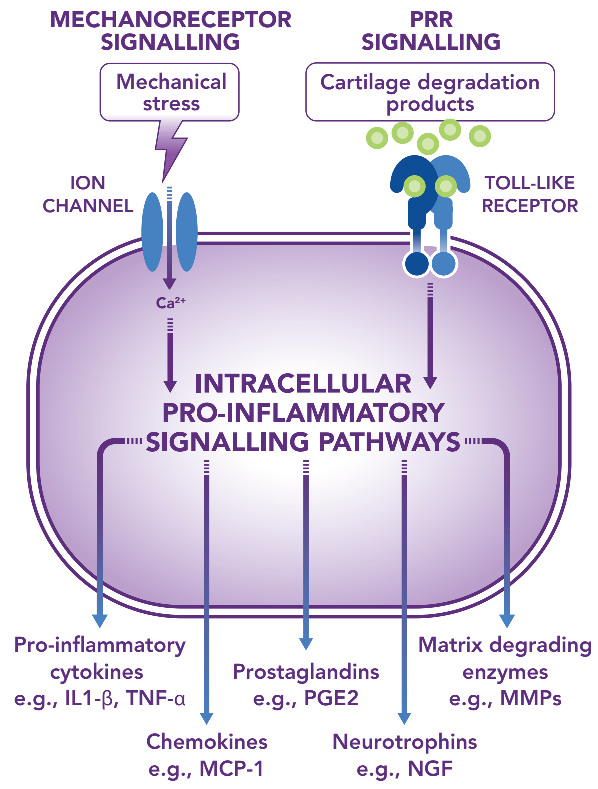
Mechanical stress on bone, cartilage and synovial cells results in the production of inflammatory nociceptive and catabolic mediators, which produce inflammation, pain and degradation of the joint.[4]

2 RECEPTORS

UPREGULATE PRO-INFLAMMATORY SIGNALLING PATHWAYS[3,4,14]:

1 Mechanoreceptors—stress opens ion channels in the cell membrane

2 Pattern recognition receptors (PRRs)—toll-like receptors recognise 'danger signals' like cartilage degradation products



Mechanical stress signals directly through mechanoreceptors and indirectly by releasing cartilage degradation products, which signal through PRRs. Intracellular pro-inflammatory signalling pathways are upregulated resulting in the release of inflammatory, nociceptive and catabolic mediators.

IL1-β: interleukin 1 beta; **MCP-1:** monocyte chemoattractant protein 1; **MMP:** matrix metalloproteinase; **NGF:** nerve growth factor; **PGE2:** prostaglandin E2; **TNF-α:** tumour necrosis factor alpha.

THE ROLE OF INFLAMMATION IN THE PATHOGENESIS OF OSTEOARTHRITIS

SYNOVITIS AMPLIFIES THE INFLAMMATORY RESPONSE TO MECHANICAL STRESS.[3]

- Induced by cartilage degradation products and inflammatory mediators[3,4]
- Characterised by synovial cell proliferation, angiogenesis, leukocyte recruitment and joint effusion[3,4]
- Results in further inflammatory and catabolic mediator production[3,4]

Synovitis is a critical stage in the development of osteoarthritis.[3,4]

Synovitis precedes structural change in the osteoarthritic joint and predicts future cartilage destruction and bone remodelling.[4]

THE VICIOUS CYCLE OF INFLAMMATION

The amplification of the inflammatory response leads to[3,14]:

