Abbreviated Prescribing Information - Inoserp™ PAN-AFRICA - For full prescribing information see the approved Summary of Product Characteristics (SPC)

Product name: Inoserp™ PAN-AFRICA. Polyvalent F(ab')$_2$ Immunoglobulin Fragments (Equine), Snake Antivenom. **Composition:** less than 1 g of total proteins (< 10%) composed of equine F(ab´)2 immunoglobulin fragments neutralizing with high specificity the venoms of sub-Saharan Africa species (list of species detailed hereafter). Excipients: sodium chloride, USP, glycine, sucrose and water for injection. **Pharmaceutical form:** lyophilized powder for injectable solution. **Indications:** Inoserp™ PAN-AFRICA is indicated for the treatment of envenoming caused by the bite of the following species: VIPERIDAE: *Echis ocellatus, Echis leucogaster, Echis pyramidum, Bitis arietans, Bitis rhinoceros, Bitis nasicornis, Bitis gabonica*; and ELAPIDAE: *Dendroaspis polylepis, Dendroaspis viridis, Dendroaspis angusticeps, Dendroaspis jamesoni, Naja nigricollis, Naja melanoleuca, Naja haje, Naja pallida, Naja nubiae, Naja katiensis* and *Naja senegalensis.* Each vial neutralizes at least 250 LD_{50} of the venom of *Echis ocellatus, Bitis arietans, Naja nigricollis* and *Dendroaspis polylepis.* **Dosage and administration:** Inoserp™ PAN-AFRICA should be administered as soon as the first signs of envenoming appear. Healthcare providers should first perform a clinical evaluation according to the following envenoming classification:

- ***Grades of edema (progressive swelling):***
  1. Localized edema reaching the nearest joint
  2. Progressive edema not exceeding 2 joints
  3. Extensive edema not exceeding the limb
  4. Edema beyond the root of the limb (anasarca)
- ***Grades of bleeding (progressive bleeding):***
  1. Persistent local bleeding over an hour
  2. Bleeding from the mouth, nose or scars
  3. Hematoma, ecchymosis, purpura, blisters
  4. Internal hemorrhage (peritoneal, meningeal, etc.)
- ***Grades of neurological disorders (progressive weakness):***
  1. Anesthesia, tingling, local "pins-and-needles" sensation
  2. Sweat and abundant saliva, vomiting, myosis
  3. Ptosis, problems with vision, hearing and swallowing
  4. Respiratory distress, communication impairment

If signs of envenoming are not present, coagulation disorders may be demonstrated by performing a whole blood clotting test (WBCT). Treatment should be initiated as soon as there are any grade 1 symptoms (edema, bleeding or neurological disorders) or in the absence of symptoms if the results of WBCT is 1 (partial coagulation) or 2 (incoagulable blood). **Initial dose should be 2 vials**. Following the administration of the initial dose, it is recommended to evaluate the patient **every 2 to 4 hours**. If major symptoms as hemorrhagic or neurologic symptoms persist, get worse or start to appear, **treatment (2 vials) should be repeated**. Regular follow-up evaluations should be performed to determine the need for repeating treatment until the critical clinical symptoms of envenoming have resolved. Larger quantities of antivenom may be required depending on the amount of inoculated venom, the severity of envenoming, the general condition of the patient, the patient's clinical evolution and the snake species involved (i.e., Elapidae or Viperidae). In contrast, the age, sex or weight of the patient should not be considered in assessing the quantity of antivenom to deliver. **Reconstitution** of the product should be performed immediately prior to administration. Do not store any reconstituted product. The lyophilized powder should be diluted with 10 ml of Sterile Water for Injection (ampoule provided in the pack). The water should be introduced in the vial containing the powder using proper sterile techniques.

The dissolution of the product is obtained after a gentle shaking in less than 60 sec. The appearance of the solution should be clear to light yellow in color and slightly opalescent with no foreign particles in suspension. If the product is not fully dissolved and contains remaining foreign particles, it should be discarded and another vial should be used instead. **Administration** of Inoserp™ PAN-AFRICA is performed through **intravenous injection.** The preferred route of administration is **direct intravenous injection** of the solution **slowly over a minimum of 3 minutes**. The product can also be administered through **a drip** (2 vials of 10 ml reconstituted solution diluted with 50 ml of sterile isotonic saline solution) **over 30** minutes. **Contraindications:** known history of allergy to equine proteins or excipients. Considering the fatal risk linked to envenoming, allergy to equine proteins is not a contraindication to the use of antivenom, provided that treatment for anaphylactic shock can be implemented immediately, if necessary. **Special warnings and precautions for use:** patients with known allergies to equine origin proteins have a higher risk of experiencing hypersensitivity reactions, as well as the patients who have received prior treatment with Inoserp™ PAN-AFRICA or other equine origin antivenoms that might have caused hypersensitivity to equine origin proteins. Envenoming in children generally leads to more severe symptoms and a higher rate of lethality and sequelae. This is due to children's smaller body weight and volume that lead to a lower dilution of venom. Dosage should be the same for adults and children, irrespective of patient weight. **Pregnancy and breastfeeding:** Taking into account the fatal risk linked to envenoming, pregnancy and breastfeeding are not contraindications to the use of antivenom. **Fertility:** there is no evidence and there are no reports or fertility problems with the use of Inoserp™ PAN-AFRICA. **Effects on ability to drive and use machines:** not relevant. **Undesirable effects:** the most frequently reported adverse events are nausea (3%), vomiting (3%) and cough (3%). Pruritus (2%), urticaria (2%), vertigo (1%), dyspnea (1%) and hypotension (< 1%) were also observed. Acute reactions: The administration of equine origin $F(ab')_2$ fragments may be associated with allergic reactions including sweating, nausea, rashes, modest fall in blood pressure; these reactions are generally of mild intensity. Anaphylactoid reactions with hypertension, dyspnea, urticaria, Quincke's edema or severe allergic shock may also occur. However, the actual generalized allergic shock only appears in an exceptional manner. In this case it is recommended to immediately suspend the infusion and to administer corticosteroids, diphenhydramine hydrochloride, as well as any therapy that the healthcare provider deems appropriate. Serum sickness: Similar reactions to serum sickness have been described after the administration of animal origin proteins that may appear roughly 6 days after treatment onset. The clinical signs are fever, pruritus, erythema or urticaria, adenopathy and arthralgias. However, these types of reactions are observed in less than 1% of the patients who are given equine origin $F(ab')_2$ fragments. **Adverse events** should be reported at: pharmacovigilance@inosanbiopharma.com. **Overdose:** due to the nature of Inoserp™ PAN-AFRICA, no overdose effects are expected. **Shelf life:** 36 months. **Special precautions for storage:** the product should be stored at room temperature (between 8°C and 30°C). Temperature excursions exceeding 30°C are permitted up to 40°C for a maxim period of 6 months. Do not freeze. **Marketing Authorisation Holder:** INOSAN BIOPHARMA, S.A. Arbea Campus Empresarial, Edificio 2. Planta 2, Carretera Fuencarral a Alcobendas, Km.3.8-28108, Alcobendas, Madrid – SPAIN. **Legal category:** POM. **Date of revision of the text:** 15/11/2019