NORTH AMERICAN CORAL SNAKE ANTIVENIN (EQUINE)- coral snake (micrurus fulvius) immune globulin antivenin (equine) injection, powder, for solution

Wyeth Pharmaceuticals LLC, a subsidiary of Pfizer Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use North American Coral Snake Antivenin (Equine) safely and effectively. See full prescribing information for North American Coral Snake Antivenin (Equine).

North American Coral Snake Antivenin (Equine)
Lyophilized Powder for Solution for Intravenous Injection
Initial U.S. Approval: 1967

INDICATIONS AND USAGE

North American Coral Snake Antivenin (Equine) is a horse-derived antivenin indicated for the treatment of envenomation caused by North American coral snakes - *Micrurus*. (1)

DOSAGE AND ADMINISTRATION

For intravenous use only.

- In adults and adolescents, the dose may vary from 3 to 5 vials, depending on the response to treatment. (2.1)
- In small children, the dose may be decreased, depending on the response to treatment. (2.1)
- Contents of each reconstituted vial can neutralize approximately 250 mouse (Lethal Dose) LD_{50} or approximately 2 mg of *M. fulvius* venom. (2.1)
- Infuse the first 1 or 2 mL over a 3- to 5-minute period, observing for allergic reaction. If tolerated, administer the rest of the dose at the rate that is comfortable for the patient based on body weight and general condition. Do not exceed 4 mL per minute for children. (2.2)

DOSAGE FORMS AND STRENGTHS

Lyophilized powder in single use vial for reconstitution for injection. (3)

CONTRAINDICATIONS

- Do not administer North American Coral Snake Antivenin (Equine) prophylactically to asymptomatic patients. (4)
- Do not use in patients with a known history of hypersensitivity to horse serum unless the benefits outweigh the risks and appropriate management for anaphylactic reactions is readily available. (4)

WARNINGS AND PRECAUTIONS

Patients sensitive to North American Coral Snake Antivenin (Equine) or horse serum may develop anaphylaxis. Prior to intravenous North American Coral Snake Antivenin (Equine) administration consider performing a proper skin test and modify therapy if indicated. (5.1)

ADVERSE REACTIONS

Adverse reactions may include anaphylaxis and serum sickness, vomiting, and abdominal pain. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer, Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

North American Coral Snake Antivenin (Equine) is indicated only for the treatment of envenomation caused by bites of North American coral snakes - *Micrurus* (including the eastern and Texas varieties).

2 DOSAGE AND ADMINISTRATION

For intravenous use only.

2.1 Dose

- Contents of each reconstituted vial can neutralize approximately 250 mouse (Lethal Dose) LD_{50} or approximately 2 mg of *Micrurus fulvius fulvius* (*M. f. fulvius)* venom.
- In adults and adolescents, the dose may vary from 3 to 5 vials, depending on the response to treatment.
- In small children, the dose may be decreased, depending on the response to treatment.

2.2 Preparation and Administration

Preparation

- Pry off the small metal disc in the cap over the diaphragms of the vials of North American Coral Snake Antivenin (Equine) and remove cap from diluent vials.
- Swab the exposed surface of the rubber diaphragms of both vials with an appropriate germicide.
- Withdraw 10 mL diluent (Sterile Water for Injection, USP) using a sterile syringe and needle, and insert the needle through the stopper of the vacuum-containing vial of North American Coral Snake Antivenin (Equine).

    - The vacuum in the North American Coral Snake Antivenin (Equine) vial will pull the diluent out of the syringe into the vial. Allow room air to be pulled into the North American Coral Snake Antivenin (Equine) vial until all vacuum is released.
    - Point the needle at the center of the lyophilized pellet of North American Coral Snake Antivenin (Equine) so that the diluent stream will wet the pellet.

- Reconstitute by swirling, not by shaking, for 1 minute, at 5-minute intervals until you observe complete dissolution of the lyophilized North American Coral Snake Antivenin (Equine). Complete reconstitution usually requires at least 30 minutes.

