**SYMPTOM RECOGNITION & DOSING REGIMEN**

**Is Your Emergency Department Prepared?**

Why send your patient to the ICU when you can send them home in under 4 hours? Make sure your hospital knows how to recognize and effectively treat scorpion envenomation symptoms, when to use ANASCORP, and how to properly dose ANASCORP.

**SYMPTOM RECOGNITION**

Symptoms can include: pain, loss of muscle control, roving or abnormal eye movements, slurred speech, respiratory distress, hypotension, arrhythmias, and coma. Symptoms are graded on a 4-point scale, adapted from O’Conner:

- **GRADE 1:** Localized pain and/or paresthesia distant from site of envenomation.
- **GRADE 2:** Pain and/or paresthesia, remote from site of envenomation.
- **GRADE 3:** Other grade 2 symptoms: Tongue fasciculations, hypersalivation, dysphagia, respiratory distress, and/or neuromuscular dysfunction.
- **GRADE 4:** Both cranial nerve AND neuromuscular dysfunction.

**ANASCORP DOSING REGIMEN**

**DOSE**

- **INITIAL DOSE:** 1 vial of 300 mg immune F(ab’)2 infused over 10 minutes
- **ADDITIONAL DOSSES:** 1 vial of 300 mg immune F(ab’)2 infused over 10 minutes (Repeat PRN)

**DECIDE**

- **OBSERVE:** For 30 minutes post-ANASCORP administration
- **SYMPTOM resolution?**
  - **YES:** Proceed to discharge
  - **NO:** Proceed to observation

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

**Hypersensitivity Reactions**

Severe hypersensitivity reactions, including anaphylaxis, are possible with ANASCORP. Prepare for monitoring and management of allergic reactions, ANASCORP. Patient monitoring with follow-up visit is recommended.

**Transmissible Infectious Agents**

ANASCORP is made from equine plasma and may contain infectious agents, e.g., viruses.

**REACTIONS**

Local reactions and generalized myalgias have been reported with the use of cresol as an injectable excipient.

**ADVERSE REACTIONS**

The most common adverse reactions observed in ≥ 2% of patients in the clinical studies for ANASCORP were: vomiting, pyrexia, rash, nausea and pruritus.

**CONTRAINDICATIONS**

None.

**INTERACTIONS**

None.

**IMMUNITY**


does not provide protection against future scorpion bites.

**IMPORTANT STOCKING CONSIDERATIONS**

- **†Sterile normal saline (0.9% NaCl).**
- **‡See Return Goods Policy for terms and conditions.**
- **© Rare Disease Therapeutics, Inc. | ANScut003PA2 | August 2022**
Localized pain and/or paresthesias at the site of envenomation.

**DECIDE**

**DONE**

An ASCORP is an antivenin indicated for the treatment of clinical signs of scorpion envenomation.

**IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

**Hypersensitivity Reactions**

Severe hypersensitivity reactions, including anaphylaxis, are possible with ANASCORP. Prepare for monitoring and management of allergic reactions, particularly in patients with a history of hypersensitivity to equine plasma or patients who have received previous therapy with antivenoms containing scorpion or equine proteins.

**Delayed Allergic Reactions (Serum Sickness)**

Delayed allergic reactions (serum sickness) may occur following treatment with ANASCORP. Patient monitoring with lidocaine uptake is recommended.

**Transmissible Infectious Agents**

ANASCORP is made from equine plasma and may contain infectious agents, e.g., viruses.

**Reaction to Creosol**

Localized reactions and generalized myalgias have been reported with the use of creosol as an injectable vehicle.

**ADVERSE REACTIONS**

The most common adverse reactions observed in ≥ 2% of patients in the clinical studies for ANASCORP were: vomiting, pyrexia, rash, nausea and pruritus. Please see full Prescribing Information at www.anascorp.com.

For educational materials, training videos, or to contact a representative, visit: www.ANASCORP.com

To order ANASCORP, call: 1-844-4RareTx (1-844-472-7389)

ANASCORP is exclusively distributed by: Rare Disease Therapeutics, Inc.

