Special warnings and precautions / Patient monitoring

- Use cautiously in haemodynamically stable patients with NYHA I* or NYHA II* heart failure
- Administer in a clinically monitored setting, appropriate for cardioversion. Only a well-qualified healthcare professional should administer vernakalant and should frequently monitor the patient for the duration of the infusion and for at least 15 minutes after the completion of the infusion for signs and symptoms of sudden decrease in blood pressure or heart rate
- Cases of severe hypotension have been reported during and immediately after vernakalant infusion is completed. Observe patients carefully for the entire duration of the infusion and for at least 15 minutes after completion of the infusion with assessment of vital signs and continuous cardiac rhythm monitoring. The patient should be further monitored for 2 hours after starting the infusion and until clinical and ECG parameters have stabilised
- In patients with valvular heart disease, there was a higher incidence of ventricular arrhythmia events in vernakalant patients until 24 hours after dosing. These patients should be closely monitored.
- Use vernakalant with caution in patients on oral antiarrhythmic drugs (class I and class III), due to limited experience. Risk of atrial flutter may be increased in patients receiving class I antiarrhythmic drugs
- Resumption or initiation of oral-maintenance antiarrhythmic therapy may be considered 2 hours after vernakalant administration
- Direct-current cardioversion may be considered for patients who do not respond to therapy. There is no clinical experience with direct-current cardioversion under two hours post-dose

Prior to BRINAVESS administration

- Patients should be checked for signs and symptoms of cardiac failure before administration of vernakalant.
- Adequately anticoagulate if necessary (*Please consult your local treatment guidelines on anticoagulation in AF*)
- Adequately hydrate and haemodynamically optimise patients
- Correct hypokalaemia to a serum potassium greater than 3.5 mmol/L

Monitoring and reporting adverse events

- Be alert for adverse events, which may occur after vernakalant administration, including hypotension, bradycardia, atrial flutter, or ventricular arrhythmia. Uncommonly, cases of severe hypotension and cardiogenic shock have been observed. During and for at least 15 minutes following infusion of vernakalant, carefully monitor patients for any of the following:
  - Signs or symptoms of a sudden decrease in blood pressure or heart rate, with or without symptomatic hypotension or bradycardia,
  - Bradycardia,
  - Hypotension,
  - ECG changes**

  Where such signs are developed, the administration of vernakalant should be immediately discontinued and these patients should receive appropriate medical management. Where such events occur during the first infusion of vernakalant, patients should not receive the second dose of vernakalant
- In clinical trials, patients with heart failure had a higher incidence of hypotension adverse reactions than patients without heart failure. Ventricular arrhythmia occurred more frequently in patients with hearth failure treated with vernakalant than with placebo
- Please report suspected adverse reactions that occur during vernakalant use in accordance with your national spontaneous reporting system's requirements. You may report suspected adverse reactions to Correvio using the contact details below:

  Lifepharma (ZAM) Ltd
  8 Agiou Nikolaou Street,
  1055 Nicosia
  Tel.: +357 22056300
  Email: PV@lifepharma.com.cy

*** New York Heart Association (NYHA) Classification:**

NYHA Class I: Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnoea or angina.
NYHA Class II: Patients with cardiac disease resulting in slight limitation of physical activity. Absence of symptoms at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea or angina.
NYHA Class III: Patients with cardiac disease resulting in marked limitation of physical activity. Absence of symptoms at rest. Less-than-ordinary activity causes fatigue, palpitation, dyspnoea or angina.
NYHA Class IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

**See BRINAVESS SmPC Section 4.4 for full details.

Consult the BRINAVESS Summary of Product Characteristics (SmPC) for further information regarding patient selection and adverse reactions.

Please call +357 22056300 or email PV@lifepharma.com.cy to report an adverse event. Report as soon as possible and in any case within 24 hours

Additional information on BRINAVESS is available upon request

APPROPRIATE USE OF BRINAVESS™

(vernakalant hydrochloride)

concentrate for solution for infusion

BRINAVESS is indicated in adults for rapid conversion of recent onset atrial fibrillation to sinus rhythm:

- **Non-surgery patients: atrial fibrillation ≤7 days duration**
- **Post-cardiac surgery patients: atrial fibrillation ≤3 days duration**

PREPARATION AND DOSING OF BRINAVESS™

concentrate for solution for infusion

For detailed instructions on preparation, dosing and administration of BRINAVESS solution, refer to BRINAVESS SmPC (section 4.2, Posology and method of administration).