Administration

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- Start an intravenous infusion of 250 to 500 mL of Sodium Chloride Injection, USP.
- Determine whether the patient has hypersensitivity to horse-serum in order to evaluate treatment decisions, and to prepare for treatment of anaphylaxis if it occurs *[see Warnings and Precautions (5.1)]*.
- After reconstitution of the lyophilized North American Coral Snake Antivenin (Equine) administer the contents of 3 to 5 vials (30 to 50 mL) intravenously by slow injection directly into the intravenous tubing or the reservoir bottle of the intravenous solution. If added to reservoir bottle, mix by gentle swirling – do not shake.
- Administer the first 1 or 2 mL over a 3- to 5-minute period with careful observation of the patient for evidence of an allergic reaction. If no signs or symptoms of anaphylaxis appear, continue the injection or intravenous infusion.
- Adjust the infusion rate by the severity of signs and symptoms of envenomation and tolerance of North American Coral Snake Antivenin (Equine). Administer at the maximum safe rate for intravenous fluids, based on body weight and general condition of the patient.

    - For adults, if given by intravenous infusion to a previously healthy adult, allow 250 or 500 mL to run in within 30 minutes;
    - For small children, allow the first 100 mL to run in rapidly but then decrease to a rate not to exceed 4 mL per minute. Response to treatment may be rapid and dramatic.

- Observe the patient carefully and administer additional North American Coral Snake Antivenin (Equine) intravenously as required.

3 DOSAGE FORMS AND STRENGTHS

Each package contains one single use vial with lyophilized North American Coral Snake

Antivenin (Equine) for dilution with 10 mL of diluent (Sterile Water for Injection, USP). Contents of each reconstituted vial can neutralize approximately 250 mouse (Lethal Dose) LD_{50} or approximately 2 mg of *M. f. fulvius* venom.

4 CONTRAINDICATIONS

- Do not administer North American Coral Snake Antivenin (Equine) prophylactically to asymptomatic patients.[1]
- Do not administer North American Coral Snake Antivenin (Equine) to patients with a known history of hypersensitivity to horse serum unless the benefits outweigh the risks and appropriate management for anaphylactic reactions is readily available.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Patients sensitive to North American Coral Snake Antivenin (Equine) or horse serum may develop anaphylaxis. Prior to intravenous North American Coral Snake Antivenin (Equine) administration, consider performing a proper skin test and modify therapy if indicated.

Consider the following precautions to manage hypersensitivity reactions:

- Emergency medical care (e.g., epinephrine, intravenous antihistamines and/or albuterol) should be readily available.
- Carefully monitor patients for signs and symptoms of an acute allergic reaction (e.g., urticaria, pruritus, erythema, angioedema, bronchospasm with wheezing or cough, stridor, laryngeal edema, hypotension, tachycardia).
- Follow-up all patients for signs and symptoms of delayed allergic reactions or serum sickness (e.g., rash, fever, myalgia, arthralgia).

Patients who receive a course of treatment with a foreign protein such as North American Coral Snake Antivenin (Equine) may become sensitized to it. Therefore, use caution when administering a repeat course of treatment with North American Coral Snake Antivenin (Equine) for a subsequent envenomation episode.

6 ADVERSE REACTIONS

The most common adverse reactions observed after treatment with North American Coral Snake Antivenin (Equine) were anaphylaxis and serum sickness, vomiting, and abdominal pain. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available human data that establish developmental toxicity related to the use of North American Coral Snake Antivenin (Equine). There are no available animal data informing the North American Coral Snake Antivenin (Equine)-associated risk. North American Coral Snake Antivenin (Equine) should be given to a pregnant woman only if clearly required. In the US general population, the background risk of major birth defects is 2–4% and of miscarriage is 15–20% in clinically recognized pregnancies.

