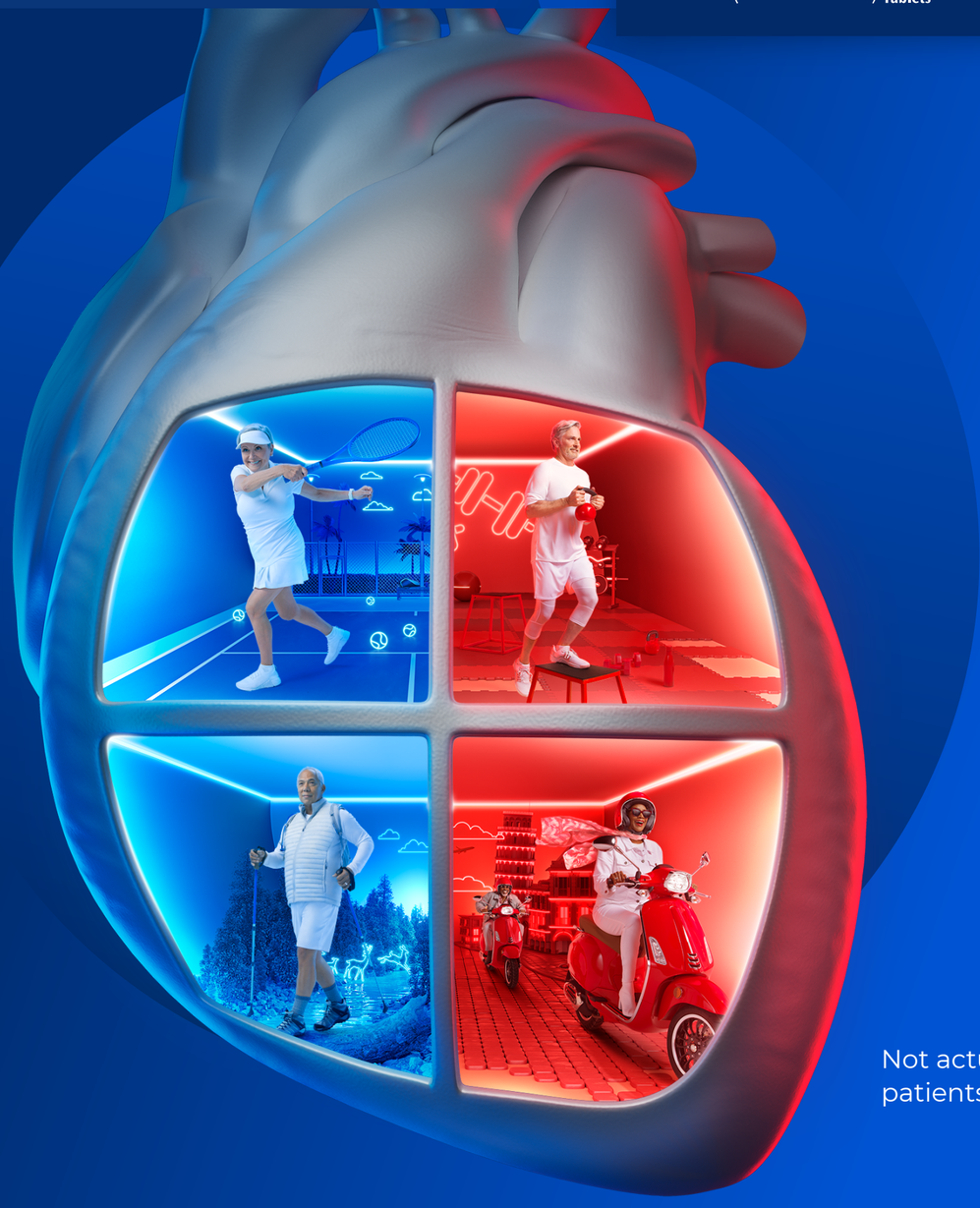
IN THE TREATMENT OF PAROXYSMAL
OR PERSISTENT AFib

MULTAQ® HELPS KEEP PATIENTS IN SINUS RHYTHM & OUT OF THE HOSPITAL

Please see Important Safety Information below and full Prescribing Information page, including **boxed WARNING.**



Not actual patients.

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

Prescribing Information AFib Guidelines Glossary References

Important Safety Information

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ is also contraindicated in patients:

- With second- or third-degree atrioventricular (AV) block or sick sinus syndrome (except when used in conjunction with a functioning pacemaker), bradycardia <50 bpm, QTc Bazett interval ≥500 ms or PR interval >280 ms
- Who are or may become pregnant (Category X) or nursing. MULTAQ may cause fetal harm when administered to a pregnant woman
- With concomitant use of strong CYP 3A inhibitors, such as ketoconazole, itraconazole, voriconazole, cyclosporine, telithromycin, clarithromycin, nefazodone, ritonavir, or drugs or herbal products that prolong the QT interval and might increase the risk of Torsade de Pointes, such as phenothiazine antipsychotics, tricyclic antidepressants, certain oral macrolide antibiotics, and Class I and III antiarrhythmics
- With liver or lung toxicity related to the previous use of amiodarone
- With severe hepatic impairment
- With hypersensitivity to the active substance or to any of the excipients

Cardiovascular Death in NYHA Class IV or Decompensated Heart Failure

MULTAQ is contraindicated in patients with NYHA Class IV heart failure or symptomatic heart failure with recent decompensation requiring hospitalization because it doubles the risk of death.

