VETERINARY PHARMACOVIGILANCE

REPORT FOR SUSPECTED ADVERSE REACTIONS IN ANIMALS OR IN HUMANS AFTER THE USE OF A VETERINARY MEDICINE

DRAFT REPORT

SENDER REPORT IDENTIFICATION-CASE REF.No: 2024-UK-013392

Safety issues in animals ☒ in humans ☐
Lack of expected efficacy ☐
Withdrawal period issues ☐
Environmental problems ☐

Reporting country: United Kingdom
Purchase country: United Kingdom
Report source: Owner

1. ADDRESS OF COMPETENT AUTHORITY

[redacted]

2. NAME AND ADDRESS OF SENDER

[redacted]

Date complaint received by sender: 8-Oct-2024 (dd-Mon-yyyy)

Type of report Initial ☒ Follow-up ☐ (date, case number)

Person who reported the reaction : veterinarian ☐ owner ☒ physician ☐ pharmacist ☐ other:

3. VETERINARIAN/ PHYSICIAN/ PHARMACIST

Name:
Address: [redacted]
Telephone No. [redacted]

4. ANIMAL OWNER / HUMAN PATIENT

Name:
Address: [redacted]
Telephone No. [redacted]

5. ANIMAL DATA **No. of animals treated: 1** **No. of animals showing signs: 1** **No. of animals died: 0**

Animal characteristics (animal(s) showing signs):

Species: Dog
Breed/ production type: Spaniel - King Charles Cavalier
Sex/ physiological status: female ☐ male ☒ pregnant ☐ neutered ☒ lactating ☐ other:
Weight (kilos): 15
Age: 8 Year(s)
State of health at time of treatment: good ☐ fair ☐ poor ☐ critical ☐ unknown ☐
Reason(s) for treatment (prevention against what disease(s) or initial diagnosis):
--UNKNOWN--

6. PRODUCT DATA #1 *See continuation page*

Trade name (include dosage form and strength): Previcox NS
M.A. number: Unknown
Active substance(s) (INN): Firocoxib
ATC vet code: QM01AH90
Batch No.: --UNKNOWN--
Expiry date: --UNKNOWN--
Storage details: --UNKNOWN--
Treatment Details: --UNKNOWN--

Dose/ frequency: 1 Dose
Route/ site of administration: Oral
Start date of treatment: 1-Jan-2021
Stop date or duration: Ongoing
Who administered the product: Unknown
veterinarian ☐ owner ☐ other ☒
Use according to label: yes ☐ unknown ☐ no ☐ explain: --UNKNOWN--
Action taken after reaction: drug withdrawn ☐ dose reduced ☐ other ☐
Did reaction abate after stopping drug? yes ☐ no ☐ not applicable ☐
Did reaction reappear after reintroduction? yes ☐ no ☐ not applicable ☐
List all other relevant medications given to animal(s):

Product name/	Company	Batch No.	Route and site of admin	Dose, frequency, indication, duration of treatment (dates of beginning and end)
Librela 10 mg Solution for Injection for Dogs (Bedinvetmab)	Zoetis Belgium S.A. (Tullamore)	UNK	Subcutaneous	1 Vial per 1 3 Year(s), (1-May-2021 - 1-May-2024)

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7. REACTION DATA

Date of onset of unexpected signs: 6-Jun-2024

Duration of reaction: --UNKNOWN--

Describe the sequence or events including administration of product(s), all clinical signs, site of reaction, severity, pertinent lab tests, necropsy results, possible contributing factors (if necessary use extra sheet): *See continuation page*

Adverse Events

An 8-year-old, male neutered, Cavalier King Charles spaniel dog, weighing 15 kilograms was administered Librela 15 mg Solution for Injection for Dogs [NCA coded overdose] on 07 JUL 2021 for 3 years and Previcox NS [dates of administration unknown]. An adverse event occurred on 06 JUN 2024. "Been in owners possession since a young puppy - diagnosed with elbow dysplasia about 4 or 5 years ago; had CT scan in [Hospital name redacted] as since had Librela injections, Previcox [NCA added Previcox NS] and Yumove; for the last several years. [Animal name redacted] has had a left hind problem that has been evident for the last 3 to 4 months; he is noticed to limp and much of the time, he holds the left hind ankle and foot at a strange angle and the ankle is very

Were the unexpected signs treated? If yes, give the details of treatment including product(s) used:

Outcome of reaction to date:

	Killed/ euthanised	died	under treatment	alive with sequelae	recovered	unknown
No of animals:	0	0	1	0	0	0
Date when:						