8.2 Lactation

Risk Summary

Lactation studies have not been conducted with North American Coral Snake Antivenin (Equine). It is not known whether North American Coral Snake Antivenin (Equine) is excreted in human milk. North American Coral Snake Antivenin (Equine) should be administered to lactating women only if clearly indicated. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for North American Coral Snake Antivenin (Equine) and any potential adverse effects on the breastfed child from North American Coral Snake Antivenin (Equine) or from the underlying maternal condition.

8.4 Pediatric Use

Controlled clinical studies of safety and effectiveness in pediatric patients have not been conducted.

Potential cases of Coral Snake envenomation and subsequent treatment with North American Coral Snake Antivenin (Equine) have been reported in pediatric patients;[2] adverse reactions included anaphylaxis (wheezing) requiring treatment with epinephrine, vomiting, and abdominal pain.

8.5 Geriatric Use

Specific studies in elderly patients have not been conducted.

11 DESCRIPTION

North American Coral Snake Antivenin (Equine) is a sterile lyophilized powder for solution for injection containing serum globulins obtained by fractionating blood from healthy horses that have been immunized with eastern coral snake (*Micrurus fulvius fulvius*) venom. Prior to lyophilization, the product contains 0.25% phenol.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

North American Coral Snake Antivenin (Equine) specifically binds to and neutralizes coral snake venom.

12.2 Pharmacodynamics

North American Coral Snake Antivenin (Equine) is standardized for potency in mice in terms of its LD_{50} neutralizing capacity per milliliter as determined by intravenous injection

of a graded series of mixtures of North American Coral Snake Antivenin (Equine) with *M. f. fulvius* venom. Based on this assay system, the reconstituted contents of each vial (10 mL) will neutralize approximately 250 mouse LD_{50} or approximately 2 mg of *M.f. fulvius* venom.

The results of cross-neutralization tests indicate that North American Coral Snake Antivenin (Equine) will neutralize the venom of *M. fulvius tenere* (Texas coral snake) but will not neutralize the venom of *Micruroides euryxanthus* (Arizona or Sonoran coral snake).

14 CLINICAL STUDIES

There have been no well-controlled clinical studies of the use of North American Coral Snake Antivenin (Equine) in patients experiencing envenomation by the Eastern Coral Snake, however a retrospective analysis[3] has been published of 387 coral snake exposures treated in a healthcare facility in Florida between 1998 and 2010, including 252 patients who were treated with North American Coral Snake Antivenin (Equine). Patients were managed according to different treatment strategies: (a) asymptomatic at ED arrival and treated empirically (n=134); (b) asymptomatic at ED arrival, but treatment withheld until symptoms appeared (n=106; 6 of the 106 received North American Coral Snake Antivenin (Equine) at some point; the remainder were never treated); (c) symptomatic at ED arrival and treated with North American Coral Snake Antivenin (Equine) (n=112); and (d) symptomatic at ED arrival but not treated with North American Coral Snake Antivenin (Equine) (n=35). The average number of vials administered to treated patients was 3.75 (range 1 – 20 vials); the 17 patients who received repeat treatment were administered 8.3 vials, on average. There was no reported usage of foreign antivenom or acetylcholinesterase inhibitors in this case series. The 387 patients were assessed for clinical outcomes, as shown in Table 1. Outcomes codes range from full recovery with no residual effects ("No Effect") to less than full recovery with significant residual effects ("Major"). Empiric treatment of asymptomatic patients resulted in more 'moderate' and 'major' outcomes compared to withholding treatment until symptoms appeared (p<.001), however, the patients were not randomized and selection biases could have affected this result.