To report SUSPECTED ADVERSE REACTIONS, contact Rare Disease Therapeutics, Inc., at 1-844-472-7389, or FDA, at 1-800-FDA-1088 or www.fda.gov/medwatch.

Poison Control Center: 1-800-222-1222

**REACTIONS SUSPECTED ADVERSE**

**To report**

**SUSPECTED ADVERSE REACTIONS,** contact Rare Disease Therapeutics, Inc., at 1-844-472-7389, or FDA, at 1-800-FDA-1088 or www.fda.gov/medwatch.

**IMPORTANT STOCKING CONSIDERATIONS**

1. Initial dose is 3 vials.
2. Stacking recommendation is a minimum of 5 vials per patient.
3. Extended holiday weekends may require having additional vials on hand.
4. ANASCORP is only available from AnNovoRx: 1-844-472-7389.
5. Free replacement for expired, unopened vials.

**INDICATION**

ANASCORP® is an antivenin indicated for the treatment of clinical signs of scorpion envenomation.

*Please see accompanying package insert for full prescribing information.

© Rare Disease Therapeutics, Inc. / ANASCORP® | August 2022

**BE PREPARED**

Why send your patient to the ICU when you can send them home in under 4 hours?

Make sure you are prepared for a bark scorpion sting emergency.

Do your best to alleviate hardships on families due to hospital admissions, transfer costs and complications of supportive care. Use ANASCORP to treat clinical signs of scorpion envenomation in your Emergency Department.
**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use ANASCORP safely and effectively. See full prescribing information for ANASCORP.

**ANASCORP®**

Centruroides (scorpion) immune F(ab')2 (equine) injection

Lyophilized for Solution

For Intravenous Use Only

Initial U.S. Approval: 2011

**INDICATIONS AND USAGE**

ANASCORP is an antivenom indicated for treatment of clinical signs of scorpion envenomation. (1)

**DOSAGE AND ADMINISTRATION**

Intravenous use only.

**Initial dose**

- 3 vials

  - Reconstitute each vial with 5 milliliters of sterile normal saline (0.9% NaCl).
  - Combine and further dilute to a total of 50 milliliters.
  - Infuse intravenously over 10 minutes.

**Additional dose(s)**

- As needed

  - Administer one vial at a time at 30-60 minute intervals.
  - Dilute to a total of 50 milliliters with sterile normal saline (0.9% NaCl).
  - Infuse intravenously over 10 minutes.

- Initiate treatment with ANASCORP as soon as possible after scorpion sting in patients who develop clinically important signs of scorpion envenomation, including but not limited to loss of muscle control, roving or abnormal eye movements, slurred speech, respiratory distress, excessive salivation, frothing at the mouth, vomiting. (2)

- Close patient monitoring is necessary. (2)

**CONTRAINDICATIONS**

None. (4)

**WARNINGS AND PRECAUTIONS**

- Severe hypersensitivity reactions, including anaphylaxis, are possible with ANASCORP. Prepare for monitoring and management of allergic reactions, particularly in patients with a history of hypersensitivity to equine (horse) proteins or patients who have received previous therapy with antivenoms containing equine proteins. (5.1)

- Delayed allergic reactions (serum sickness) may occur following treatment with ANASCORP. Patient monitoring with a follow-up visit is recommended. (5.2)

- ANASCORP is made from equine plasma and may contain infectious agents, e.g. viruses. (5.3)

- Localized reactions and generalized myalgias have been reported with the use of cresol as an injectable excipient. (5.4)

**ADVERSE REACTIONS**

The most common adverse reactions observed in ≥ 2% of patients in the clinical studies for ANASCORP were: vomiting, pyrexia, rash, nausea, and pruritus. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Rare Disease Therapeutics, Inc., at 1-844-472-7389, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**USE IN SPECIFIC POPULATIONS**

Pregnancy: No human or animal data. Use only if clearly needed. (8.1)

See Section 17 for PATIENT COUNSELING INFORMATION

Revised: 08/2022

**FULL PRESCRIBING INFORMATION: CONTENTS**

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
  5.1 Hypersensitivity Reactions
  5.2 Delayed Allergic Reactions (Serum Sickness)
  5.3 Transmissible Infectious Agents
  5.4 Reactions to Cresol
6 ADVERSE REACTIONS
  6.1 Clinical Trials Experience
  6.2 Postmarketing Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
  8.1 Pregnancy
  8.2 Lactation
  8.4 Pediatric Use
  8.5 Geriatric Use
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
  12.1 Mechanism of Action
  12.3 Pharmacokinetics
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

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

1 INDICATIONS AND USAGE
ANASCORP® [centruroides (scorpion) immune F(ab’)_2 (equine) injection] is an equine-derived antivenom indicated for treatment of patients with clinical signs of scorpion envenomation.