Preparation

- BRINAVESS is supplied as sterile concentrate containing vernakalant hydrochloride 20 mg/ml
- **BRINAVESS concentrate must be diluted prior to administration to produce a solution with a vernakalant hydrochloride concentration of 4 mg/ml**
- Suitable diluents include 0.9% Sodium Chloride for Injection, Lactated Ringer's for Injection and 5% Glucose for Injection

Dosing and administration

- Vernakalant should be administered by intravenous infusion by qualified medical staff in a clinically monitored setting appropriate for cardioversion
- Only a well-qualified healthcare professional should administer vernakalant
- Administer vernakalant by intravenous infusion within 10 minutes (for each infusion). During this time, the patient should be carefully monitored for any signs or symptoms of a sudden decrease in blood pressure or heart rate. Where such signs are developed, with or without symptomatic hypotension or bradycardia, the infusion should be stopped immediately and the patient should not receive the second dose
- A pre-infusion checklist is provided with the product. Prior to administration, the prescriber is asked to determine eligibility of the patient through use of the supplied checklist. The checklist should be placed on the infusion container to be read by the healthcare professional who will administer vernakalant
- Vernakalant should only be administered by intravenous infusion. Do not administer as an intravenous push or bolus
- Determine the correct dose of vernakalant based on patient's body weight

Body weight: ≥40 kg and <113 kg

1. Administer the initial infusion: Total dose=**3 mg/kg** over a 10-minute period
2. Monitor the patient following completion of the initial infusion. If conversion to sinus rhythm has not occurred within 15 minutes after completing the initial infusion, administer a second infusion
3. Second infusion (if necessary): Total dose=**2 mg/kg** over a 10-minute period

Body weight: ≥113 kg

1. Administer the initial infusion: Total dose=**339 mg** over a 10-minute period
2. Monitor the patient following completion of the initial infusion. If conversion to sinus rhythm has not occurred within 15 minutes after completing the initial infusion, administer a second infusion
3. Second infusion (if necessary): Total dose=**226 mg** over a 10-minute period

Cumulative doses above 565 mg have not been evaluated.

- If conversion to sinus rhythm occurs during either the initial or second infusion, that infusion should be continued through completion
- If haemodynamically stable atrial flutter is observed after the initial infusion, the second infusion of vernakalant may be administered, as patients may convert to sinus rhythm
- Other intravenous rhythm-control antiarrhythmics (class I and class III) are contraindicated within 4 hours prior to, as well as in the first 4 hours after, vernakalant administration
- Resumption or initiation of oral-maintenance antiarrhythmic therapy may be considered 2 hours after vernakalant administration

APPROPRIATE USE OF BRINAVESS™

concentrate for solution for infusion

Contraindications

- Hypersensitivity to the active substance or to any of the ingredients of the concentrate
- Patients with severe aortic stenosis, patients with systolic blood pressure <100 mm Hg, and patients with heart failure class NYHA III* or NYHA IV*
- Patients with prolonged QT at baseline (uncorrected >440 msec), severe bradycardia, sinus node dysfunction, or second- and third-degree heart block in the absence of a pacemaker
- Use of intravenous rhythm-control antiarrhythmics (class I and class III) within 4 hours prior to, and in the first 4 hours after, vernakalant administration
- Acute coronary syndrome (including myocardial infarction) within the last 30 days

BRINAVESS is not recommended for patients

- With previously documented left ventricular ejection fraction ≤35%
- Who previously received other intravenous rhythm-control antiarrhythmics (class I and class III) between 4 and 24 hours prior to planned vernakalant administration, due to lack of data
- With clinically significant valvular stenosis
- With hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy or constrictive pericarditis
- With advanced hepatic impairment

Use of other intravenous anti-arrhythmic drugs

- Use of intravenous rhythm-control antiarrhythmics (class I and class III) is **contraindicated** within 4 hours prior to, as well as in the first 4 hours after, vernakalant administration
- Vernakalant is **not recommended** for patients who previously received other intravenous rhythm-control antiarrhythmics (class I and class III) between 4 and 24 hours prior to planned vernakalant administration, due to lack of data

Pre-infusion checklist

- Use the pre-infusion checklist provided with vernakalant to confirm the patient's eligibility