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The incidence of adverse events reported that were possibly or probably related to CARTROPHEN VET was 0.0296% per course (per 4 weekly injections). Or, one adverse effect reported per 3,300 courses administered. The data is based on commercial history in the United Kingdom from 1991 to 1999.

Based on the information from the UK Veterinary Medicines Directorate, it is believed that 10% of all adverse events for all products including CARTROPHEN VET are reported. Hence, an estimated real incidence of adverse events for CARTROPHEN VET is 0.296% per course administered or 0.074% per dose administered.

**A Disease Modifying Osteoarthritis Drug (DMOAD)**

CARTROPHEN VET (pentosan polysulfate sodium or PPS) is a treatment for osteoarthritis (OA or also known as degenerative joint disease or DJD) and related musculoskeletal disorders which provides pain relief by acting on the pathology within the joint that causes pain and lameness.

CARTROPHEN VET has therefore been classified as a disease modifying osteoarthritis drug (DMOAD) and importantly, it protects and supports the recovery of joint cartilage that is damaged by the arthritic process.

With 20% of dogs over one year of age suffering from OA and CARTROPHEN VET being an effective treatment in 80% of dogs treated, CARTROPHEN VET and DMOAD represent the rational approach to the medical treatment of OA.

**DMOAD Actions**

The PPS in CARTROPHEN VET has been shown to exhibit the following actions:

1. **Improve the quality of cartilage** – Stimulates chondrocytes to synthesize cartilage matrix.
2. **Improve the quantity and quality of synovial fluid** – Stimulates synoviocyte biosynthesis of hyaluronan, improving both the quantity and molecular weight.
3. **Reduce the levels of cartilage degrading enzymes** – Metalloproteinase (as collagenase) and elastase are significantly reduced and tissue inhibitor of metalloproteinase (TIMP) is increased.
4. **Stimulates stem cell activity and cartilage cell differentiation** – Promotes mesenchymal precursor cell (MPC) proliferation and cartilage cell differentiation. Importantly, the frequency of MPCs is elevated in OA cartilage.
5. **Increased blood supply and nutrition to the joint and subchondral bone** – Mobilizes thrombi and fibrin deposits, lipids and cholesterol in both synovial tissues and subchondral blood vessels.
6. **Strong anti-inflammatory properties** – The potent anti-inflammatory activities of PPS have been consistently demonstrated in different models of severe inflammation.
7. **Eliminates free radicals** – Stimulates the release of the free radical scavenging enzyme, superoxide dismutase (SOD).
8. **Stimulates important growth factors that promote cartilage growth** – Increases the production of the essential trophic factor for cartilage, insulin-like growth factor-1 (IGF-1), which stimulates incorporation of sulfate and encourages cartilage growth.
9. **Affinity for cartilage** – The strong binding of the drug to cartilage protein results in therapeutic concentrations for 4 days.

**CARTROPHEN VET is safe**

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When it comes to osteoarthritic joint pain and lameness, CARTROPHEN VET is equal or superior to the potent analgesic and anti-inflammatory, carprofen. This is the first time a DMOAD has been proven to offer significant pain relief comparable to that afforded by non-steroidal anti-inflammatory drugs (NSAIDs). CARTROPHEN VET has a slightly slower onset of ameliorating effects but longer persistence of these after the recommended four week course of treatment.

CARTROPHEN VET has shown to be an effective treatment in over 80% of dogs treated. In a Japanese open clinical trial of canine OA, according to the veterinarian’s impression 96% of cases improved with CARTROPHEN VET treatment.

CARTROPHEN VET as a treatment for osteochondritis dissecans (OCD) and fragmented coronoid process (FCP) is rapid with long-term efficacy equivalent to surgical treatments.

CARTROPHEN VET is recommended for use in the treatment of lameness and/or pain caused by OA and related musculoskeletal disorders. With 20% of dogs over 1 year affected by OA combined with CARTROPHEN VET’s broad applications for the treatment of joint disorders, there are many opportunities for positive results.

CARTROPHEN VET will benefit acute through to chronic OA due to the progressive nature of this disease. Early intervention with CARTROPHEN VET in acute injuries will maximise the restoration of normal connective tissue function.

CARTROPHEN VET dosage and when to use?

CARTROPHEN VET has an optimal clinical efficacy in dogs at 3mg/kg s.c. on four occasions at weekly intervals.

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Why is DMOAD and specifically CARTROPHEN VET important?

- **Heal and Repair** – Enacts natural biological processes that encourage the healing and repair processes, modifying the OA disease and subsequently reducing the symptoms of pain and lameness.
- **Protects** – Acts as a prophylactic, guarding against the progression of the OA process in both age related circumstances or a consequence of physical stress and trauma, providing optimal joint performance for longer periods.
- **Metabolic normalisation** – Normalisation of joint health, restoring metabolic balance that ensures lasting clinical results well beyond the treatment period.

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12. Data on file, Biopharm Australia Pty Ltd
14. Data on file at Biopharm Australia Pty Ltd