# DOSAGE FORMS AND METHODS FOR ENANTIOMERICALLY ENRICHED OR PURE BUPROPION

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## CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. provisional patent application numbers 62/971,174, filed February 6, 2020; 62/978,626, filed February 19, 2020; and 62,992,060, filed March 19, 2020; this application is also a continuation-in-part of 16/830,637, filed March 26, 2020; this application is also a continuation-in-part of PCT/US2019/052210, filed September 20, 2019; this application is also a continuation-in-part of 16/907,691, filed June 22, 2020; all of which are incorporated by reference herein in their entirety.

## BACKGROUND

Bupropion is approved for human use as a racemic mixture. It was believed by many that bupropion and its metabolites rapidly racemize in the human body.

## SUMMARY

Described herein are dosage forms containing an enantiomeric excess of (*S*)-bupropion, enantiomerically enriched (*S*)-bupropion, or enantiomerically pure (*S*)-bupropion and methods of using those dosage forms. These dosage forms may be administered to human beings in a reduced amount as compared to the amount of racemic bupropion that would be administered in the same situation.

Some examples include a method of providing bupropion to the plasma of a human being, comprising: selecting a human patient in need of a pharmacokinetic profile provided by orally administering a reference dosage form containing a first amount of racemic bupropion at a first dosing frequency; and orally administering a dosage form containing a second amount of (*S*)-bupropion that is at least 95% enantiomerically pure at the first dosing frequency to achieve the same pharmacokinetic profile that would be achieved by administering the reference dosage form at the first dosing frequency; wherein the first dosing frequency is once daily or twice daily;

and wherein the second amount is about 20-70%, about 40-60%, about 45-55%, or about 50% of the first amount. For example, if a particular pharmacokinetic profile is achievable by orally administering a dosage form containing 150 mg of racemic bupropion and the second amount is 40-60% of the first amount, the second amount is 60-90 mg. Thus, in this situation, 60-90 mg of (*S*)-bupropion would be administered once daily to achieve the same pharmacokinetic profile as would be achieved by administering 150 mg of racemic bupropion once daily; or 60-90 mg of (*S*)-bupropion would be administered twice daily to achieve the same pharmacokinetic profile as would be achieved by administering 150 mg of racemic bupropion twice daily.

For the purposes of this disclosure, if the dosage form containing enantiomerically pure (*S*)-bupropion is recognized by the FDA as bioequivalent to a dosage form containing racemic bupropion, then the two dosage forms have the same pharmacokinetic profile.

Some examples include a method of treating a condition that is treatable with racemic bupropion, comprising: selecting a human patient having the condition that is treatable by orally administering a reference dosage form containing a first amount of racemic bupropion at a first dosing frequency; and orally administering a dosage form containing a second amount of (*S*)-bupropion that is at least 95% enantiomerically pure at the first dosing frequency to achieve the same therapeutic effect that would be achieved by administering the reference dosage form at the first dosing frequency; wherein the first dosing frequency is once daily or twice daily; and wherein the second amount is about 20-70%, about 40-60%, about 45-55%, or about 50% of the first amount. For example, if a condition is treatable by orally administering a dosage form containing 150 mg of racemic bupropion and the second amount is 40-60% of the first amount, the second amount is 60-90 mg. Thus, in this situation, 60-90 mg of (*S*)-bupropion would be administered once daily to treat a condition so that the same therapeutic effect is achieved as would be achieved by administering 150 mg of racemic bupropion once daily; or 60-90 mg of (*S*)-bupropion would be administered twice daily to treat a condition so that the same therapeutic effect is achieved as would be achieved by administering 150 mg of racemic bupropion twice daily.

Some examples include a method of treating a human being, comprising orally administering a dosage form containing (*S*)-bupropion that is at least 95% enantiomerically pure, one or two times per day, to the human being.

Some examples include a dosage form for treating a condition in a human being, comprising (*S*)-bupropion that is at least 95% enantiomerically pure, wherein the dosage form is orally administered one or two times per day to the human being.

Some examples include use of (*S*)-bupropion that is at least 95% enantiomerically pure in the manufacture of a medicament for treating a condition in a human being, wherein the medicament is orally administered one or two times per day to the human being.

