SUMMARY

[0010a] In one aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient having a left ventricular ejection fraction of less than 35%. In another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who does not exhibit atrial fibrillation or atrial flutter. In another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient having heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification. In another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient having advanced heart failure. In another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating ischemic heart failure in a patient. In another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who has had a myocardial infarction. In another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who has a pretreatment level of NT-proBNP of at least 2,000 pg/mL. In yet another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who has low blood pressure, symptomatic hypotension, impaired renal function, or bradycardia. In yet another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who is unable to tolerate one or more of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, diuretics, aldosterone antagonists, inotropes, neprilysin inhibitors, digitalis, and digoxin. In yet another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for preventing stroke in a patient suffering from heart failure with reduced ejection fraction (HFrEF). In yet another aspect, the present disclosure relates to use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for reducing the risk of heart failure events or death from cardiovascular causes in a heart failure.

[0011] Provided herein are methods of treating heart failure in a patient having a left ventricular ejection fraction (LVEF) of less than 35% (such as less than 30%, less than 28%, less than 25%, or less than 22%) comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0012] Also provided herein are methods of treating heart failure in a patient who does not exhibit atrial fibrillation or atrial flutter comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0013] Also provided herein are methods of treating heart failure in a patient having heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0014] Also provided herein are methods of treating heart failure in a patient having advanced heart failure comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0015] The disclosure further provides methods of treating ischemic heart failure in a patient comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0016] Also provided herein are methods of treating heart failure in a patient who has had a myocardial infarction comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0017] Also provided herein are methods of treating heart failure in a patient having a NT-proBNP level of at least 2,000 pg/mL prior to start of omecamtiv mecarbil treatment comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0018] Also provided herein are methods of treating heart failure in a patient who has low blood pressure, symptomatic hypotension, impaired renal function, or bradycardia comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0019] Also provided herein are methods of treating heart failure in a patient who is unable to tolerate one or more of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, diuretics, aldosterone antagonists, inotropes, neprilysin inhibitors, digitalis, and digoxin comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

[0020] Also provided herein is a method of preventing stroke in a patient suffering from heart failure with reduced ejection fraction (HFrEF) comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil as described herein.

What is Claimed:

1. ~~A method of treating heart failure in a patient having a left ventricular ejection fraction (LVEF) of less than 35% comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient having a left ventricular ejection fraction of less than 35%.

2. The ~~method~~ use of claim 1, wherein the patient has a LVEF of less than 30%, less than 28%, less than 25% or less than 22%.

~~3. The method of claim 1, wherein the patient has a LVEF of less than 28%.~~

~~4. The method of claim 1, wherein the patient has a LVEF of less than 25%.~~

~~5. The method of claim 1, wherein the patient has a LVEF of less than 22%.~~

~~6.~~3. ~~A method of treating heart failure in a patient who does not exhibit atrial fibrillation or atrial flutter comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who does not exhibit atrial fibrillation or atrial flutter.

~~7.~~4. The ~~method~~ use of claim ~~3~~6, wherein the patient has a LVEF of less than 35%, less than 30%, less than 28%, less than 25% or less than 22%.

~~8. The method of claim 6, wherein the patient has a LVEF of less than 30%.~~

~~9. The method of claim 6, wherein the patient has a LVEF of less than 28%.~~

~~10. The method of claim 6, wherein the patient has a LVEF of less than 25%.~~

~~11. The method of claim 6, wherein the patient has a LVEF of less than 22%.~~

~~12.~~5. ~~A method of treating heart failure in a patient having heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient having heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification.

~~13.~~6. ~~A method of treating heart failure in a patient having advanced heart failure comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient having advanced heart failure.

~~14.~~7. The ~~method~~ use of claim ~~13~~6, wherein the patient has heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification; optionally wherein the patient has a LVEF of less than 30%; optionally wherein the patient has had at least one heart failure hospitalization within 6 months prior to the treatment; optionally wherein the patient does not exhibit atrial fibrillation or atrial flutter.

~~15. The method of claim 13 or 14, wherein the patient has a LVEF of less than 30%.~~

~~16. The method of any one of claims 13-15, wherein the patient has had at least one heart failure hospitalization within 6 months prior to the treatment.~~

~~17. The method of any one of claims 13-16, wherein the patient does not exhibit atrial fibrillation or atrial flutter.~~

~~18.~~8. ~~A method of treating ischemic heart failure in a patient comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating ischemic heart failure in a patient.

~~19.~~9. ~~A method of treating heart failure in a patient who has had a myocardial infarction comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who has had a myocardial infarction.

~~20.~~10. ~~A method of treating heart failure in a patient who has a pretreatment level of NT-proBNP of at least 2,000 pg/mL comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who has a pretreatment level of NT-proBNP of at least 2,000 pg/mL.

~~21.~~11. The use of claim 10, ~~method of claim 20~~, wherein the patient has a LVEF of less than 35%, less than 30%, less than 28%, less than 25% or less than 22%.

~~22. The method of claim 20, wherein the patient has a LVEF of less than 30%.~~

~~23. The method of claim 20, wherein the patient has a LVEF of less than 28%.~~

~~24. The method of claim 20, wherein the patient has a LVEF of less than 25%.~~

~~25. The method of claim 20, wherein the patient has a LVEF of less than 22%.~~

~~26.~~12. The ~~method of any one of claims 20-25~~use claim 10 or 11, wherein the patient does not exhibit atrial fibrillation or atrial flutter.

~~27.~~13. ~~A method of treating heart failure in a patient who has low blood pressure, symptomatic hypotension, impaired renal function, or bradycardia comprising administering to the patient a therapeutically effective amount of~~Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who has low blood pressure, symptomatic hypotension, impaired renal function, or bradycardia.