8. ATTENDING VETERINARIAN'S LEVEL OF SUSPICION THAT DRUG CAUSED

possible ☐ unlikely ☐ no attending vet ☐ --UNKNOWN--

9. PREVIOUS EXPOSURE AND REACTION(S) TO PRODUCT(S)

Previous exposure to the suspect product? no ☐ yes ☐ Date(s): Unknown

Previous reaction to the suspect product? no ☐ yes ☐ Describe: Unknown

De-challenge information: --UNKNOWN--

10. DETAILS OF SUSPECTED ADVERSE REACTION(S) IN HUMANS

Patient details Sex: --UNKNOWN-- Pregnant ☐ Age/ date of birth: --UNKNOWN-- Occupation (if relevant): --UNKNOWN--

Date of exposure: --UNKNOWN-- Date of reaction: --UNKNOWN--

Nature and duration of exposure, reaction details (including symptoms) and outcome:

--UNKNOWN--

[redacted]

[redacted]

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6. PRODUCT DATA # 2

Trade name (include dosage form and strength): M.A. number: 42058/5030

Librela 10 mg Solution for Injection for Dogs; Dosage Form: Solution for injection

Active substance(s) (INN): Bedinvetmab ATC vet code: QN02BG91

Batch No.: --UNKNOWN-- Expiry date: --UNKNOWN-- Storage details: --UNKNOWN--

Treatment details:

--UNKNOWN--

Dose/ frequency: 1 Vial per 1 Route/ site of administration: Subcutaneous

Start date of treatment: Stop date or duration: Who administered the product: Veterinarian

1-May-2021 1-May-2024 veterinarian ☐ owner ☐ other ☒

Use according to label: yes ☐ unknown ☐ no ☒ explain: Treatment regimen Off-Label

Did reaction abate after stopping drug? yes ☐ no ☐ not applicable ☐

Did reaction reappear after reintroduction? yes ☐ no ☐ not applicable ☐

8. ATTENDING VETERINARIAN'S LEVEL OF SUSPICION THAT DRUG CAUSED

Possible ☐ unlikely ☐ no attending vet ☐ --UNKNOWN--

9. PREVIOUS EXPOSURE AND REACTION(S) TO PRODUCT(S)

Previous exposure to the suspect product? no ☐ yes ☐ Date(s): Unknown

Previous reaction to the suspect product? no ☐ yes ☐ Describe: Unknown

De-challenge information: --UNKNOWN--

[redacted]

7. REACTION DATA (continued)

Adverse Events

swollen/thickened; the problem is gradually getting worse. Otherwise [animal name redacted] is a bright happy healthy dog. Right thoracic limb: no abnormalities noted. Left pelvic limb: moderate proximal limb muscle atrophy; the hock is thickened and rotationally unstable but is apparently comfortably on manipulation. Right pelvic limb: there is mild lateral soft tissue thickening / effusion of the hock; comfortable range of movement with no palpable instability. 4. Blood tests: haematology, biochemistry & electrolytes; no significant abnormalities 5. Radiographic Examination: Left hock: the talus is caudally displaced relative to the distal tibia; the distal tibia is malformed with apparent erosion / loss of the caudal bone; marked soft tissue swelling / effusion centred over the talo-crural joint; a thin corridor of periosteal / mineralised new bone is visible caudal to the distal tibia and talus. Right hock: moderate soft tissue thickening / effusion centred over the talo-crural joint; the medial aspect of the joint space is wider than the lateral which could be consistent with osteochondrosis of the medial trochlear ridge of the talus 6. Palpation under sedation: Left hock: grossly unstable with proximal-distal, medial-lateral and rotational instabilities. Right hock: mild swelling/thickening but no palpable instability 7. Synovial aspirates: Left hock: 1ml of relatively normal appearing synovial fluid; slightly less viscous than normal and mild blood staining. Cytology; Nucleated Cell Count : 1.72 x 10*9/L (Ref Range : less than 3.0 x 10*9/L, Protein : 48.0 g/L (Ref Range : less than 48.0 g/L), Viscosity is good on visual estimate. Approximately 60% neutrophils, 33% small mononuclear cells (mainly lymphocytes, some quiescent synoviocytes) and 7% large mononuclear cells. Subjectively, neutrophils appear markedly increased relative to numbers expected to be contributed by the background blood. No infectious agents are seen. Right hock: <0.1ml of normal appearing synovial joint fluid. Nucleated Cell Count : 0.62 x 10*9/L (Ref Range : less than 3.0 x 10*9/L). Protein : 56.0 g/L (Ref Range : less than 48.0 g/L). Viscosity is good on visual estimate. Approximately 33% neutrophils, 64%, small mononuclear cells (mainly lymphocytes, some

