ANNEX

Conditions or restrictions with regard to the safe and effective use of the medicinal product to be implemented by the Member States

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The Member States should ensure that all conditions or restrictions with regard to the safe and effective use of the medicinal product described below are implemented:

The Marketing Authorisation Holder shall ensure that all Healthcare Professionals (HCP) involved in the administration of BRINAVESS are provided with a healthcare professional information pack containing the following:

Educational material for Healthcare Professionals
Summary of Product Characteristics, Package Leaflet and Labelling

Key elements to be included in the educational material:

1. BRINAVESS should be administered by intravenous infusion in a monitored clinical setting appropriate for cardioversion. Only a well-qualified healthcare professional should administer BRINAVESS 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 a sudden decrease in blood pressure or heart rate (see section 4.4).

2. Appropriate measures to manage and minimize the risks, including the need for close monitoring during and after administration of BRINAVESS.

3. Patient selection criteria, including contraindications, special warnings and precautions for use and information about patient populations with limited information from clinical trials.

- Alert HCP on BRINAVESS contraindications:
  - Patients with prolonged QT at baseline (uncorrected > 440 msec), or severe bradycardia, sinus node dysfunction or second degree and third degree heart block in the absence of a pacemaker.
  - Use of intravenous rhythm control anti-arrhythmics (class I and class III) within 4 hours prior, as well as in the first 4 hours after, to BRINAVESS administration.
  - Acute coronary syndrome (including myocardial infarction) within the last 30 days
  - Patients with severe aortic stenosis, patients with systolic blood pressure <100 mm Hg, and patients with heart failure class NYHA III and NYHA IV.

- Alert HCP about BRINAVESS special warnings and precautions in patients with, clinically meaningful valvular stenosis, hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, or constrictive pericarditis, previously documented LVEF ≤ 35%, advanced hepatic impairment.
- Alert HCP about the need of precautions when using BRINAVESS in haemodynamically stable patients with congestive heart failure NYHA I and NYHA II and the need to monitor patients with valvular heart disease closely.
- Alert HCP for adverse events, which may occur after BRINAVESS administration, including hypotension, bradycardia, atrial flutter, or ventricular arrhythmia.
- Alert HCP for use of AADs (anti-arrhythmic drugs) prior to or after BRINAVESS.
  - BRINAVESS can not be recommended in patients previously administered intravenous AADs (class I and III) 4-24 hours prior to vernakalant, due to lack of data.
  - BRINAVESS should be used with caution in patients on oral AADs (class I and III), due to limited experience. Risk of atrial flutter may be increased in patients receiving class I AADs.
  - Resumption or initiation of oral-maintenance antiarrhythmic therapy can be considered 2 hours after BRINAVESS administration.
  - Intravenous rhythm control AADs should not be used in the first 4 hours after BRINAVESS administration.

4. Instructions on dose calculation, preparation of the solution for infusion, and method of administration.

5. BRINAVESS may be available in different vial sizes [available vial sizes to be inserted locally]. The number of vials of BRINAVESS concentrate required to prepare the appropriate quantity of solution for the treatment of an individual patient will depend on the patient's weight, and the vial size.