2 DOSAGE AND ADMINISTRATION
For intravenous use only.
Initiate treatment with ANASCORP as soon as possible after scorpion sting in patients who develop clinically important signs of scorpion envenomation, including but not limited to loss of muscle control, roving or abnormal eye movements, slurred speech, respiratory distress, excessive salivation, frothing at the mouth and vomiting. (2)

Initial Dose: 3 vials
- The initial dose of ANASCORP is 3 vials.
- Reconstitute the contents of each vial with 5 milliliters of sterile normal saline (0.9% NaCl) and mix by continuous gentle swirling.
- Combine the contents of the reconstituted vials promptly and further dilute to a total volume of 50 milliliters with sterile normal saline (0.9% NaCl).
- Inspect the solution visually for particulate matter and discoloration prior to administration. Do not use if turbid.
- Infuse intravenously over 10 minutes.
- Monitor patient closely during and up to 60 minutes following the completion of infusion to determine if clinically important signs of envenomation have resolved.
- Discard partially used vials.

Additional Dosing
- Additional doses may be used if needed.
- Infuse one vial at a time at intervals of 30 to 60 minutes.
- Reconstitute the contents with 5 milliliters of sterile normal saline (0.9% NaCl) and mix by continuous gentle swirling.
- Further dilute to a total volume of 50 milliliters with sterile normal saline (0.9% NaCl). Inspect the solution visually for particulate matter or discoloration prior to administration.
- Infuse intravenously over 10 minutes.
- Monitor patient closely during and up to 60 minutes following the completion of infusion to determine if clinically important signs of envenomation have resolved.
- Discard partially used vials.

3 DOSAGE FORMS AND STRENGTHS
Each vial of ANASCORP contains a sterile, lyophilized preparation containing not more than 35 milligrams total protein and not less than 150 LD50 (mouse) neutralizing units.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity Reactions
Severe hypersensitivity reactions, including anaphylaxis, may occur with ANASCORP. Close patient monitoring for hypersensitivity reactions and readiness with intravenous therapy using epinephrine, corticosteroids, and diphenhydramine hydrochloride is recommended during the infusion of ANASCORP. If an anaphylactic reaction occurs during the infusion, terminate administration at once and administer appropriate emergency medical care.
Patients with known allergies to horse protein are particularly at risk for an anaphylactic reaction. Patients who have had previous
therapy with ANASCORP or another equine antivenom/antitoxin may have become sensitized to equine proteins and be at risk for a severe hypersensitivity reaction.

5.2 Delayed Allergic Reactions (Serum Sickness)
Monitor patients with follow-up visit(s) for signs and symptoms of delayed allergic reactions or serum sickness (e.g., rash, fever, myalgia, arthralgia), and treat appropriately if necessary. Eight out of 1,534 (0.5%) patients in the clinical trials exhibited symptoms suggestive of serum sickness. (6.1)

5.3 Transmissible Infectious Agents
ANASCORP is made from equine (horse) plasma, it may therefore carry a risk of transmitting infectious agents, e.g., viruses.

5.4 Reactions to Cresol
Trace amounts of cresol from the manufacturing process are contained in ANASCORP. Localized reactions and generalized myalgias have been reported with the use of cresol as an injectable excipient.

6 ADVERSE REACTIONS
The most common adverse reactions observed in ≥ 2% of patients in the clinical studies for ANASCORP were: vomiting, pyrexia, rash, nausea, and pruritus.

