Healthcare Professional Information Sheet for MULTAQ®

To ensure appropriate use of MULTAQ®, a Risk Management Plan has been implemented in Canada.
To this effect, before prescribing/dispensing MULTAQ®, please take note of the following important safety information.

INDICATION AND DOSING FORMATION

MULTAQ® is indicated for the treatment of patients with paroxysmal or persistent atrial fibrillation (AF) who are in sinus rhythm or who are intended to be cardioverted, to reduce the risk of cardiovascular hospitalization due to AF. MULTAQ® should only be prescribed after alternative treatment options have been considered.

MULTAQ® is administered as one 400 mg tablet taken with the morning and evening meals. Patients should be warned to avoid grapefruit or grapefruit juice beverages while taking MULTAQ®. There is limited information on the optimal timing to switch from amiodarone to MULTAQ®. It should be considered that amiodarone may have a long duration of action after discontinuation due to its long half-life. If a switch is considered, this should be done under the supervision of a specialist.

CONTRAINDICATIONS

DO NOT PRESCRIBE MULTAQ® if

- Permanent AF of any duration in which sinus rhythm cannot be restored and attempts to restore it are no longer considered;
- History of, or current heart failure, regardless of NYHA functional class;
- Unstable hemodynamic conditions;
- Left ventricular systolic dysfunction;
- Second- or third-degree AV 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);
- Liver and lung toxicity related to the previous use of amiodarone.

Prescribers should also be aware of other important contraindications, including:

- Co-administration with strong CYP 3A4 inhibitors, medicinal products inducing Torsade de Pointes, or Class I and III antiarrhythmics agents;
- Bradycardia < 50 bpm;
- QTc Bazett interval ≥ 500 msec;
- Severe hepatic impairment;
- Pregnancy or nursing mother;
- History of hypersensitivity reactions to dronedarone or any of its excipients or component of the container.

MULTAQ® is not recommended with:

- Grapefruit juice;
- Potent CYP3A4 inducers including rifampicin, phenobarbital, carbamazepine, phenytoin, St John's Wort.
- Digitalis

Use MULTAQ® with caution in association with:

- Digoxin *(close monitoring of serum levels, especially during the 1st week of co-administration. Clinical and ECG monitoring are recommended and digoxin dose should be adjusted as appropriate).*
- Beta blockers, calcium antagonists, statins, tacrolimus, sirolimus.
- Vitamin K antagonists such as warfarin.

RELEVANT INFORMATION INCLUDED

Please consider the following Warnings and Precautions – including monitoring recommendations - for ensuring appropriate use when prescribing MULTAQ® to your patients:

CARDIOVASCULAR

- QT prolongation: MULTAQ® may induce a moderate (~10 msec) QTc Bazett prolongation, which is linked to its therapeutic effect and does not reflect toxicity.
  - → If QTc Bazett interval is ≥ 500 msec, MULTAQ® should be stopped.
- Congestive heart failure (CHF) or Left Ventricular Systolic Dysfunction: MULTAQ® is contraindicated for use in patients in unstable hemodynamic conditions, history of, or current heart failure or left ventricular systolic dysfunction.
  - → Patients should be advised to consult a physician if they develop or experience worsening signs or symptoms of heart failure, such as weight gain, dependent edema, or increasing shortness of breath.
- It is recommended to perform an ECG at least every 6 months while patients are receiving MULTAQ®.
  - → If patients develop permanent AF, heart failure or left ventricular systolic dysfunction, treatment with MULTAQ® should be discontinued.
- Coronary Artery Disease: Caution is needed in patient with coronary artery disease.

ANTICOAGULATION THERAPY

- Patient should be appropriately anticoagulated.
- International Normalized Ratio (INR) should be closely monitored after initiating MULTAQ® in patients taking vitamin K antagonists as per their label.
- The concomitant use of dabigatran and MULTAQ® is not recommended since it may increase the risk of bleeding.

HEPATIC

- Hepatocellular liver injury, including acute liver failure requiring transplant, has been reported in patients treated with MULTAQ® in the post-marketing setting.
- Advise patients to immediately report symptoms suggesting hepatic injury, such as anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching.
- Obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment, should be considered.
- If hepatic injury is suspected, MULTAQ® should be discontinued immediately and followed by necessary blood tests.
- The safety of restarting MULTAQ® in patients who have sustained liver injury from any cause is unknown; accordingly, its use in such patients is not recommended.

RENAL

- Plasma creatinine increase: MULTAQ® often induced an increase in plasma creatinine (~10 µmol/L) early after treatment initiation that reached a plateau after 7 days. Values returned to baseline within one week of treatment discontinuation.
  - → Larger increases in creatinine after MULTAQ® initiation have been reported in post-marketing experience. Some cases also reported increases in blood urea nitrogen, possibly due to hypoperfusion secondary to developing CHF (pre-renal azotemia). In such case, MULTAQ® should be stopped. Consequently, renal function should be monitored periodically and consider further investigations as needed.

RESPIRATORY

- Interstitial lung disease, including pneumonitis and pulmonary fibrosis, have been reported in post-marketing experience.
- Patient should be carefully evaluated clinically for onset of dyspnea or non-productive cough as it may be related to pulmonary toxicity.
- If pulmonary toxicity is confirmed, treatment with MULTAQ® should be discontinued.

SPECIAL POPULATIONS / GERIATRICS

- Caution is needed in elderly patients ≥ 75 years with multiple co-morbidities.

Refer to the full Product Monograph (PM) for additional contraindications, warnings, precautions, and drug-drug interactions. This PM can be found at www.sanofi.ca or by contacting the sponsor at 1-800-265-7927.

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