

## **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 shall ensure that the Marketing Authorisation Holder complies with the following requirements in their Member State:

The Marketing Authorisation Holder shall ensure that Health care professionals who intend to prescribe or dispense MULTAQ are provided with an SPC and the MULTAQ Information Card. The content and format of the MULTAQ Information Card, together with the communication and distribution plan should be agreed with the National Competent Authority in each Member State prior to distribution.

### **1. The MULTAQ Information Card should contain the following key safety messages:**

- That MULTAQ must not be used in patients with unstable haemodynamic conditions including patients with symptoms of heart failure at rest or with minimal exertion (corresponding to NYHA class IV and unstable class III patients).
- That the use of MULTAQ is not recommended in patients with recent (1-3 months) stable NYHA class III heart failure or with LVEF <35%.
- That liver function tests should be performed prior and during treatment. If ALT levels are confirmed to be  $\geq 3 \times \text{ULN}$  after re-measurement, treatment with dronedarone should be withdrawn.
- That plasma creatinine levels may rise initially due to inhibition of the renal tubular excretion of creatinine and are not necessarily indicative of a deterioration in renal function.
- As the MULTAQ Information Card does not include all warnings or contraindications, the SPC should be referred to prior to prescribing MULTAQ and also prior to prescribing additional drugs to a patient already taking MULTAQ.
- That patients should be counselled that:
  - ❖ they should consult a physician if they develop or experience worsening signs or symptoms of heart failure;
  - ❖ they should immediately report to a physician any symptoms of potential liver injury;
  - ❖ MULTAQ interacts with a number of medicines;
  - ❖ if they consult other doctors they should inform them that they are taking MULTAQ;
  - ❖ they should not take St John's Wort with MULTAQ;
  - ❖ they should avoid grapefruit juice.

### **2. The MULTAQ Information Card should contain a list of drugs which interact with MULTAQ classified according to the seriousness of the interaction (eg contraindication, not recommended, use with caution).**

- Contraindication:
  - CYP3A inhibitors including ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefazodone and ritonavir.
  - potential torsades de pointes inducers including phenothiazines, cisapride, bepridil, tricyclic antidepressants, terfenadine and certain oral macrolides.
  - Class I or Class III antiarrhythmics.
- Not recommended/to be avoided:
  - grapefruit juice,
  - potent CYP3A4 inducers including rifampicin, phenobarbital, carbamazepine, phenytoin, St John's Wort

- dabigatran.
- Use with caution: in association with digoxin, beta blockers, calcium antagonists, statins and vitamin K antagonists.