LEGEND MULTI DOSE- hyaluronate sodium injection, solution
Merial, Inc.

Legend® Multi Dose
(hyaluronate sodium)
Injectable Solution

For Intravenous Use in Horses Only

Not for Intra-Articular Use

CAUTION:

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:

LEGEND Multi Dose Injectable Solution is a clear, colorless solution of low viscosity. LEGEND Multi Dose Injectable Solution is pyrogen free and sterile. It is administered by intravenous injection.

Hyaluronic acid, the conjugate acid of hyaluronate sodium, is extracted from the capsule of *Streptococcus* spp. and purified, resulting in a form which is essentially free of protein and nucleic acids.

LEGEND Multi Dose Injectable Solution is supplied in 20 mL vials. Each mL contains 10 mg hyaluronate sodium, 8.5 mg sodium chloride, 0.223 mg sodium phosphate dibasic, 0.04 mg sodium phosphate monobasic and 15.63 mg benzyl alcohol as a preservative. The pH is adjusted to between 6.5 and 8.0 with sodium hydroxide or hydrochloric acid.

CHEMISTRY:

Hyaluronic acid, a glycosaminoglycan, can exist in the following forms depending upon the chemical environment in which it is found: as the acid, hyaluronic acid; as the sodium salt, sodium hyaluronate (hyaluronate sodium); or as the hyaluronate anion. These terms may be used interchangeably but in all cases, reference is made to the glycosaminoglycan composed of repeating subunits of D-glucuronic acid and N-acetyl-D-glucosamine linked together by glycosidic bonds. Since this product originates from a microbial source, there is no potential for contamination with dermatan or chondroitin sulfate or any other glycosaminoglycan.

CLINICAL PHARMACOLOGY:

Hyaluronic acid is a naturally occurring substance present in connective tissue, skin, vitreous humour and the umbilical cord in all mammals. High concentrations of hyaluronic acid are also found in the synovial fluid. It also constitutes the major component of the capsule of certain microorganisms. The hyaluronic acid produced by bacteria is of the same structure and configuration as that found in mammals.

The actual mechanism of action for hyaluronate sodium in the healing of degenerative joint disease is not completely understood. One major function appears to be the regulation of normal cellular constituents. This effect decreases the impact of exudation, enzyme release and subsequent degradation of joint integrity. Additionally, hyaluronate sodium exerts an anti-inflammatory action by inhibiting the movement of granulocytes and macrophages.[1] Hyaluronate molecules are long chains which form a filter network interspersed with normal cellular fluids.

INDICATIONS:

LEGEND Multi Dose Injectable Solution is indicated in the treatment of joint dysfunction of the carpus or fetlock in horses due to non-infectious synovitis associated with equine osteoarthritis.

DOSAGE AND ADMINISTRATION:

4 mL (40 mg) injected intravenously. Treatment may be repeated at weekly intervals for a total of three treatments.

Use aseptic technique and inject slowly into the jugular vein.

Horses should be given stall rest after treatment before gradually resuming normal activity.

CONTRAINDICATIONS:

There are no known contraindications for the use of LEGEND Multi Dose Injectable Solution in horses.

RESIDUE WARNING:

Do not use in horses intended for human consumption.

HUMAN WARNINGS:

Not for use in humans. Keep this and all other drugs out of reach of children.

ANIMAL SAFETY WARNINGS:

Not for Intra-articular use. The Intra-articular safety of hyaluronate sodium with benzyl alcohol has not been evaluated.

PRECAUTIONS:

Radiographic evaluation should be carried out in cases of acute lameness to ensure that the joint is free from serious fracture.

The safety of LEGEND Multi Dose Injectable Solution has not been evaluated in breeding stallions or in breeding, pregnant or lactating mares.

ADVERSE REACTIONS:

No local or systemic side effects were observed in the field studies using LEGEND Injectable Solution.

Post-Approval Experience: While all adverse reactions are not reported, the following adverse reactions are based on voluntary post-approval reporting for LEGEND Injectable Solution: Occasional depression, lethargy, and fever.

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, contact Merial at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation.

EFFECTIVENESS:

Effectiveness studies utilizing LEGEND Multi Dose Injectable Solution were not performed. LEGEND Multi Dose Injectable Solution was approved based on the conclusion that the effectiveness of LEGEND Multi Dose Injectable Solution will not differ from that demonstrated for the original formulation of LEGEND Injectable Solution.

Twenty-one horses with lameness in either the carpal or fetlock joints were treated intravenously with LEGEND Injectable Solution in a well-controlled field study conducted at four locations. One, two or three injections were given based on clinical improvement. Overall clinical improvement was judged as excellent or good in 90% of the cases treated intravenously with LEGEND Injectable Solution.

ANIMAL SAFETY:

Animal safety studies utilizing LEGEND Multi Dose Injectable Solution were not performed. LEGEND Multi Dose Injectable Solution was approved based on the conclusion that the safety of LEGEND Multi Dose Injectable Solution will not differ from that demonstrated for the original formulation of LEGEND Injectable Solution.

LEGEND Injectable Solution was administered to normal horses at one, three and five times the

recommended intravenous dosage of 40 mg. Treatments were given once weekly for nine consecutive weeks (three times the maximum duration). No systemic clinical signs were observed nor were there any adverse effects upon hematology or clinical chemistry parameters.

STORAGE:

Do not store above 40° C (104° F).

HOW SUPPLIED:

LEGEND Multi Dose Injectable Solution is supplied in 20 mL bottles.

NADA 140-883, Approved by FDA

Manufactured for: Merial, Inc., Duluth, GA 30096-4640, U.S.A.

