Special warnings and precautions/Patient monitoring

- Use cautiously in haemodynamically stable patients with NYHA I* or NYHA II* heart failure
- Administer in a monitored clinical setting with facilities and qualified medical personnel 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 serious hypotension have been reported during and immediately following vernakalant infusion. 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 the start of 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. Within the first 2 hours, ventricular arrhythmia occurred in 6.4% of patients treated with vernakalant versus none after placebo These patients should be monitored closely
- 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 can be considered 2 hours after vernakalant administration

Before giving BRINAVESS

- A **Pre-infusion Checklist** is provided with BRINAVESS. Prior to administration the prescriber is asked to determine elegibility 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
- Patients should be studied 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 (serum potassium < 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 have been observed. During and for at least 15 minutes following infusion of vernakalant, carefully monitor patients for:
  - Any signs or symptoms of a sudden decrease in blood pressure or heart rate, with or without symptomatic hypotension or bradycardia;
  - Bradycardia;
  - Hypotension;
  - ECG changes**

  If such signs develop, the administration of vernakalant should be immediately discontinued and these patients should receive appropriate medical management. If these 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. In heart failure patients, ventricular arrhythmia occurred more frequently with vernakalant than with placebo
- Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie
- You may report suspected adverse reactions to Correvio using the contact details below:

  Correvio
  UK Tel: +44 2030028114
  International Tel: +41 848 00 79 70
  Email: medinfo@correvio.com

* **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, dyspnea or anginal pain.

NYHA Class II: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.

NYHA Class III: Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less-than-ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.

NYHA Class IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the 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.

APPROPRIATE USE OF BRINAVESS™

(vernakalant)

concentrate for solution for infusion

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

- **Non-surgery patients with AF ≦7 days duration**
- **Post–cardiac surgery patients with AF ≦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 the 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 Administration

- A **Pre-infusion Checklist** is provided with BRINAVESS. 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
- Administer vernakalant by intravenous infusion over 10 minutes (for each infusion). During this period the patient should be carefully monitored for any signs or symptoms of a sudden decrease in blood pressure or heart rate. If such signs develop, with or without symptomatic hypotension or bradycardia, the infusion should be stopped immediately
- 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** delivered 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 can be considered 2 hours after vernakalant administration

APPROPRIATE USE OF **BRINAVESS™**

(vernakalant) concentrate for solution for infusion

Contraindications

- Hypersensitivity to the active substance or to any of the inactive ingredients
- 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), or 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, as well as 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 meaningful valvular stenosis
- With hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, or constrictive pericarditis
- With advanced hepatic impairment

Use of other intravenous anti-arrhythmic drugs (IV AADs)

- 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