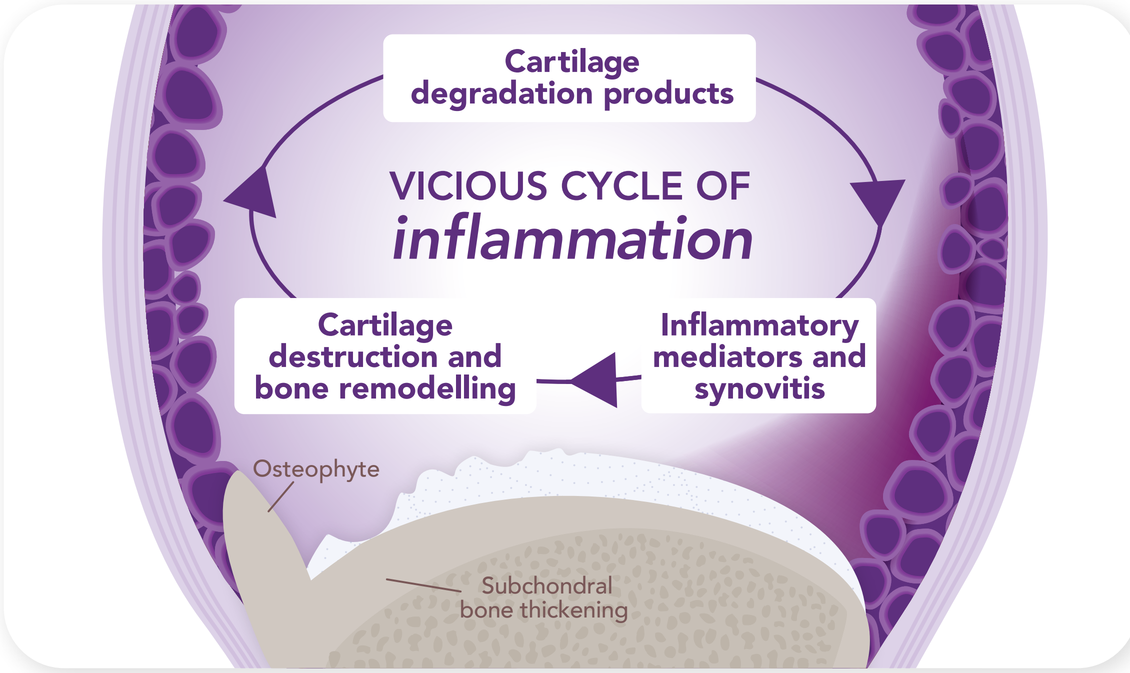
Cartilage destruction

- Cartilage cell apoptosis
- Matrix degradation

Bone remodelling

- Subchondral sclerosis
- Osteophyte formation

Ongoing release of cartilage degradation products leads to a vicious cycle of inflammation with progressive cartilage destruction and bone remodelling.[2–4]



Chronic inflammation is a major driver of ongoing joint degeneration.[4]

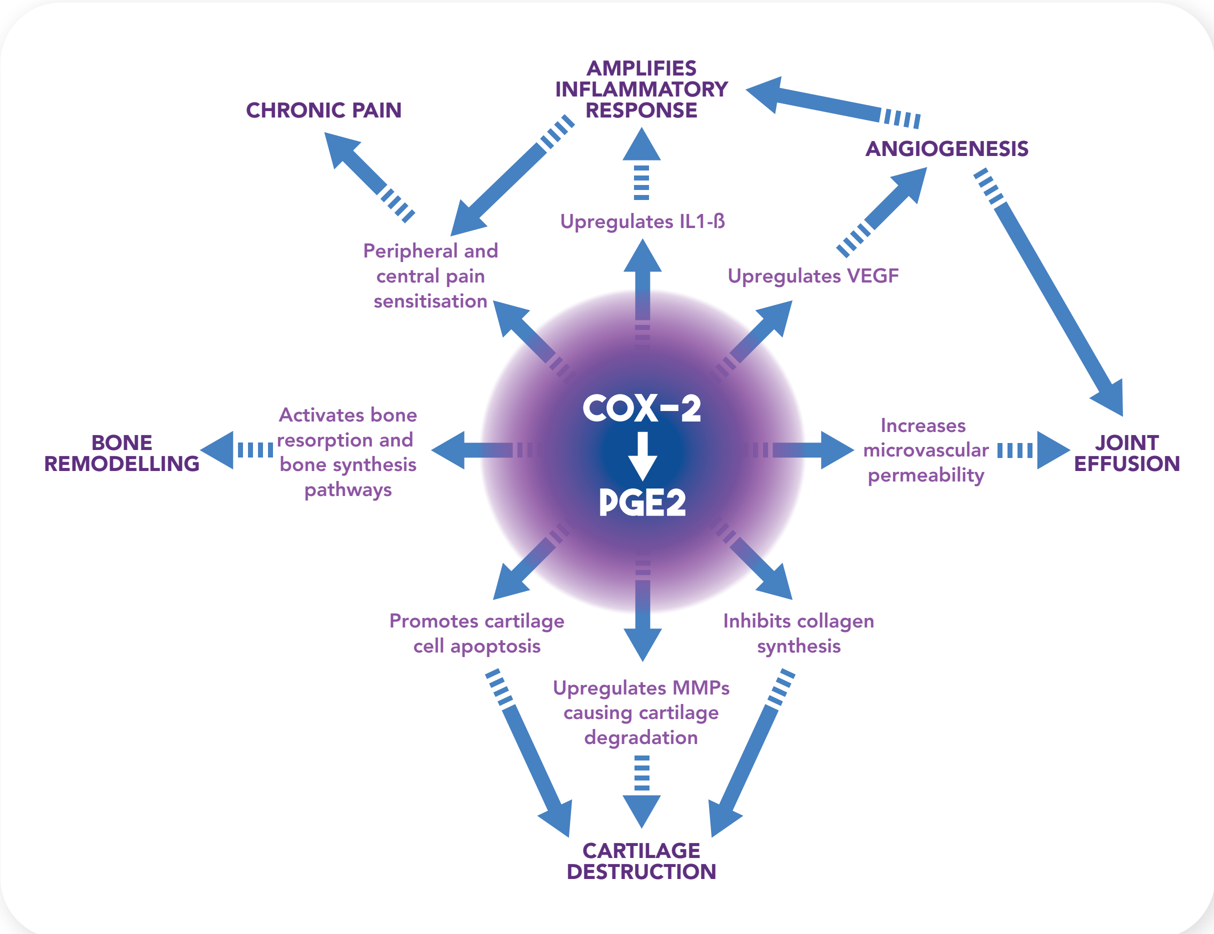
COX-2 AND PGE2 ARE CENTRAL TO THE PATHOGENESIS OF OSTEOARTHRITIS

