the symptoms of cervical dystonia, thereby extending treatment interval duration for the individual.

[0015] In another of its examples, this disclosure provides injectable compositions comprising botulinum toxin non-covalently associated with a positively charged carrier molecule used to treat cervical dystonia. In preferred examples, the compositions of the disclosure possess one or more advantages over conventional commercial botulinum toxin formulations, such as BOTOX® or MYOBLOC®. For instance, in certain examples, the compositions may exhibit one or more advantages over conventional injectable botulinum formulations, including reduced antigenicity, a reduced tendency to undergo diffusion into surrounding tissue following injection, increased duration of clinical efficacy or enhanced potency relative to conventional botulinum toxin formulations, faster onset of clinical efficacy, and/or improved stability.

[0016] A further example of this disclosure is the recognition that certain non-native molecules (i.e., molecules not found in botulinum toxin complexes obtained from *Clostridium botulinum* bacteria) can be added to botulinum toxin, botulinum toxin complexes, and in particular reduced botulinum toxin complexes (as defined herein), to improve toxin diffusion through tissues in the treatment of cervical dystonia. The non-native molecules associate non-covalently with the toxin and act as penetration enhancers that improve the ability of the toxin to reach target structures after injection. Furthermore, the non-native molecules may increase the stability of the toxin prior to and after injection. By way of example, the penetration enhancers may be positively charged carriers, such as cationic peptides, which have no inherent botulinum-toxin-like activity and which also contain one or more protein transduction domains as described herein.

[0017] Another example of this disclosure is to provide a composition comprising botulinum toxin, a botulinum toxin complex (or a reduced protein botulinum toxin complex including just the 150 kD neurotoxin itself, or the neurotoxin with some, but not all, of the native complex proteins) and a positively charged carrier for use in a method of treatment for cervical dystonia.

[0017a] In one example, the present disclosure refers to a pharmaceutical composition in a sterile injectable formulation for use in treating cervical dystonia in an individual in need thereof, said composition comprising:

a Type A, 150 kD botulinum toxin in a dose of 100 U to 300 U,

a positively charged carrier component having an amino acid sequence of SEQ ID NO: 4; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein said dose of the composition provides a single treatment having at least a 20 week duration of effect in reducing the symptoms of cervical dystonia in the individual.

[0017b] In one aspect, the present disclosure refers to use of a Type A, 150 kD botulinum toxin for the manufacture of an injectable composition for the treatment of cervical dystonia in an individual in need thereof, said composition comprising:

the botulinum toxin in a dose of 100 U to 300 U,

a positively charged carrier component having an amino acid sequence of SEQ ID NO: 4; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein said dose of the composition provides a single treatment having at least a 20 week duration of effect in reducing the symptoms of cervical dystonia in the individual.

[0017c] In one example, the present disclosure refers to a pharmaceutical composition in a sterile injectable formulation for use in treating cervical dystonia in an individual in need thereof who has been treated previously with the injectable composition, said composition comprising:

a Type A, 150 kD botulinum toxin in a dose of 100 U to 300 U,

a positively charged carrier component having an amino acid sequence of SEQ ID NO: 4; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein said individual was previously treated with the dose and had a duration of effect of at least 20 weeks in reducing the symptoms of cervical dystonia in the individual and the treatment of said subject was at least 20 weeks after the previous treatment.

[0017d] In one aspect, the present disclosure refers to use of a Type A, 150 kD botulinum toxin for the manufacture of an injectable composition for a treatment of cervical dystonia in an individual in need thereof who has been treated previously with the injectable composition, said composition comprising:

the botulinum toxin in a dose of 100 U to 300 U,

a positively charged carrier component having an amino acid sequence of SEQ ID NO: 4; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein said individual was previously treated with the dose and had a duration of effect of at least 20 weeks in reducing the symptoms of cervical dystonia in the individual and the treatment of said subject was at least 20 weeks after the previous treatment.

[0018] In another example, the disclosure provides effective doses and amounts of the compositions of this disclosure in the treatment of cervical dystonia that afford a long-lasting, sustained efficacy e.g., a response rate of long duration, following administration by injection to

Claims:

1. Use of a Type A, 150 kD botulinum toxin for the manufacture of an injectable composition for the treatment of cervical dystonia in an individual in need thereof, said composition comprising:

the botulinum toxin in a dose of 100 U to 300 U,

a positively charged carrier component having an amino acid sequence of SEQ ID NO: 4; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein said dose of the composition provides a single treatment having at least a 20 week duration of effect in reducing the symptoms of cervical dystonia in the individual.

2. The use according to claim 1, wherein the composition does not locally diffuse from the site of injection following injection.

3. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 20 weeks.

4. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 24 weeks.

5. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 5 months.

6. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 6 months.

7. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 7 months.

8. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 8 months.

9. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises greater than 9 months.

10. The use according to claim 1 or claim 2, wherein the duration of treatment effect comprises at least 6 months through 10 months.

11. Use of a Type A, 150 kD botulinum toxin for the manufacture of an injectable composition for a treatment of cervical dystonia in an individual in need thereof who has been treated previously with the injectable composition, said composition comprising:

the botulinum toxin in a dose of 100 U to 300 U,

a positively charged carrier component having an amino acid sequence of SEQ ID NO: 4; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein said individual was previously treated with the dose and had a duration of effect of at least 20 weeks in reducing the symptoms of cervical dystonia in the individual and the treatment of said subject was at least 20 weeks after the previous treatment.