Some examples include a kit comprising a dosage form and a label, wherein the dosage form comprises (*S*)-bupropion that is at least 95% enantiomerically pure, and the label states that the dosage form is orally administered one or two times per day to the human being for treating a condition in the human being.

In one aspect, the present disclosure provides use of (*S*)-bupropion that is at least 95% by weight enantiomerically pure, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a neurological disorder or a central nervous system disorder in a human being, wherein the medicament is to be orally administered in a dosage form one or two times per day to the human being, wherein the dosage form includes 80 mg to 120 mg of the (S)-bupropion, wherein the (S)-bupropion is to be administered in the dosage form that provides sustained release of (S)-bupropion, wherein the dosage form comprises a sustained release polymer, and wherein the dosage form is formulated to have a Tmax of (S)-bupropion that is 2 hours to 4 hours, and wherein the dosage form is substantially free of any active pharmaceutical agent other than (S)-bupropion.

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts the $AUC_{0-12}$ values for bupropion and hydroxybupropion in healthy volunteers after dosing S-bupropion and racemic bupropion tablets.

FIG. 2 shows the mean plasma levels of bupropion and hydroxybupropion after dosing (S)-bupropion or (R)-bupropion tablets.

FIG. 3 shows the $C_{max}$ of *R,R*-hydroxybupropion after dosing (S)-bupropion or (R)-bupropion tablets.

## DETAILED DESCRIPTION

The (*S*)-bupropion administered to the human being may be enantiomerically pure or enantiomerically enriched. For example, the (*S*)-bupropion may be at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.9%, or at least 99.99% enantiomerically pure, up to (or nearly) 100% enantiomerically pure. (*S*)-bupropion that is 99.99% enantiomerically pure contains 99.99% (*S*)-bupropion and 0.001% (*R*)-bupropion. For convenience, any of the above may be referred to as "(*S*)-bupropion." This type of dosage form may be useful in treating conditions where increased levels of (*S*)-

**What Is Claimed Is**:

1. Use of (*S*)-bupropion that is at least 95% by weight enantiomerically pure, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a neurological disorder or a central nervous system disorder in a human being, wherein the medicament is to be orally administered in a dosage form one or two times per day to the human being, wherein the dosage form includes 80 mg to 120 mg of the (S)-bupropion, wherein the (S)-bupropion is to be administered in the dosage form that provides sustained release of (S)-bupropion, wherein the dosage form comprises a sustained release polymer, and wherein the dosage form is formulated to have a Tmax of (S)-bupropion that is 2 hours to 4 hours, and wherein the dosage form is substantially free of any active pharmaceutical agent other than (S)-bupropion.

2. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of claim 1, wherein the (*S*)-bupropion or the pharmaceutically acceptable salt thereof is to be administered once daily.

3. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of claim 1, wherein the (*S*)-bupropion or the pharmaceutically acceptable salt thereof is to be administered in two doses per day, and wherein the sum of the two doses per day is a daily dose.

4. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1, 2, or 3, wherein the (*S*)-bupropion or the pharmaceutically acceptable salt thereof is to be administered for at least 8 consecutive days.

5. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1, 2, or 3, wherein the (*S*)-bupropion or the pharmaceutically acceptable salt thereof is to be administered for at least 14 consecutive days.

6. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1, 2, or 3, wherein the (*S*)-bupropion or the pharmaceutically acceptable salt thereof is to be administered for at least 21 consecutive days.

7. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1, 2, or 3, wherein the (*S*)-bupropion or the pharmaceutically acceptable salt thereof is to be administered for at least 28 consecutive days.

8. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1-7, wherein the dosage form provides an $AUC_{0\text{-}12}$ of (*S*)-bupropion in the human being that is at least about 300 ng·hr/mL.

9. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1-7, wherein the dosage form provides an $AUC_{0\text{-}12}$ of (*S*)-bupropion in the human being that is at least about 400 ng·hr/mL.

10. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1-9, wherein the dosage form provides an $AUC_{0\text{-}12}$ of (*S*)-bupropion in the human being that is 500 ng·hr/mL to 900 ng·hr/mL.

11. The use of (*S*)-bupropion or the pharmaceutically acceptable salt thereof of any one of claims 1-10, wherein the dosage form provides a $C_{max}$ of (*S*)-bupropion in the human being that is 60 ng/mL to 140 ng/mL.