quiescent synoviocytes) and 6% large mononuclear cells. 8. Surgery: 2 October 2024: Left pantarsal arthrodesis. Placed: 10 hole medial 2.7/2.0mm hybrid PTA plate, 3.5mm calcaneo-tibial positional screw & 1cc of VTB DBM bone graft. Routine surgery; no problems or complications. 3 October 2024; [animal name redacted] has recovered well from the surgery; Right thoracic limb: no abnormalities noted. Left pelvic limb: moderate proximal limb muscle atrophy; the hock is thickened and rotationally unstable but is apparently comfortably on manipulation. Right pelvic limb: there is mild lateral soft tissue thickening / effusion of the hock; comfortable range of movement with no palpable instability. 4. Blood tests: haematology, biochemistry & electrolytes; no significant abnormalities. 5. Radiographic Examination: Left hock: the talus is caudally displaced relative to the distal tibia; the distal tibia is malformed with apparent erosion / loss of the caudal bone; marked soft tissue swelling / effusion centred over the talo-crural joint; a thin corridor of periosteal / mineralised new bone is visible caudal to the distal tibia and talus. Right hock: moderate soft tissue thickening / effusion centred over the talo-crural joint; the medial aspect of the joint space is wider than the lateral which could be consistent with osteochondrosis of the medial trochlear ridge of the talus 6. Palpation under sedation: Left hock: grossly unstable with proximal-distal, medial-lateral and rotational instabilities. Right hock: mild swelling/thickening but no palpable instability. 7. Synovial aspirates: Left hock: 1ml of relatively normal appearing synovial fluid; slightly less viscous than normal and mild blood staining. Cytology; Nucleated Cell Count : 1.72 x 10*9/L (Ref Range : less than 3.0 x 10*9/L, Protein : 48.0 g/L (Ref Range : less than 48.0 g/L), Viscosity is good on visual estimate. Approximately 60% neutrophils, 33% small mononuclear cells (mainly lymphocytes, some quiescent synoviocytes) and 7% large mononuclear cells. Subjectively, neutrophils appear markedly increased relative to numbers expected to be contributed by the background blood. No infectious agents are seen. Right hock: <0.1ml of normal appearing synovial joint fluid. Nucleated Cell Count : 0.62 x 10*9/L (Ref Range : less than 3.0 x 10*9/L), Protein : 56.0 g/L (Ref Range : less than 48.0 g/L). Viscosity is good on visual estimate. Approximately 33% neutrophils, 64% small mononuclear cells (mainly lymphocytes, some quiescent synoviocytes) and 6% large mononuclear cells. As discussed and as per emails of 2nd October, the reason for [animal name redacted] left ankle instability is not clear. There is a growing body of anecdotal evidence suggesting that Librela can cause catastrophic joint instability or collapse in a very small number of dogs. How or why is unclear. We cannot definitely prove that Librela has caused this unusual problem of [animal name redacted] left ankle joint; but equally there is not another good explanation. Test results from fluid taken from [Animal name redacted] left and right ankle joints is very unusual. Infection is ruled out. The cell distribution of increased numbers of neutrophils but within a normal cell count is highly unusual and difficult to explain". The dog was treated and is reported as not yet recovered. No further information is expected.

NCA comment 13 NOV 2024: Duplicate detected, narrative states "An 8-year-old, male neutered, King Charles Cavalier Spaniel dog, weighing 15 kilograms was administered Librela 10 mg Solution for Injection for Dogs on 01 MAY 2021 for 3 years [most recent date of administration unknown], an adverse event occurred on 01 MAY 2024. "Left hock collapse with gross instability; right hock similar changes, less severe. There seems to be a growing body of evidence Librela that in a small (undefined) group of dogs, Librela has associated side effects (causes) of 1. Rapidly Progressive Osteoarthritis, and 2. catastrophic joint instability". The dog was treated and is reported as not yet recovered. No further information is expected". Main difference between the cases is product strength selected, altered to Librela 10 mg Solution for Injection for Dogs. Otherwise no major differences.
Zoetis follow-up 16Dec2024: administration dates and strength updated as per NCA 13Nov2024 follow-up. Zoetis reason for assessment was also updated. [redacted]
Zoetis follow-up 25Apr25: follow up from online news article from pet owner: After three years of having injections every six weeks (owners name redacted) noticed eight-year-old (animals name redacted) had started walking with his back leg bowing and his foot rolling underneath him. He stopped taking Librela shortly before his operation, Oct24. The surgery was very invasive and he was in a terrible state afterwards. He became incontinent and was peeing all over the house, which he had never done before. It became so severe that he had to wear a belly band to save the soft furnishings.
Since (Animal name redacted) had his last Librela injection in September (owners name redacted) said she has seen massive changes in his behaviour which she attributes to stopping the drug. His leg is recovering and although he can't bend his leg, he is adapting, she said. He is going to hydrotherapy and can swim well again, which is what he always enjoyed doing.
Veddra code added incontinence. Added end date of Librela as approx. 30Sep24 and frequency every 6 weeks (off-label treatment program not respected).

Case closed.
(Osteochondritis, Abnormal posture NOS, Bone and joint disorder NOS, Synovial fluid, high protein level, Neuromuscular disorder NOS, Arthritis, Abnormal radiograph finding, Lameness, Synovial fluid, high red blood cell count, Arthritis, Bone and joint disorder NOS, Arthritis, Urinary incontinence), (Outcome : Unknown)

Medical History