There is increasing evidence to support the use of neuroactive steroids, *e.g.,* a neuroactive steroid as described herein, *e.g.,* progesterone and its metabolites; in the treatment and prevention of tremor (e.g., essential tremor), depression (e.g., postpartum depression, major depressive disorder), and anxiety disorder.

SUMMARY

The disclosure features, *inter alia*, a method, the method comprising administering a neuroactive steroid, *e.g.,* a neuroactive steroid as described herein, *e.g.,* pregnanolone, allopregnanolone, alphadalone, ganaxolone, alphaxolone, or Compound 9 as described below, or a pharmaceutical composition comprising a neuroactive steroid (e.g., brexanolone) to a subject, for example to treat a CNS-related disorder such as tremor, depression (e.g., postpartum depression, major depressive disorder), or anxiety disorder. In some embodiments, the neuroactive steroid is formulated for parenteral delivery (*e.g.*, intravenous delivery (IV)). The disclosure features methods of treating a subject having a CNS disorder, *e.g.,* tremor, *e.g.,* essential tremor; depression, *e.g.,* postpartum depression; and anxiety disorder, the methods comprising administering to the subject a composition described herein, *e.g.,* a neuroactive steroid, *e.g.,* pregnanolone, allopregnanolone, alphadalone, ganaxolone, or alphaxolone, 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®. The disclosure also features, *inter alia*, compositions comprising a neuroactive steroid, *e.g.,* pregnanolone, allopregnanolone, alphadalone, ganaxolone, or alphaxolone; 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®.

In one aspect, the present disclosure refers to use of allopregnanolone in the manufacture of a medicament for treating post-partum depression in a human subject in need thereof, wherein allopregnanolone is to be administered at a dosing regimen over a time period of about 60 hours, wherein the dosing regimen comprises a continuous infusion of:

30 mg/kg/hour from about hour 0 to about hour 4;

60 mg/kg/hour from about hour 4 to about hour 24;

90 mg/kg/hour from about hour 24 to about hour 52;

60 mg/kg/hour from about hour 52 to about hour 56; and

30 mg/kg/hour from about hour 56 to about hour 60.

The present disclosure also provides a method for treating a human subject, the method comprising: identifying a subject at risk of suffering from depression (e.g., postpartum depression) or an anxiety disorder; and administering (e.g., orally, intraveneously) to the subject a therapeutically effective amount of a therapeutic agent (e.g., a neuroactive steroid as described herein (e.g., allopregnanolone)) or

a pharmaceutical composition comprising a therapeutic agent (e.g., a pharmaceutical composition as described herein, e.g., brexanolone). In some embodiments, the therapeutic agent is administered to the subject within 3 days, 2 days, 1 day, or 24 hours of delivery of a baby (e.g., within 12 hours, within 6 hours, within 3 hours, within 2 hours, within 1 hour, within 30 minutes).

In some embodiments, the subject is identified to be at risk through a screening method (e.g., Edinburgh Postnatal Depression Scale (EPDS), e.g., a score of 10 or more on the EPDS, a score of 13 or more on the EPDS). In some embodiments, the subject is identified to be at risk through screening instruments such as Patient Health Questionnaire (PHQ) in various forms or the Hospital Anxiety and Depression Scales or Geriatric Depression Scale.

CLAIMS

1. Use of allopregnanolone in the manufacture of a medicament for treating post-partum depression in a human subject in need thereof, wherein allopregnanolone is to be administered at a dosing regimen over a time period of about 60 hours, wherein the dosing regimen comprises a continuous infusion of:

30 mg/kg/hour from about hour 0 to about hour 4;

60 mg/kg/hour from about hour 4 to about hour 24;

90 mg/kg/hour from about hour 24 to about hour 52;

60 mg/kg/hour from about hour 52 to about hour 56; and

30 mg/kg/hour from about hour 56 to about hour 60.

2. The use according to claim 1, wherein allopregnanolone is in a sterile aqueous solution comprising allopregnanolone and sulfobutylether-b-cyclodextrin.

3. The use according to claim 2, wherein the sterile aqueous solution is buffered with citrate.

4. The use according to claim 3, wherein the sterile aqueous solution comprises about 0.1 mg/mL to about 10 mg/mL of allopregnanolone.

5. The use according to claim 4, wherein the sterile aqueous solution comprises about 0.1 mg/mL to about 5 mg/mL of allopregnanolone.

6. The use according to claim 5, wherein the sterile aqueous solution comprises about 1 mg/mL of allopregnanolone.

7. The use according to claim 3, wherein the sterile aqueous solution comprises about 1% to about 30% by weight of sulfobutylether-b-cyclodextrin per volume of sterile aqueous solution.

8. The use according to claim 7, wherein the sterile aqueous solution comprises about 1% to about 15% by weight of sulfobutylether-b-cyclodextrin per volume of sterile aqueous solution.

9. The use according to claim 8, wherein the sterile aqueous solution comprises about 1% to about 5% by weight of sulfobutylether-b-cyclodextrin per volume of sterile aqueous solution.

10. The use according to claim 9, wherein the sterile aqueous solution comprises about 5% by weight of sulfobutylether-b-cyclodextrin per volume of sterile aqueous solution.