Synovetin OA®

[Homogeneous Tin (^{117m}Sn) Colloid]
Veterinary Device for Use in Dogs

NAME: Synovetin OA®
Tin (^{117m}Sn) stannic colloid in ammonium salt. It is supplied as a 2–4 mCi (74–148 MBq)/mL suspension for intra-articular (IA) injection.

NET QUANTITY
Vials contain a prescribed dose up to 6.0 mCi (222 MBq) at the date and time to treat one dog.

1 mL of suspension contains 2–4 mCi (74–148 MBq) of tin (^{117m}Sn) stannic colloid in ammonium salt at the date and time of end use.

PRODUCT DESCRIPTION
Synovetin OA® is a conversion electron therapeutic veterinary device comprising a colloidal, sterile suspension with a pH between 6.5 and 9.0 where at least 90% of the particles have a size between 1.5 µm and 20 µm (HORIBA light scatter instrument). The ^{117m}Sn emits monoenergetic conversion electrons (significant energies 127–158 keV; emission probability 113%) and imageable gamma radiation (159 keV, 86% abundant). Accompanying low-energy emissions are Auger electrons (<22 keV) and X-rays (<30 keV). The half-life of ^{117m}Sn is 14 days. ^{117m}Sn decays by isomeric transition to stable ^{117}Sn.

Excipients include ammonium carbonate ($(NH_4)_2CO_3$), ammonium chloride (NH_4Cl), ammonium iodide (NH_4I), and trace tin (Sn) salts.

MECHANISM OF ACTION
Synovetin OA® is a veterinary device consisting of a homogeneous tin colloid which emits discrete (<300 µm) low-energy conversion electrons confined to the joint space. The colloid is composed of microparticles (1.5 µm to 20 µm) that are retained in the joint space of the dog. The particles are absorbed and retained by synoviocytes and macrophages in the synovium, resulting in apoptosis and reduction of inflammatory cells. Elimination of the pro-inflammatory cells reduces inflammation of the joint synovium, thereby reducing pain associated with synovitis. The data, including radiographic evidence, supports use in Grade 1, 2, and 3 osteoarthritis (OA) of the elbow joint.

CAUTION
Federal law restricts this device to sale by or on the order of a licensed veterinarian trained in the use of radioactive veterinary medical products.

Use of this product is restricted to facilities with a compatible Radioactive Materials (RAM) license.

INTENDED USE
Synovetin OA® is intended to reduce synovitis and associated pain of canine elbow joints afflicted with osteoarthritis.

WARNINGS
Do not exceed 6.0 mCi (222 MBq) of radiation activity per dog per treatment. Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental injection or ingestion by humans.

PRECAUTIONS
Injection should be performed only by a licensed veterinarian skilled in the delivery of intra-articular (IA) injections who is located at a facility that has a RAM license.

Rigorous aseptic technique must be ensured during injection.

DIRECTIONS FOR USE
Use the chart below to determine the appropriate dose. Doses were determined using the elbow joint.

For example, a dog weighing 25 lbs. receives an IA dose of 0.9 mCi in each elbow to be treated.

Dog Weight (lbs.)	Synovetin OA® Dose per Elbow Joint (mCi)*
10–19 lbs.	0.6
20–29 lbs.	0.9
30–39 lbs.	1.2
40–49 lbs.	1.5
50–59 lbs.	1.7
60–69 lbs.	1.9
70–79 lbs.	2.2
80–89 lbs.	2.4
90–99 lbs.	2.6
100–109 lbs.	2.8
110 lbs. and over	3.0

***Dose will be limited to 3.0 mCi/elbow joint when weight exceeds 110 lbs., with the total body dose not exceeding 6.0 mCi (i.e., two elbow joints in 110-lb. or greater-sized dogs).**

PREPARATION FOR USE
Synovetin OA® is provided in a 3 mL glass vial within a lead cylinder. Each vial is for use with a single dog.

The product should be stored in the cardboard shipping container until needed for use. The **prescribed dose** should be **administered on the date noted** on the certificate accompanying the Synovetin OA®; however, it can be administered the day before or after if circumstances require injection on a different day. Always use proper personal protection equipment and precautions for handling radioactive medical products, including nitrile gloves, splash shield, safety goggles, back-fastening gowns, head covers, booties, and surgical masks.

STEP 1: When ready to withdraw the dose into a syringe and prior to removing the shrink wrap around the lead cylinder, gently **shake the lead cylinder for approximately 10 seconds to ensure proper mixing** of the product.

STEP 2: Remove the shrink wrap from the lead cylinder and dispose of it appropriately.

STEP 3: Remove the lead cylinder lid, but do not remove the glass vial from the lead cylinder.

STEP 4: Remove the colored flip cap from the vial and retain for placement on the vial after the dose is withdrawn.

STEP 5: Attach a plastic syringe (3 mL or other appropriate volume) to a 22-ga. needle. Where practical, use a syringe shield to maintain operator radiation doses as low as reasonably achievable and to meet existing license conditions.

STEP 6: While holding the container at an approximate 45° angle, insert the needle through the septum.

STEP 7: **Draw the prescribed volume into the syringe** for an individual elbow. **Under no circumstances should the volume be modified.** Repeat immediately for the second elbow dose. If both elbows are to be treated, both doses will be contained in a single vial. If there are any questions or concerns, contact Exubrion Therapeutics® Customer Service at 833-942-1247.