~~28.~~14. The ~~method~~ use of claim ~~27~~13, wherein the patient has not previously been treated with one or more of an angiotensin-converting enzyme inhibitor, an angiotensin II receptor blocker, a beta blocker, a diuretic, an aldosterone antagonist, an inotrope, neprilysin inhibitors, digitalis, and digoxin.

~~29.~~15. ~~A method of treating heart failure in a patient who is unable to tolerate one or more of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, diuretics, aldosterone antagonists, inotropes, neprilysin inhibitors, digitalis, and digoxin comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for treating heart failure in a patient who is unable to tolerate one or more of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, diuretics, aldosterone antagonists, inotropes, neprilysin inhibitors, digitalis, and digoxin.

~~30.~~16. The ~~method~~ use of claim 15~~29~~, wherein the patient has low blood pressure, symptomatic hypotension, impaired renal function, or bradycardia.

~~31.~~17. ~~A method of preventing stroke in a patient suffering from heart failure with reduced ejection fraction (HFrEF) comprising administering to the patient a therapeutically effective amount of~~ Use of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for preventing stroke in a patient suffering from heart failure with reduced ejection fraction (HFrEF).

~~32.~~18. The ~~method~~ use of claim 17~~31~~, wherein the stroke is non-fatal or fatal; optionally wherein the stroke is ischemic; optionally wherein the stroke is ischemic with hemorrhagic transformation; optionally wherein the stroke is hemorrhagic.

~~33. The method of claim 31, wherein the stroke is fatal.~~

~~34. The method of any one of claim 31 to 33, wherein the stroke is ischemic.~~

~~35. The method of any one of claim 31 to 33, wherein the stroke is ischemic with hemorrhagic transformation.~~

~~36. The method of any one of claim 31 to 33, wherein the stroke is hemorrhagic.~~

~~37.~~19. ~~A method of reducing the risk of heart failure events or death from cardiovascular causes in a heart failure patient comprising administering to the patient a therapeutically effective amount of~~ Use

of omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof in the manufacture of a medicament for reducing the risk of heart failure events or death from cardiovascular causes in a heart failure.

38.20. The method use of claim 3719, wherein the method use reduces the risk of heart failure events in the patient; optionally wherein the patient has chronic heart failure with reduced ejection fraction; optionally wherein the heart failure events are an urgent clinic visit, emergency department visit or hospitalization for worsening heart failure leading to treatment intensification beyond changed oral diuretic therapy.

39. The method of claim 37 or 38, wherein the patient has chronic heart failure with reduced ejection fraction.

40. The method of any one of claims 37-39, wherein the heart failure events are an urgent clinic visit, emergency department visit or hospitalization for worsening heart failure leading to treatment intensification beyond changed oral diuretic therapy.

41.21. The method use of any one of claims 37-40claim 19 or 20, wherein the patient has a LVEF of less than 30%, less than 28%, less than 25% or less than 22%.

42. The method of any one of claims 37-40, wherein the patient has a LVEF of less than 28%.

43. The method of any one of claims 37-40, wherein the patient has a LVEF of less than 25%.

44. The method of any one of claims 37-40, wherein the patient has a LVEF of less than 22%.

45.22. The method use of any one of claims 19-2137-44, wherein the patient does not exhibit atrial fibrillation or atrial flutter; optionally wherein the patient has advanced heart failure; optionally wherein the patient has heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification; optionally wherein the patient has had at least one heart failure hospitalization within 6 months prior to the treatment.

46. The method of any one of claims 37-45, wherein the patient has advanced heart failure.

47. The method of any one of claims 37-46, wherein the patient has heart failure classified as Class III or IV as determined using the New York Heart Association (NYHA) classification.

48. The method of any one of claims 37-47, wherein the patient has had at least one heart failure hospitalization within 6 months prior to the treatment.

49.23. The method use of any one of claims 1-4822, wherein the patient is an inpatient or an outpatient.

50. The method of any one of claims 1-48, wherein the patient is an outpatient.

51.24. The usemethod of any one of claims 1-5023, wherein omecamtiv mecarbil is to be administered orally; optionally wherein omecamtiv mecarbil is to be administered as a tablet .

52. The method of claim 51, wherein omecamtiv mecarbil is administered as a tablet.

53.25. The method use of any one of claims 1-2452, comprising administering to the patient a therapeutically effective amount of omecamtiv mecarbil dihydrochloride hydrate to be administered to the patient.

54.26. The method use of any one of claims 1-5325, wherein omecamtiv mecarbil, or a hydrate, a salt, or a salt of a hydrate thereof is to be administered as a modified release matrix tablet.

55.27. The method use of any one of claims 1-5426, wherein omecamtiv mecarbil is to be administered twice daily.

56.28. The method use of claim 5527, wherein omecamtiv mecarbil is to be administered in a dosage of 25 mg, 37.5 mg, or 50 mg twice daily.

57. The method of claim 55, wherein omecamtiv mecarbil is administered in a dosage of 37.5 mg twice daily.

58. The method of claim 55, wherein omecamtiv mecarbil is administered in a dosage of 50 mg twice daily.

59.29. The method use of any one of claims 1-2858, wherein the patient has undergone cardiac resynchronization therapy (CRT) prior to treatment, optionally wherein the patient has an implantable cardioverter defibrillator (ICD) device.

60. The method of any one of claims 1-59, wherein the patient has an implantable cardioverter defibrillator (ICD) device.

61.30. The method use of any one of claims 1-6029, further comprising administering to the patient a therapeutically effective amount of an angiotensin-converting enzyme inhibitor is to be administered to the patient.

62.31. The method use of any one of claims 1-6130, further comprising administering to the patient a therapeutically effective amount of a mineralocorticoid receptor antagonist is to be administered to the patient.