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

A total of 1534 patients were treated with ANASCORP, ranging from less than one month to 90 years old. The patient population was comprised of 802 males and 732 females. Patients were monitored for signs and symptoms of adverse reactions, including acute hypersensitivity reactions and serum sickness. Follow-up telephone interviews were conducted at 24 hours, 7 days, and 14 days after treatment to assess symptoms suggestive of ongoing venom effect, serum sickness, and any other adverse reactions.

Table 1 shows the adverse reactions occurring in patients across all clinical trials for ANASCORP. Twenty-seven percent (421/1534) of patients receiving ANASCORP reported at least one adverse reaction.

<table>
<thead>
<tr>
<th>ADVERSE REACTION</th>
<th>ANASCORP [n=1534] n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>72 (4.7)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>63 (4.1)</td>
</tr>
<tr>
<td>Rash</td>
<td>41 (2.7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>32 (2.1)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>31 (2.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>29 (1.9)</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>28 (1.8)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>25 (1.6)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>24 (1.6)</td>
</tr>
<tr>
<td>Cough</td>
<td>22 (1.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20 (1.3)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>17 (1.1)</td>
</tr>
</tbody>
</table>

No patients died or discontinued study participation for severe adverse reactions.

Eight patients were considered to have serum sickness (Type III hypersensitivity); no patient manifested the full serum sickness syndrome. Three patients were treated with systemic corticosteroids and five others received either no treatment or symptomatic therapy.

34 patients experienced a total of 39 severe adverse reactions such as respiratory distress, aspiration, hypoxia, ataxia, pneumonia, and eye swelling. It is not clear whether these adverse reactions were related to ANASCORP, envenomation, or a combination of both².
6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of ANASCORP. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Chest tightness, palpitations, rash and pruritus.

7 DRUG INTERACTIONS

No drug interaction studies have been conducted with ANASCORP.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Animal reproduction studies have not been conducted with ANASCORP. It is also not known whether ANASCORP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. ANASCORP should be given to a pregnant woman only if clearly needed.

8.2 Lactation

Risk Summary

It is not known whether ANASCORP is excreted in human breast milk. Because many drugs are excreted in human milk, caution should be exercised when ANASCORP is administered to a nursing woman.

8.4 Pediatric Use

Seventy-eight percent of the patients enrolled in the clinical studies were pediatric subjects (1204/1534), with ages ranging from less than one month to 18.7 years of age. Patient age groups were as follows: <2 years of age, 29%, 2 to 5 years, 37%, 5 to 18 years, 34%. The efficacy and safety of ANASCORP is comparable in pediatric and adult patients.

8.5 Geriatric Use

Specific studies in elderly patients have not been conducted. ANASCORP was administered to 77 patients over the age of 65 years with comparable efficacy and safety to the overall patient population.

11 DESCRIPTION

ANASCORP [centruroides (scorpion) immune F(ab')2 (equine) injection] is a sterile, nonpyrogenic, lyophilized, polyvalent preparation of equine immune globulin F(ab')2 fragments, manufactured from plasma of horses immunized with venom of C. noxius, C. l. limpidus, C. l. tecomanus, and C.s.suffusus. The product is obtained by pepsin digestion of horse plasma to remove the Fc portion of immune globulin, followed by fractionation and purification steps. The F(ab')2 content is not less than 85%, F(ab) content is not more than 7%, and the product contains less than 5% intact immunoglobulin. Each vial of ANASCORP contains 13.00-25.00 milligrams of sodium chloride, 27.00-52.00 milligrams of sucrose, and 61.00-102.00 milligrams of glycine as stabilizers. Trace amounts of pepsin, cresol (<0.058 mg/vial), borates (< 1 mg/vial), and sulfates (< 1.7 mg/vial) may be present from the manufacturing process. Each vial contains no more than 35 milligrams of protein and will neutralize at least 150 LD50 of Centruroides scorpion venom in a mouse neutralization assay.

The manufacturing procedures that contribute to the reduction of risk of viral transmission include pepsin digestion, ammonium sulfate precipitation/heat treatment, and nanofiltration.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ANASCORP is composed of venom-specific F(ab')2 fragments of immunoglobulin G (IgG) that bind and neutralize venom toxins, facilitating redistribution away from target tissues and elimination from the body. ¹

12.3 Pharmacokinetics
Eight clinically healthy volunteers (6 males and 2 females, age: 17 to 26 years) received a bolus intravenous dose of 47.5 mg of centruroides (scorpion) immune F(ab')2, (equine) injection. Blood samples were collected till 504 hours (21 days) and pharmacokinetic parameters were estimated by non-compartmental analysis which are summarized in Table 2.