STEP 8: The dose should be resuspended by gently inverting the syringe if more than 10 minutes has elapsed since dose was drawn into the syringe.

STEP 9: Following use of Synovetin OA®, replace the colored flip cap on the vial, then place the lid on the lead container and secure the lid with tape. Mark the vial with a tentative disposal date 5 months from the present date. After 5 months, the vial should be measured with a handheld rate meter (GM detector) to verify that radioactivity has decayed. If the vial is less than or equivalent to background radiation, it can then be disposed of as regular trash. All waste disposals should be documented according to your radioactive materials license and federal or state regulations. Do not return the vial, any packaging components, or supplies to the manufacturer.

The shielded syringe or syringes and needles that are used for administration should be placed in shielded sharps containers for radionuclides of similar half-lives (two weeks) and disposed of according to local, state, and federal regulations.

ROUTE OF ADMINISTRATION

Intra-articular injection. The product must NOT be administered by any other route. Confirmation of needle placement is recommended, whether by anatomical landmarks, fluoroscope, C-arm, ultrasound, or radiography.

DIRECTIONS FOR ADMINISTRATION

Dogs should be appropriately anesthetized or sedated prior to administration. With the canine elbow positioned at 45 degrees of flexion, inject Synovetin OA® through a 22-ga. needle into the joint. This can be done between the lateral condyle of the humerus and the triceps tendon, but other approaches to the joint can be used. Following injection, gently flex and extend the treated joint through a range of motion to disperse the colloid throughout the joint compartments.

FREQUENCY OF ADMINISTRATION

If needed, Synovetin OA® can be readministered to a previously treated elbow at least 12 months after the last treatment.

DURATION OF EFFECT FROM ADMINISTRATION

Effectiveness has been shown to last up to 12 months following a single treatment of dogs with naturally occurring OA of the elbow.

MAXIMUM ANNUAL DOSE

Total radiation dose per joint should not exceed 3.0 mCi/joint, with the total body dose not exceeding 6.0 mCi (i.e., two elbow joints during a 12-month period).

ADVERSE REACTIONS

Dogs participating in clinical studies to evaluate safety and effectiveness (n=74 dogs, 97 elbow joints) exhibited no significant adverse reactions when administered Synovetin OA®. If adverse events are observed or suspected, please report them by calling Exubrion Therapeutics® Customer Service at 833-942-1247.

POST-INJECTION CARE

Following administration of Synovetin OA®, the dog can recover with other post-operation animals in the general clinic population. Once the dog has fully recovered, it can be discharged to go home with the approval of the facility radiation safety officer or authorized user. All treatment site policies and license requirements should be observed.

FACILITY CONTAMINATION ASSESSMENT

Removable radioactive contamination is assessed by using filter paper to wipe a known area (typically 100 cm^2), then count the number of interactions on the filter paper using a radiation detector with a known efficiency for counting the specific isotope in question. Empirical data using a Ludlum model 3 rate meter and 44-9 GM probe show the efficiency for ^{117m}Sn detection to be approximately 20% under 2D geometry. With a background rate of 100 counts per minute (cpm), this radiation detection system has a minimum detectable activity (MDA) of approximately 400 disintegrations per minute (dpm). The standard regulatory threshold for removable contamination in an unrestricted area is 2000 dpm for similar isotopes. Therefore, a Ludlum rate meter and GM is an adequate instrument to use for compliance measurements of removable contamination.

Note, ^{117m}Sn has a similar gamma emission as the commonly used medical radioisotope ^{99m}Tc along with several low-energy conversion electron emissions which would only aid in the detection efficiency of contamination.

EXPOSURE RATE MEASUREMENTS

Radioactive materials licenses require daily closeout surveys of all areas where unsealed radioactive material was used. These surveys can be completed with any rate meter capable of detecting the type of radiation emitted by the radioactivity. Further, license conditions require that release exposure rate measurements be completed prior to releasing animals who have been administered radioactivity. Most license conditions require the measurement taken not exceed 0.5 mR/h at 1 meter from the treatment site. The exposure rate release measurement and daily closeout surveys can be completed with either a standard volume ion chamber such as the Ludlum 9DP or Victoreen 451P, a Ludlum Model 3 rate meter and energy compensated GM probe 44-38, or a Ludlum 26-1 DOSE with energy flattening cover. While the ion chamber is the gold standard for exposure rate measurements, the Ludlum model 26-1 DOSE is the most practical because it can satisfy both contamination and exposure rate measurements (with dose flattening cover).

OWNER INSTRUCTIONS FOR POST-TREATMENT CARE

When the level of radiation is determined to be below the established levels for release, the dog can be discharged. The dog will, however, retain a low level of radioactivity in the treated joint(s) for a short period of time. There is no requirement for rehabilitation or restraint of the dog, and it can resume its normal level of activity. Specific written instructions based on the post-treatment radiation dosimetry for care and proximity to the treated dog will be provided by the radiation safety officer (RSO) or authorized user (AU) of a radioactive materials (RAM)-licensed veterinary hospital to the dog owner. A RAM-licensed veterinary hospital RSO or AU should contact Exubrion Therapeutics® if there are specific questions.

MANUFACTURED BY Theragenics Corporation for Exubrion Therapeutics®

Manufacturer's contact information:
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STORAGE INSTRUCTIONS

Store in the shipping container at controlled room temperature (10°–30°C or 50°–86°F) until ready to use.

EXUBRION®
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