Cardiovascular Death and Heart Failure in Permanent AFib

MULTAQ doubles the risk of cardiovascular death (largely arrhythmic) and heart failure events in patients with permanent AFib. Patients treated with MULTAQ should undergo monitoring of cardiac rhythm no less often than every 3 months. Cardiovert patients who are in AFib (if clinically indicated) or discontinue MULTAQ. MULTAQ offers no benefit in subjects in permanent AFib.

Increased Risk of Stroke in Permanent AFib

In a placebo-controlled study in patients with permanent AFib, dronedarone was associated with an increased risk of stroke, particularly in the first two weeks of therapy. MULTAQ should only be initiated in patients in sinus rhythm who are receiving appropriate antithrombotic therapy.

New Onset or Worsening Heart Failure

New onset or worsening of heart failure has been reported during treatment with MULTAQ in the postmarketing setting. In a placebo-controlled study in patients with permanent AFib, increased rates of heart failure were observed in patients with normal left ventricular function and no history of symptomatic heart failure, as well as those with a history of heart failure or left ventricular dysfunction.

Advise patients to consult a physician if they develop signs or symptoms of heart failure, such as weight gain, dependent edema, or increasing shortness of breath. If heart failure develops or worsens and requires hospitalization, discontinue MULTAQ.

Liver Injury

Hepatocellular liver injury, including acute liver failure requiring transplant, has been reported in patients treated with MULTAQ in the postmarketing setting. Advise patients treated with MULTAQ to report immediately symptoms suggesting hepatic injury (such as anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching). Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment. It is not known whether routine periodic monitoring of serum enzymes will prevent the development of severe liver injury. If hepatic injury is suspected, promptly discontinue MULTAQ and test serum enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase, as well as serum bilirubin, to establish whether there is liver injury. If liver injury is found, institute appropriate treatment and investigate the probable cause. Do not restart MULTAQ in patients without another explanation for the observed liver injury.

Pulmonary Toxicity

Cases of interstitial lung disease including pneumonitis and pulmonary fibrosis have been reported in patients treated with MULTAQ in the post-marketing setting. Onset of dyspnea or non-productive cough may be related to pulmonary toxicity and patients should be carefully evaluated clinically. If pulmonary toxicity is confirmed, MULTAQ should be discontinued.

Hypokalemia and Hypomagnesemia with Potassium-Depleting Diuretics

Hypokalemia and hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be within the normal range prior to administration of MULTAQ and maintained in the normal range during administration of MULTAQ.

QT Interval Prolongation

MULTAQ induces a moderate (average of about 10 ms but much greater effects have been observed) QTc (Bazett) prolongation. If the QTc Bazett interval is ≥500 ms, discontinue MULTAQ.

Renal Impairment and Failure

Marked increase in serum creatinine, pre-renal azotemia and acute renal failure, often in the setting of heart failure or hypovolemia, have been reported in patients taking MULTAQ. In most cases, these effects appear to be reversible upon drug discontinuation and with appropriate medical treatment. Monitor renal function periodically.

Small increases in creatinine levels (about 0.1 mg/dL) following MULTAQ treatment initiation have been shown to be a result of inhibition of creatinine's tubular secretion. The elevation has a rapid onset, reaches a plateau after 7 days and is reversible after discontinuation.

Women of Childbearing Potential

Premenopausal women who have not undergone a hysterectomy or oophorectomy must use effective contraception while using MULTAQ. Dronedarone caused fetal harm in animal studies at doses equivalent to recommended human doses. Counsel women of childbearing potential regarding appropriate contraceptive choices.

Drug-Drug Interactions

- Treatment with Class I or III antiarrhythmics or drugs that are strong inhibitors of CYP 3A must be stopped before starting MULTAQ (see Contraindications)
- Patients should be instructed to avoid grapefruit juice beverages while taking MULTAQ
- Calcium channel blockers with depressant effects and beta-blockers could increase the bradycardia effects of MULTAQ on conduction
- In the ANDROMEDA (patients with recently decompensated heart failure) and PALLAS (patients with permanent AFib) trials, baseline use of digoxin was associated with an increased risk of arrhythmic or sudden death in MULTAQ-treated patients compared to placebo. In patients not taking digoxin, no difference in risk of sudden death was observed in the MULTAQ vs placebo groups.

  Digoxin can potentiate the electrophysiologic effects of MULTAQ (such as decreased AV-node conduction). MULTAQ increases exposure to digoxin.