### Table 2: Pharmacokinetic parameters of scorpion antivenom

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± sd</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC(0-∞) (μg*hr/mL)</td>
<td>706 ± 352</td>
</tr>
<tr>
<td>Clearance (mL/hr)</td>
<td>83.5 ± 38.4</td>
</tr>
<tr>
<td>Half-life (hrs)</td>
<td>159 ± 57</td>
</tr>
<tr>
<td>Vss (liters)</td>
<td>13.6 ± 5.4</td>
</tr>
</tbody>
</table>

14 CLINICAL STUDIES
The efficacy of ANASCORP was assessed in a prospective double-blinded randomized placebo-controlled study, four open-label studies and one retrospective study in various treatment settings in the United States and Mexico, where scorpion envenomation is common. A total of 1534 patients ranging from less than one month to 90 years old were treated. The majority of patients (78%, 1204/1534) were pediatric, ranging from less than one month to 18.7 years of age. Male (52.3%) and female patients (47.7%) were equally represented. Treatment success was determined by resolution of clinically important signs of scorpion envenomation within four hours of starting infusion. The randomized placebo study enrolled 15 subjects, eight to the ANASCORP treated group and seven to the placebo. The symptom resolution success rate was 100% for the ANASCORP treated and 14.3% for the placebo group.

A retrospective hospital chart review provided historical data from envenomated patients (n=97) who did not receive antivenom but were treated with sedatives and supportive care for symptoms of envenomation. These data were used as a historical control for expected outcomes in the absence of antivenom treatment. The historical controls were pediatric patients admitted to two pediatric intensive care units between 1990 and 2003 for the treatment of scorpion envenomation with supportive care only. The proportion of patients that required intensive care support four hours after intensive care unit admission, and the overall duration of the intensive care support requirement were calculated.

Overall, 95-100% of patients were relieved of systemic signs associated with scorpion envenomation in less than four hours after initiating ANASCORP treatment. In the historical control database, only 3.1% of patients experienced relief of symptoms within 4 hours of hospital admission.

In 1396/1534 patients the mean time from start of ANASCORP infusion to resolution of clinical signs and symptoms of envenomation was 1.42 hours (0.2 to 20.5 hours). Pediatric patients generally experienced a slightly faster time to resolution (1.28 ± 0.8 hours) compared with that of adult patients (1.91 ±1.4 hours). The time to resolution of symptoms was not affected by use of sedatives (474 patients who received sedatives resolved in 1.49 ± 1.1 hours and 922 patients who did not receive sedatives resolved in 1.38 ± 0.9 hours).

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING
ANASCORP is supplied as a sterile lyophilized preparation in a single-use vial. When reconstituted, each vial contains not more than 7.0 milligrams per milliliter of protein, and not less than 150 mouse LD50 neutralizing units.

Each carton NDC 66621-0150-2 contains 1 vial of ANASCORP NDC 66621-0150-1.
Store at room temperature (up to 25 °C (77 °F)). Brief temperature excursions are permitted up to 40 °C (104°F).
DO NOT FREEZE.
Discard partially used vials.

17 PATIENT COUNSELING INFORMATION

Serious Allergic Reactions

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 [see Hypersensitivity Reactions (5.1)].

Manufactured by:
Laboratorios Silanes, S.A. de C.V.
Toluca, Estado de Mexico, Mexico
Silanes® and the Silanes logo are registered trademarks in Mexico of Laboratorios Silanes, S.A. de C.V.

Manufactured for:
Rare Disease Therapeutics, Inc.
2550 Meridian Blvd., Suite 150
Franklin, TN 37067
www.raretx.com
RDT® and the RDT logo are registered trademarks of Rare Disease Therapeutics, Inc.

U.S. License No. 1860

RDT Part No: ANS-PI-009
Silanes Part No. 360891-7