Table 1 – Outcome by Treatment Strategy

Treatment Strategy	**Empiric (N = 134)**	**Withhold (N = 106)**	**Symptomatic with AV (N = 112)**	**Symptomatic without AV (N = 35)**
Primary outcome				
Endotracheal intubation (%)	3 (2.2)	1 (0.94)	7 (6.25)	0 (0)
Secondary outcomes				
Days intubated Avg. (SD)	5.67 (2.89)	24 (N/A)	8 (6.22)	0 (0)
ICU admission (%)*	97 (72.39)	49 (46.23)	90 (80.36)	9 (25.71)
ICU LOS Avg.(SD)	1.5 (1.18)	1.73 (3.28)	2.25 (3.35)	1.3 (0.5)
Total LOS Avg.(SD)	1.58 (1.56)	1.17 (2.94)	2.47 (3.68)	0.94 (0.85)
Antivenom ADR	26 (19.4)	0 (0)	20 (17.86)	0 (0)

(%)*	20 (19.4)	0 (0)	20 (17.86)	0 (0)
Outcome code %*				
No Effect	4.76	29.29	0	0
Minor	71.43	56.57	34.23	63.64
Moderate	20.63	13.13	54.05	36.36
Major	3.17	1.01	11.71	0

ADR, adverse drug reaction; AV, antivenom; Avg, average; LOS, length of stay; ICU, intensive care unit.

* $p < 0.01$ between empiric and withhold strategies.

Adverse reactions associated with North American Coral Snake Antivenin (Equine) administration were documented in 46 (18.25%) cases. The most common adverse reactions were hives, rash and/or welts (12%); itching (9%); shortness of breath (8%); hypotension (2%) and angioedema (1%). Antihistamines were administered to 46 patients, corticosteroids to 40, and epinephrine to 10 cases to treat these adverse reactions.

15 REFERENCES

1. Bowden, C and Krenzelok, E: Clinical applications of commonly used contemporary antidotes, a US perspective. Drug Safety 1997; 16(1):9-47.
2. Sasaki, J et al: Coral snake bites and envenomation in children, A case series. Ped Emerg Care 2014; 30(4):262-5.
3. Wood A, Schauben J, Thundiyil J, et al. Review of Eastern coral snake (Micrurus fulvius fulvius) exposures managed by the Florida Poison Information Center Network: 1998-2010. Clin Toxicol 2013; 51(8):783-8.

16 HOW SUPPLIED/STORAGE AND HANDLING

North American Coral Snake Antivenin (Equine) is supplied as a sterile lyophilized powder in single use vial (NDC 0008-0423-01) in a carton (NDC 0008-0423-03).

Store vials between 2 and 8°C (36 and 46° F). Do not freeze.

Use the reconstituted and diluted product within 4 hours.

17 PATIENT COUNSELING INFORMATION

Advise patients to contact the physician or emergency department immediately if they experience any signs and symptoms of delayed allergic reactions or serum sickness up to 14 days following hospital discharge. Symptoms include rash, pruritus, joint pain, arthralgia, fever, lymphadenopathy, and malaise.

U.S. Govt. License No. 3

This product's label may have been updated. For current full prescribing information, please visit www.pfizer.com.

Manufactured by
Wyeth Pharmaceuticals LLC
A subsidiary of Pfizer Inc, Philadelphia, PA 19101

