MULTAQ® PRESCRIBER GUIDE

This guide contains important safety information for the safe use of dronedarone (Multaq®)

Aim of this Guide:

To provide Multaq® (dronedarone) prescribers with a guide to:

1. Screen patients before treatment initiation
2. Monitor patients during treatment
3. Discontinue Multaq® when required
4. Counsel patients about its use

This is additional to the Summary of Product Characteristics (SmPC) and Patient Information Leaflet. Thus, it does not include the full prescribing information.

Safe Use:

- Treatment with Multaq® should only be:
  - Initiated and monitored under specialist supervision
  - Prescribed after alternative treatment options have been considered
- Treatment with Multaq® can be initiated in an outpatient setting.

Call for Reporting

Healthcare professionals are encouraged to report all the adverse events suspected to be associated with the use of Multaq® to the Medicines Authority. Report Form can be downloaded from **http://www.medicinesauthority.gov.mt/adrportal** and sent to Post-licensing Directorate, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000 Malta, or by email to **postlicensing.medicinesauthority@gov.mt**
Alternatively any suspected adverse reactions and medication error can be reported to Sanofi Srl, Viale Luigi Bodio, 37/b - 20158 Milano, Italy at **PharmacovigilanceMalta@sanofi.com**

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BEFORE TREATMENT INITIATION

If **any** of the 'Yes' criteria **(Red Buttons)** apply, do not prescribe Multaq®. You should only prescribe Multaq® if **all** 'No' criteria **(Green Buttons)** apply. Contraindications should be confirmed by **ECG, serum creatinine and, liver and pulmonary tests**.

Multaq® is **indicated** for the maintenance of sinus rhythm after successful cardioversion in clinically stable adult patients with paroxysmal or persistent atrial fibrillation (AF)

If any red 'Yes' applies do not initiate Multaq®

Atrial Fibrillation

- Yes — Hypersensitivity to the active substance or to any of the excipients.
- No
- Yes — **Permanent AF with an AF duration ≥6 months (or duration unknown) and attempts to restore sinus rhythm no longer considered by the physician**
- No

Heart Failure

- Yes — Second- or third- degree atrio-ventricular block, complete bundle branch block, distal block, sinus node dysfunction, atrial conduction defects or sick sinus syndrome (except when used in conjunction with a functioning pacemaker).
- Yes — QTc Bazett interval ≥ 500 milliseconds.
- Yes — **History of, or current heart failure or left ventricular systolic dysfunction (LVSD)**
- Yes — Unstable hemodynamic conditions
- Yes — Pre-renal azotaemia (functional impairment)
- Yes — Bradychardia <50 beats per minute (bpm)
- No

Drug – Drug Interactions

- Yes — Potential torsades de pointes inducers *(phenothiazines, cisapride, bepridil, tricyclic antidepressants, terfenadine and certain oral macrolides)*
- Yes — Potent cytochrome P 450 (CYP) 3A4 inhibitors *(ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefazodone and ritonavir)*
- Yes — Class I or Class III antiarrhythmics
- Yes — Dabigatran
- No

Liver & Lung

- Yes — Severe hepatic impairment
- Yes — Liver and lung toxicity related to the previous use of amiodarone
- No

Kidney

- Yes — Severe renal impairment (CrCl <30 ml/min)
- No

Multaq® can be initiated

MONITORING DURING TREATMENT

The following assessments are recommended during treatment with Multaq®. Criteria for discontinuation are also described. If **any** of the 'Yes' criteria **(Red Buttons)** arise during treatment, Multaq® should be discontinued.

ECG:
Serially, at least every 6 months

→ Patient develops permanent AF — Yes

SYMPTOMS OF:
- Heart failure
- LVSD (monitoring of left ventricular function)

→ Patient develops heart failure or LVSD — Yes

USE WITH CAUTION *(in association with):*
- Digitalis
- Beta blockers, calcium antagonists with heart rate lowering properties, statins
- Drug modifying INR (warfarin)
- Sirolimus and tacrolimus

NOT RECOMMENDED *(in association with):*
Grapefruit juice, potent CYP3A4 inducers including rifampicin, phenobarbital, carbamazepine, phenytoin, St John's Wort

LIVER FUNCTION TESTS:
After 1 week → after 1 month → monthly for 6 months → at months 9 and 12 → periodically

→ ALT levels are confirmed to be ≥3 ULN — Yes

PULMONARY FUNCTION TESTS

→ Pulmonary toxicity — Yes

SERUM CREATININE*: After 1 week → after a further 7 days if ↑ creatinine

→ Serum creatinine continues to ↑ — Yes

Plasma creatinine levels may rise initially due to inhibition of renal tubular excretion of creatinine and are not necessarily indicative of a deterioration in renal function

If any red 'Yes' applies Multaq® must be discontinued

PATIENT COUNSELLING

Patients should be informed that during treatment with Multaq® **blood tests and ECGs** will be performed, and should be advised on the following:

To consult a physician if they develop: *palpitations, sensation of rapid or irregular heart beats*

To consult a physician if they develop: *weight gain, dependent oedema, increased dyspnoea*

Multaq® interacts with a number of medicines:
- **To inform any other doctor** that they are under treatment with Multaq®
- They **should not take** St. John's Wort
- They should **avoid** grapefruit juice

To report immediately if they develop: *new-onset abdominal pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine or itching*
To consult a physician if they develop: *non-productive cough, breathlessness*

Reporting **suspected adverse drug reactions** is important for continued monitoring of the benefit/risk balance. Healthcare professionals are asked to report any suspected adverse reactions to **Medicines Authority** at **postlicensing.medicinesauthority@gov.mt** or to **Sanofi Srl** at **PharmacovigilanceMalta@sanofi.com**