epilepticus, non-convulsive status epilepticus, the methods comprising administering to the subject a composition described herein, e.g., a neuroactive steroid, e.g., allopregnanolone, and optionally a cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., CAPTISOL®..

Provided herein is use of an effective amount of a dosage formulation of allopregnanolone in a cyclodextrin carrier in the manufacture of a medicament for treating a traumatic brain injury in an individual in need thereof for treatment of a central nervous system injury.

In one aspect, there is provided an aqueous pharmaceutical composition formulated for parental administration comprising allopregnanolone at a concentration of 5 mg/mL, sulfo butyl ether-β cyclodextrin at a concentration between 200-400 mg/mL, and a buffer, wherein the pH of the composition is 6 and the buffer is citrate buffer.

In one aspect, there is provided use of the aqueous pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a CNS disorder, wherein the CNS disorder is a traumatic brain injury, a seizure or status epilepticus.

In another aspect, there is provided use of the aqueous pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a traumatic brain injury.

In another aspect, there is provided an aqueous pharmaceutical composition formulated for parenteral administration comprising allopregnanolone at a concentration of 5 mg/mL, sulfo butyl ether-β-cyclodextrin at a concentration between 25-400 mg/mL, and a buffer, wherein the pH of the composition is 6 and the buffer is citrate buffer.

Provided herein is use of an effective amount of a dosage formulation of allopregnanolone in the manufacture of a medicament for treating a CNS disorder in a subject, wherein the CNS disorder is a seizure or status epilepticus.

In one embodiment, the disclosure features a composition, the composition comprising a neuroactive steroid, e.g., allopregnanolone, and cyclodextrin, e.g., a neuroactive steroid, e.g., allopregnanolone, and optionally a cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., CAPTISOL®, complex. a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., CAPTISOL®, complex.

In some embodiments, the neuroactive steroid is a progestin derivative, e.g., allopregnanolone. In an embodiment, the neuroactive steroid is allopregnanolone.

In some embodiments, the cyclodextrin is a β-cyclodextrin. In an embodiment, the cyclodextrin is a sulfo butyl ether β-cyclodextrin. In an embodiment, the cyclodextrin is CAPTISOL®. In some embodiments, the cyclodextrin is a β-cyclodextrin disclosed in U.S. Patent Nos. 5,874,418; 6,046,177; or 7,635,733, which are herein incorporated by reference.

In some embodiments, the neuroactive steroid is a progestin derivative, e.g., allopregnanolone, and the cyclodextrin is a β-cyclodextrin. In an embodiment, the neuroactive steroid is allopregnanolone and the cyclodextrin is CAPTISOL®.

In some embodiments, the neuroactive steroid, e.g., allopregnanolone, and cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g., CAPTISOL®, complex is formulated for parenteral administration. In an embodiment, the neuroactive steroid, e.g., allopregnanolone, and cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β-cyclodextrin, e.g.,

We claim:

1. An aqueous pharmaceutical composition formulated for parenteral administration comprising allopregnanolone at a concentration of 5 mg/mL, sulfo butyl ether-β-cyclodextrin at a concentration between 200-400 mg/mL, and a buffer, wherein the pH of the composition is 6 and the buffer is citrate buffer.

2. An aqueous pharmaceutical composition as claimed in claim 1, comprising sulfo butyl ether-β-cyclodextrin at a concentration of 250mg/mL.

3. An aqueous pharmaceutical composition as claimed in claim 1 or 2, wherein the formulation comprises an antioxidant.

4. An aqueous pharmaceutical composition as claimed in any one of claims 1 to 3, wherein the composition is formulated for intravenous administration.

5. An aqueous pharmaceutical composition as claimed in any one of claims 1 to 3, wherein the composition is formulated for intramuscular (IM) injection, subcutaneous (SC) injection, intrathecal administration, or administration via the pulmonary, nasal or mucosal routes.

6. An aqueous pharmaceutical composition as claimed in any one of claims 1 to 3, wherein the composition is formulated for intramuscular (IM) injection.

7. Use of the aqueous pharmaceutical composition as claimed in any one of claims 1 to 6 in the manufacture of a medicament for treating a CNS disorder, wherein the CNS disorder is a traumatic brain injury, a seizure or status epilepticus.

8. The use of claim 7, wherein the status epilepticus disorder is refractory status epilepticus or non-convulsive status epilepticus and wherein the seizure is an acute repetitive seizure or a cluster seizure.

9. The use of claim 7, wherein the CNS disorder is a traumatic brain injury.

10. Use of the aqueous pharmaceutical composition as claimed in any one of claims 1 to 6 in the manufacture of a medicament for treating a traumatic brain injury.

11. An aqueous pharmaceutical composition formulated for parenteral administration comprising allopregnanolone at a concentration of 5 mg/mL, sulfo butyl ether-β-cyclodextrin at a concentration between 25-400 mg/mL, and a buffer, wherein the pH of the composition is 6 and the buffer is citrate buffer.