Musculoskeletal adverse events in dogs receiving Librela™ (bedinvetmab injection)

Dear Colleagues,

In the interest of continued open communication and transparency, I'm writing to share a recent publication titled **"Atypical radiographic changes seen in dogs treated with bedinvetmab (Librela)"** (Budsberg SC, Clements DN, Regan DP, Wennemuth J).[1]

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The authors are an external, multidisciplinary panel of veterinary specialists. Zoetis began to collaborate with this expert panel in early 2025, and we are pleased this publication is now available to veterinarians.

The expert panel was provided access to the adverse events reported globally during the five-year period ending December 31, 2025 coinciding with the administration of Librela, and wrote the paper independently from Zoetis. The goal of the study was to describe any consistent patterns of clinical-radiographic signs of musculoskeletal (MSK) adverse events reported in a small subset of dogs receiving bedinvetmab for osteoarthritis (OA)-associated pain.

This paper describes a subset of MSK adverse events characterized by a radiographic pattern that the authors consider atypical. During the study period (November 2020 through December 2025), cases with a minimum amount of medical information were eligible for expert review, and 319 cases fit the criteria. Review of these cases found 186 having atypical radiographic findings. **Abnormal Periarticular Bone Remodeling (APBR)** was the most common change noted.[1] Over 34 million doses of Librela were distributed globally during the five-year period, and in total 7,205 MSK adverse events were reported.[1,2] This category includes muscle weakness, musculoskeletal NOS (not otherwise specified), lameness, arthritis, bone and joint disorder NOS, etc. Globally, MSK adverse events have been reported rarely (through Dec 2025)[†], and APBR reports are a subset of those.

In Context

With over five years of global clinical experience, Librela has benefited millions of dogs with OA pain. Pet owner and veterinarian overall satisfaction with Librela remains strong.[3,4] OA severely impacts a dog's quality of life,[1] and in a clinical trial Librela improved quality of life in dogs.[5] OA is also a major cause of morbidity and mortality in dogs, highlighting the

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importance of continuous pain management (i.e., chronic musculoskeletal conditions are commonly associated with decisions to euthanize).[1]

However, like any medication, there are adverse events reported, and Librela is no different. Zoetis stands behind the efficacy of Librela for the management of OA pain and its positive benefit-risk profile.

As this is a newly described condition in dogs, there have been several publications recently describing these reported adverse events.[6-13] These publications have used different terminology to refer to similar clinical signs (now defined by the expert panel as APBR).[1]

In practice, many cases which have been previously reported are consistent with APBR. APBR is different from OA (and OA that progresses fast) and Rapidly Progressive Osteoarthritis (RPOA) in humans:

- APBR is characterized by marked joint and soft tissue swelling, extensive, irregular periosteal and ectopic mineralized tissue formation extending beyond the normal margins of the joint into the metaphyseal and, in some cases, diaphyseal regions of the bone[1]. In contrast to typical osteoarthritis, articular joint surfaces may remain relatively preserved. These extensive periarticular changes are not seen with normal progression of OA.
- Some cases of OA can progress rapidly[14, 15] (without anti-NGF treatment).
- RPOA is a distinct condition described in humans since the 1950s. RPOA also differs from APBR as there is no alteration of soft tissue in RPOA. The main features of RPOA in humans are cartilage loss (RPOA type I) and subchondral bone collapse (RPOA type II).[16-18]

Importantly, this new publication by Budsberg et al.[1] is the most comprehensive analysis based on a minimum set of medical information and radiographs. **Cases screened included all global pharmacovigilance cases of MSK adverse events reported over a five-year period with radiographic images available, and included the cases with radiographs described in those previous publications.**

As with normal post-approval monitoring process, Zoetis is engaged with regulators globally on adverse event reports and taking action where appropriate and in line with applicable regulatory requirements, and can share the following progress:

- Updates to the UK Librela label (Summary of Product Characteristics (SPC)) was approved on 21 May 2026.

- Updates to the EU Librela SPC were approved by the European Commission on 02 July 2026.

The EU and UK regulators have confirmed that the **benefit-risk balance** for bedinvetmab for the alleviation of OA pain in dogs **remains positive**.

It is normal and expected that label updates may occur at different times in different markets based on differences in jurisdictional regulatory processes. We expect updates to occur in other markets.

Why This Matters

The paper's findings support increased awareness and prompt evaluation if a dog presents with new or worsening joint swelling, pain and/or restricted range of motion. If these clinical signs occur, the dog should be examined and have affected joints radiographed to help rule out differential diagnoses (e.g., normal progression of OA, septic arthritis, trauma, immune-mediated disease, neoplasia, Lyme) and to guide management. A clear name, and recognizable pattern will enable an appropriate response if these clinical signs or joint changes occur in dogs treated with Librela (bedinvetmab injection).

Because there are no known predictors, and APBR appears idiosyncratic, veterinary rechecks and careful owner observation are most important.

Treatment is individualized and typically focuses on symptom control, along with a case-by-case decision on whether to continue Librela, since some dogs may still need it to maintain acceptable pain control and quality of life.

With rare adverse events, clinical studies will not be sensitive enough to detect cases.[19-22] Pharmacovigilance reporting is not an indicator of prevalence, but remains the best means of monitoring safety of medications. Globally, musculoskeletal adverse events are reported rarely†, and APBR reports are a subset of those.

We recommend adding information on this adverse event to your benefit–risk discussion before treatment with pet owners, which is good practice for any therapy.

We will continue to investigate all reported adverse events and share important updates with you that may inform your clinical decision making. Zoetis continues to evaluate which factors or conditions may predispose dogs to APBR. Whether APBR is unique to dogs treated with Librela or also occurs in dogs not treated with Librela remains unknown.

Zoetis is taking deliberate steps to directly address veterinarians' questions and concerns and to ensure a clear understanding of Librela's benefit-risk profile, including expanding

medical education, partnering with experts to share efficacy and safety information, and investing in post-launch studies to generate additional real-world insights.[13]

To report a possible adverse event associated with any Zoetis product, please contact our Veterinary Medical Information Support team.

Sincerely,
Richard Goldstein, DVM, DACVIM (SAIM)
Chief Medical Officer, Zoetis

IMPORTANT SAFETY INFORMATION:

Librela is for use in dogs only. Women who are pregnant, trying to conceive or breastfeeding should take extreme care to avoid self-injection. Hypersensitivity reactions, including anaphylaxis, could potentially occur with self-injection. Librela should not be used in breeding, pregnant, or lactating dogs. Librela should not be administered to dogs with known hypersensitivity to bedinvetmab. Adverse events reported post-approval include ataxia (lack of balance/coordination), anorexia (loss of appetite), lethargy (tiredness), emesis (vomiting), and polydipsia (increased drinking). The most common adverse events reported in a clinical study were urinary tract infections, bacterial skin infections and dermatitis (skin irritation/inflammation). For complete safety information, refer to the full prescribing information at LibrelaPI.com.

[†]Globally, musculoskeletal adverse events have been reported rarely (through Dec 2025);[2] APBR cases are a subset of all musculoskeletal AEs. According to European Medicines Agency classification, 'rare' means an event has been reported in between 1 and 10 in 10,000 treated animals (where one dose equals one treated animal).[23]

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