CYCLO-OXYGENASE 2 (COX-2)[4]:

- Upregulated in osteoarthritic bone, cartilage and synovial cells by inflammatory mediator and cartilage degradation product signalling
- Increases production of prostaglandins

PROSTAGLANDIN E2 (PGE2):

- Promotes inflammation and angiogenesis[15,16]
- Promotes chronic pain through peripheral and central pain sensitisation[15–17]
- Promotes cartilage destruction and bone remodelling[14,15,18]



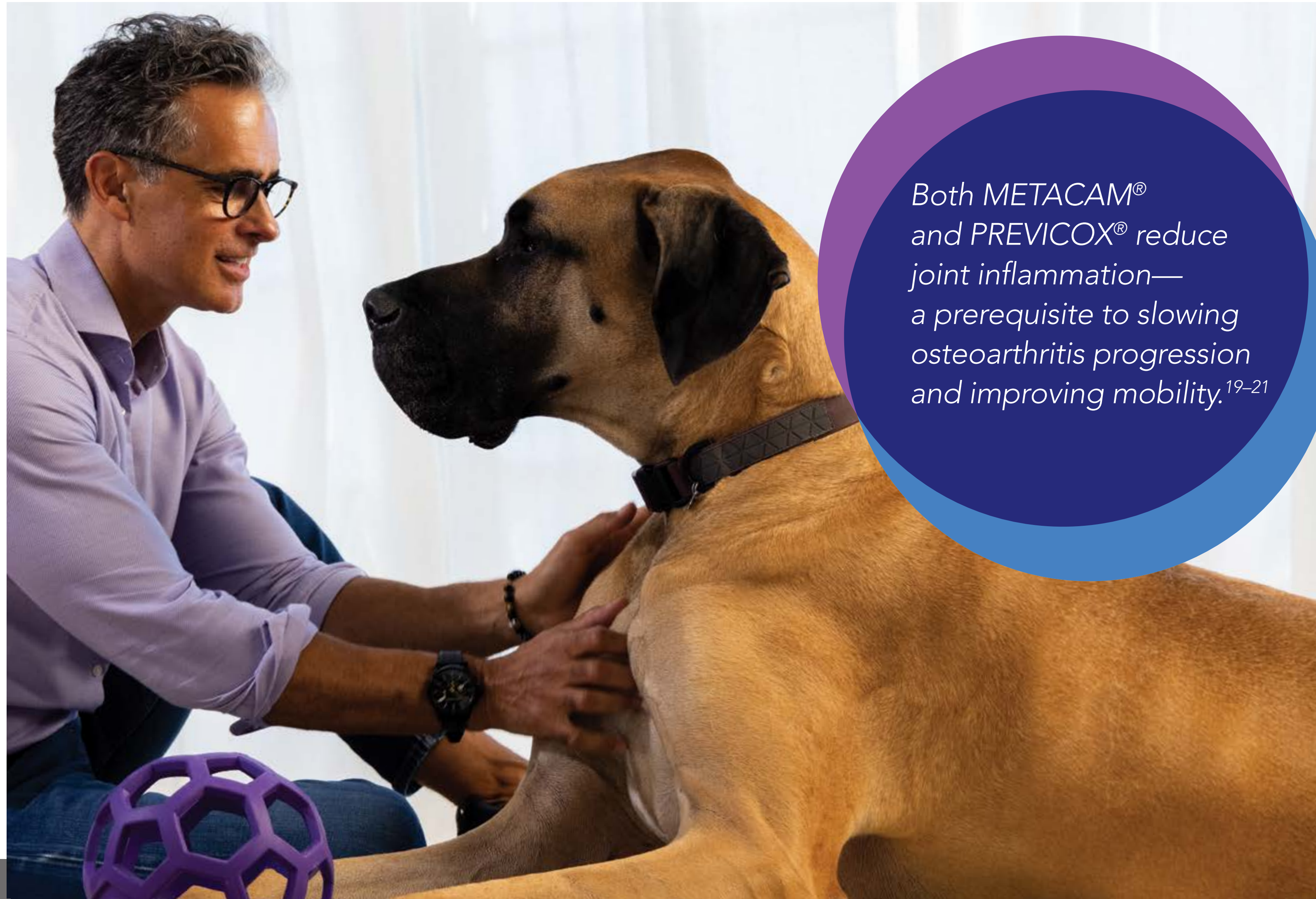
VEGF: vascular endothelial growth factor.