REFERENCE:

[1]Swanstrom, O.G. 1978. Hyaluronate (hyaluronic acid) and its use, Proc. American Assoc. Equine Pract., 24th annual convention, pp. 345-348.

Made in USA

1050-8683-01, Rev. 05-2015

84671924

PRINCIPAL DISPLAY PANEL - 20 mL Bottle Carton

Legend® Multi Dose
(hyaluronate sodium)
Injectable Solution 10 mg/mL

MERIAL

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For the treatment of joint dysfunction of the carpus or fetlock in horses due to non-infectious synovitis associated with equine osteoarthritis.

20 mL

Manufactured for:
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NADA 140-883, Approved by FDA

84671932

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NADA 140-883, Approved by FDA

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Made in USA
1030-8680-00, Rev. 04-2015

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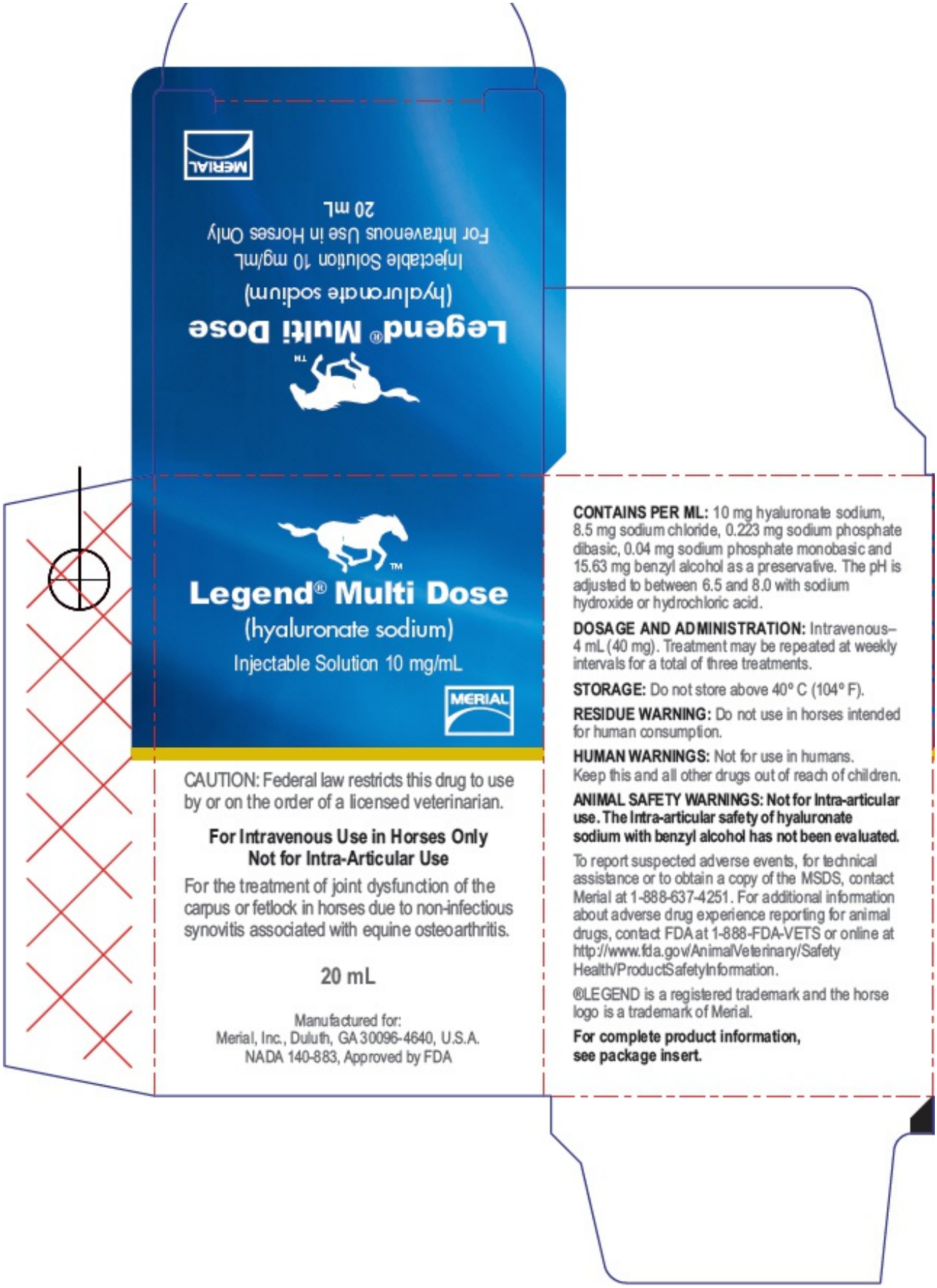
Lot:

Exp.:



LEGEND MULTI DOSE

hyaluronate sodium injection, solution

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:50604-3142
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
hyaluronate sodium (UNII: YSE9PPT4TH) (hyaluronic acid - UNII:S270N0TRQY)	hyaluronate sodium	10 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
Sodium Chloride (UNII: 451W47IQ8X)	8.5 mg in 1 mL
Sodium Phosphate, Dibasic (UNII: GR686LBA74)	0.223 mg in 1 mL
Sodium Phosphate, Monobasic (UNII: 3980JIH2SW)	0.04 mg in 1 mL
Benzyl Alcohol (UNII: LKG8494WBH)	15.63 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50604-3142-1	1 in 1 CARTON		
1		20 mL in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA140883	03/02/2015	

Labeler - Merial, Inc. (799641006)

Revised: 5/2015 Merial, Inc.