LAB-0726-7.0

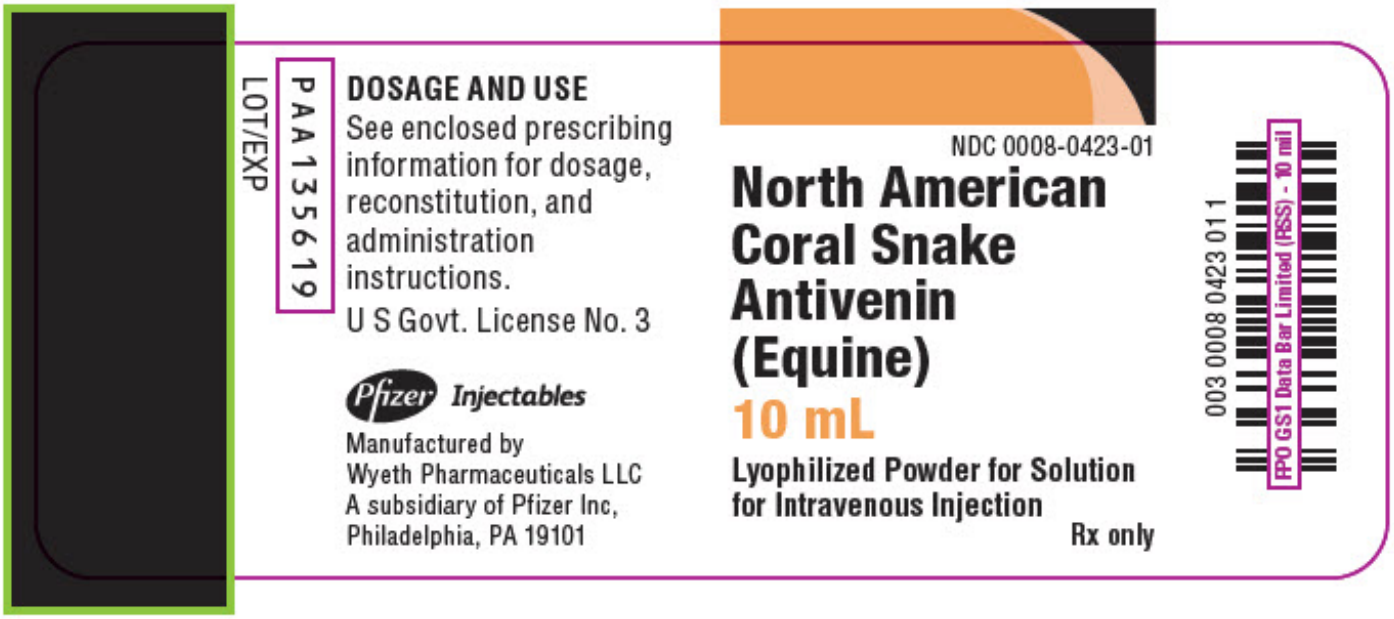
PRINCIPAL DISPLAY PANEL - 10 mL Vial Label

NDC 0008-0423-01

North American
Coral Snake
Antivenin
(Equine)
10 mL

Lyophilized Powder for Solution
for Intravenous Injection

Rx only



PRINCIPAL DISPLAY PANEL - 10 mL Vial Carton

NDC 0008-0423-03
Contains 1 of NDC 0008-0423-01

North American
Coral Snake
Antivenin
(Equine)