OSTEOARTHRITIS REQUIRES MORE THAN PAIN RELIEF. MANAGING INFLAMMATION IS KEY.

The goal of osteoarthritis management is to reduce pain and inflammation, increase mobility and slow progression of disease.[2]

As COX-2 is a major driver of inflammation and subsequent joint degeneration,[4] NSAIDs are the foundation of osteoarthritis management by[5]:

Relieving pain	Reducing inflammation	Improving mobility



TOGETHER WE CAN RELIEVE MORE THAN CHRONIC PAIN

Gold standard care for osteoarthritis requires the relief of pain, inflammation and mechanical stress. The **Osteoarthritis 5-Point Integrated Care Plan** is a multimodal approach that provides relief from all three.

OSTEOARTHRITIS 5-POINT INTEGRATED CARE PLAN

1 METACAM® or PREVICOX®

NSAIDs effectively inhibit inflammatory processes and by this relieve:

- Inflammation ✓
- Pain ✓

2 DIET

Obesity is a pro-inflammatory condition and achieving or maintaining an ideal weight relieves:

- Mechanical stress ✓
- Inflammation ✓

3 EXERCISE AND REHABILITATION

By restoring musculoskeletal strength and joint mobility, exercise and physical rehabilitation relieve:

- Pain ✓
- Mechanical stress ✓

4 ENVIRONMENTAL MODIFICATION

Simple modifications around the home aid a pet's mobility by relieving:

- Mechanical stress ✓
- Pain ✓

5 MONITORING

Daily monitoring helps owners notice changes in their pet's pain, inflammation and mobility earlier, helping to relieve:

- Pain ✓
- Inflammation ✓
- Mechanical stress ✓

KEY TAKEAWAYS ABOUT MECHANOFLAMMATION

- Chronic inflammation is a major driver of ongoing joint degeneration[4]
- NSAIDs, which effectively reduce pain and inflammation, are the foundation of osteoarthritis management[5]
- Both METACAM® and PREVICOX® reduce joint inflammation—a prerequisite to slowing osteoarthritis progression and improving mobility[19–21]
- The **Osteoarthritis 5-Point Integrated Care Plan** is a clinical care standard for osteoarthritis management, providing a multimodal approach for the relief of pain, inflammation and mechanical stress

Ask your Boehringer Ingelheim sales representative for further information about the Osteoarthritis 5-Point Integrated Care Plan.

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WE'RE ALWAYS READY TO LISTEN

Please speak with your Boehringer Ingelheim sales representative today about how METACAM® and PREVICOX® can assist you with pain, inflammation and mobility solutions.

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