SUMMARY

In one aspect, the present disclosure pertains to a use of a compound that is [((1R,2S,5R)-2-isopropyl-5-methyl-cyclohexanecarbonyl)-amino]-acetic acid isopropyl ester, or a pharmaceutically acceptable salt, hydrate, or solvate thereof, in the manufacture of a medicament for the treatment of refractory chronic cough (RCC) or idiopathic chronic cough (ICC).

One example of the disclosure pertains to a compound that is [((1R,2S,5R)-2-isopropyl-5-methyl-cyclohexanecarbonyl)-amino]-acetic acid isopropyl ester (also referred to herein as “AX-8” or “Gly-O-iPr”), or a pharmaceutically acceptable salt, hydrate, or solvate thereof, as described herein, for use in a method of treatment of the human or animal body by therapy, more specifically, for use in a method of treatment of chronic cough (CC), including, for example, refractory chronic cough (RCC) and idiopathic chronic cough (ICC), and as described herein.

Another example of the present disclosure pertains to use a compound that is [((1R,2S,5R)-2-isopropyl-5-methyl-cyclohexanecarbonyl)-amino]-acetic acid isopropyl ester (also referred to herein as “AX-8” or “Gly-O-iPr”), or a pharmaceutically acceptable salt, hydrate, or solvate thereof, as described herein, in the manufacture of a medicament for treatment, more specifically, for the treatment of chronic cough (CC), including, for example, refractory chronic cough (RCC) and idiopathic chronic cough (ICC), and as described herein.

Another example of the present disclosure pertains to a method of treatment, more specifically, a method of treatment of chronic cough (CC), including, for example, refractory chronic cough (RCC) and idiopathic chronic cough (ICC), and as described herein, comprising administering to a patient in need of treatment a therapeutically effective amount of a compound that is [((1R,2S,5R)-2-isopropyl-5-methyl-cyclohexanecarbonyl)-amino]-acetic acid isopropyl ester (also referred to herein as “AX-8” or “Gly-O-iPr”), or a pharmaceutically acceptable salt, hydrate, or solvate thereof, as described herein, preferably in the form of a pharmaceutical composition.

Another example of the present disclosure pertains to a kit comprising (a) a compound that is [((1R,2S,5R)-2-isopropyl-5-methyl-cyclohexanecarbonyl)-amino]-acetic acid isopropyl ester (also referred to herein as “AX-8” or “Gly-O-iPr”), or a pharmaceutically acceptable salt, hydrate, or solvate thereof, as described herein, preferably provided as a pharmaceutical composition and in a suitable container and/or with suitable packaging; and (b) instructions for its use, for example, written instructions on how to administer the compound for the treatment of chronic cough (CC), including, for example, refractory chronic cough (RCC) and idiopathic chronic cough (ICC), and as described herein.

As will be appreciated by one of skill in the art, features and preferred examples of one example of the disclosure will also pertain to other examples of the disclosure.

CLAIMS

1. Use of a compound that is [((1R,2S,5R)-2-isopropyl-5-methyl-cyclohexanecarbonyl)-amino]-acetic acid isopropyl ester, or a pharmaceutically acceptable salt, hydrate, or solvate thereof, in the manufacture of a medicament for the treatment of refractory chronic cough (RCC) or idiopathic chronic cough (ICC).

2. The use according to claim 1, wherein:
the chronic cough is idiopathic chronic cough (ICC).

3. The use according to claim 1, wherein:
the chronic cough is refractory chronic cough (RCC).

4. The use according to claim 1, wherein:
the chronic cough is refractory chronic cough (RCC) that persists after assessment and treatment of a cough-related condition.

5. The use according to claim 1 wherein:
the chronic cough is refractory chronic cough (RCC) that persists after assessment and treatment of: asthma, eosinophilic bronchitis, post-nasal drip syndrome (PNDS), gastro-oesophageal reflux disease (GORD), bronchiectasis chronic obstructive pulmonary disease (COPD), or idiopathic pulmonary fibrosis (IPF).

6. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is associated with allotussia.

7. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is associated with hypertussia.

8. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is associated with cough hypersensitivity syndrome (CHS).

9. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is associated with cough hypersensitivity reflex (CHR).

10. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is associated with laryngeal paraesthesia.

11. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is associated with laryngeal hypersensitivity syndrome (LHS).

12. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough (ICC) is sensory neuropathic cough.

13. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough is associated with peripheral sensitization; central sensitization (cough centre); and/or cortical and/or subcortical maladaptive plasticity.

14. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough is associated with vagal neuropathy.

15. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough is associated with airway inflammation.

16. The use according to any one of claims 1 to 5, wherein:
the refractory chronic cough (RCC) or idiopathic chronic cough is associated with neurogenic inflammation and/or neuroinflammation.

17. The use according to any one of claims 1 to 16, wherein:
the treatment is to reduce cough frequency;
the treatment is to reduce hourly cough frequency;
the treatment is to reduce median hourly cough frequency;
the treatment is to reduce mean hourly cough frequency;
the treatment is to reduce awake hourly cough frequency;
the treatment is to reduce awake median hourly cough frequency;
the treatment is to reduce awake mean hourly cough frequency;
the treatment is to reduce asleep hourly cough frequency;
the treatment is to reduce asleep median hourly cough frequency;
the treatment is to reduce asleep mean hourly cough frequency;
the treatment is to reduce cough severity;
the treatment is to reduce urge-to-cough; and/or
the treatment is to reduce throat irritation.

18. The use according to any one of claims 1 to 17, wherein:
the treatment is by topical oral administration of the compound;
the treatment is by topical oromucosal administration of the compound;
the treatment is by topical buccal administration of the compound;
the treatment is by topical sublingual administration of the compound;
the treatment is by topical intranasal administration of the compound; or
the treatment is by topical transmucosal administration of the compound.

19. The use according to any one of claims 1 to 18, wherein:
the treatment is with a dose in the range of from 1 µg to5 mg of the compound per kilogram body weight of the subject per day;
the treatment is with a dose in the range of from 5 µg to2 mg of the compound per kilogram body weight of the subject per day;
the treatment is with a dose in the range of from 15 µg to0.7 mg of the compound per kilogram body weight of the subject per day;
the treatment is with a dose in the range of from 30 µg to 0.4 mg of the compound per kilogram body weight of the subject per day; or
the treatment is with a dose in the range of from 70 µg to 0.3 mg of the compound per kilogram body weight of the subject per day.

20. The use according to any one of claims 1 to 18, wherein:
the treatment is with a dose in the range of from 0.07 mg to 350 mg of the compound per day;
the treatment is with a dose in the range of from 0.35 mg to 140 mg of the compound per day;
the treatment is with a dose in the range of from 1 mg to 50 mg of the compound per day;
the treatment is with a dose in the range of from 2 mg to 30 mg of the compound per day; or
the treatment is with a dose in the range of from 5 mg to 20 mg of the compound per day.

21. The use according to any one of claims 1 to 20, wherein:
the treatment is by a treatment regimen of 1 to 5 administrations daily;
the treatment is by a treatment regimen of 1 to 4 administrations daily;
the treatment is by a treatment regimen of 2 to 5 administrations daily;
the treatment is by a treatment regimen of 2 to 4 administrations daily;
the treatment is by a treatment regimen of 2 administrations daily;
the treatment is by a treatment regimen of 3 administrations daily; or
the treatment is by a treatment regimen of 4 administrations daily.

22. The use according to any one of claims 1 to 21, wherein:
the treatment is by a *pro re nata* (PRN) treatment regimen.

23. The use according to any one of claims 1 to 22, wherein:
the compound is formulated as a tablet;
the compound is formulated as an orally disintegrating tablet (ODT);
the compound is formulated as a spray;
the compound is formulated as a mist; or
the compound is formulated as an aerosol.