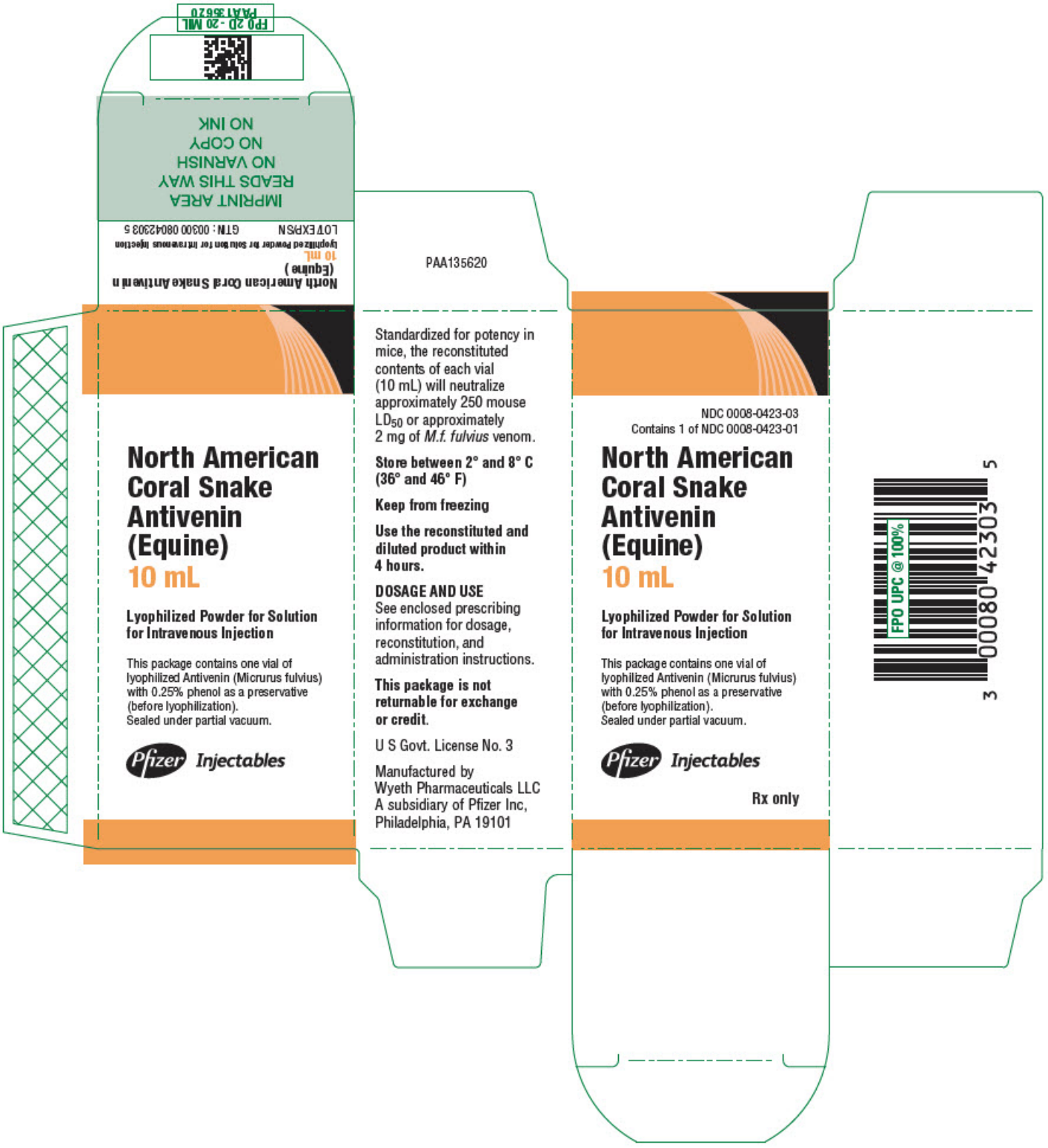
10 mL

Lyophilized Powder for Solution
for Intravenous Injection

This package contains one vial of
lyophilized Antivenin (Micrurus fulvius)
with 0.25% phenol as a preservative
(before lyophilization).
Sealed under partial vacuum.

Pfizer Injectables

Rx only



NORTH AMERICAN CORAL SNAKE ANTIVENIN (EQUINE)

coral snake (micrurus fulvius) immune globulin antivenin (equine) injection, powder, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0008-0423
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CORAL SNAKE (MICRURUS FULVIUS) IMMUNE GLOBULIN ANTIVENIN (EQUINE) (UNII: Y605XBM2GL) (CORAL SNAKE (MICRURUS FULVIUS) IMMUNE GLOBULIN ANTIVENIN (EQUINE) - UNII:Y605XBM2GL)	CORAL SNAKE (MICRURUS FULVIUS) IMMUNE GLOBULIN ANTIVENIN (EQUINE)	250 [arb'U] in 10 mL

Inactive Ingredients

Ingredient Name	Strength
PHENOL (UNII: 339NCG44TV)	
THIMEROSAL (UNII: 2225PI3MOV)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0008-0423-03	1 in 1 CARTON	10/12/2016	
1	NDC:0008-0423-01	10 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101099	10/12/2016	

Labeler - Wyeth Pharmaceuticals LLC, a subsidiary of Pfizer Inc. (113008515)

Establishment

Name	Address	ID/FEI	Business Operations
Pharmacia & Upjohn Company LLC		618054084	ANALYSIS(0008-0423) , API MANUFACTURE(0008-0423) , LABEL(0008-0423) , MANUFACTURE(0008-0423) , PACK(0008-0423)

Revised: 11/2022 Wyeth Pharmaceuticals LLC, a subsidiary of Pfizer Inc.