  Consider discontinuing digoxin. If digoxin treatment is continued, halve the dose of digoxin, monitor serum levels closely, and observe for toxicity.
- Postmarketing cases of increased INR with or without bleeding events have been reported in warfarin-treated patients initiated with MULTAQ. Monitor INR after initiating MULTAQ in patients taking warfarin
- Statins: Avoid simvastatin doses greater than 10 mg daily. Follow statin label recommendations for use with CYP 3A and P-gP inhibitors such as MULTAQ

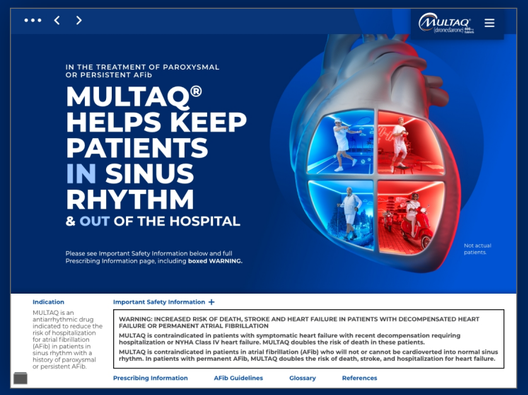
Adverse Reactions

In studies, the most common adverse reactions observed with MULTAQ were diarrhea, nausea, abdominal pain, vomiting, and asthenia.

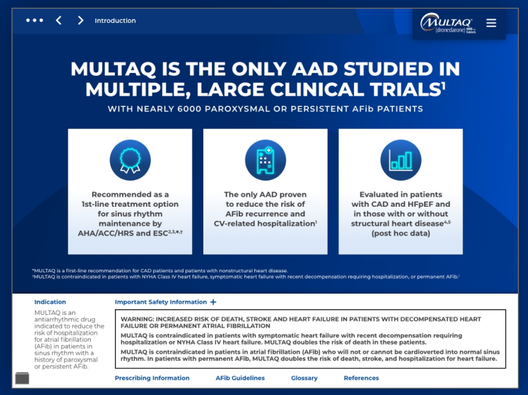
Click here for full Prescribing Information, including boxed WARNING.

Click here to learn more about Sanofi's commitment to fighting counterfeit drugs.

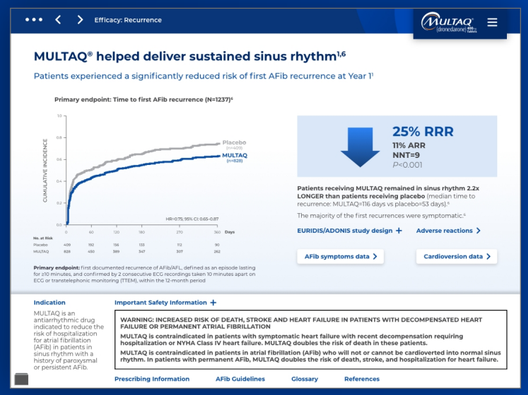
Home



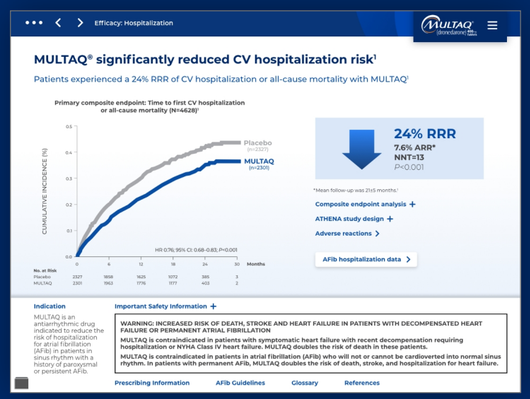
Introduction



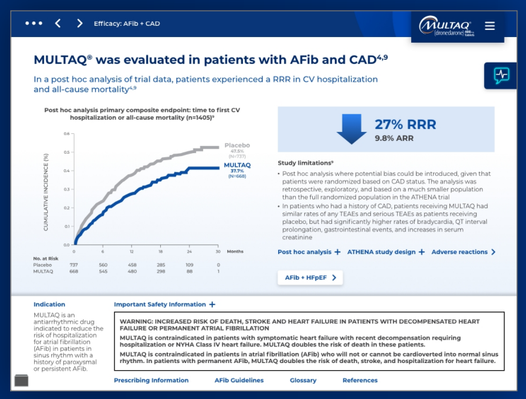
Efficacy: Recurrence



Efficacy: Hospitalization

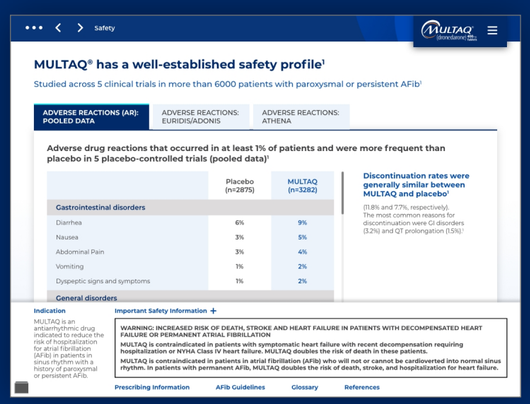


Efficacy: AFib + CAD

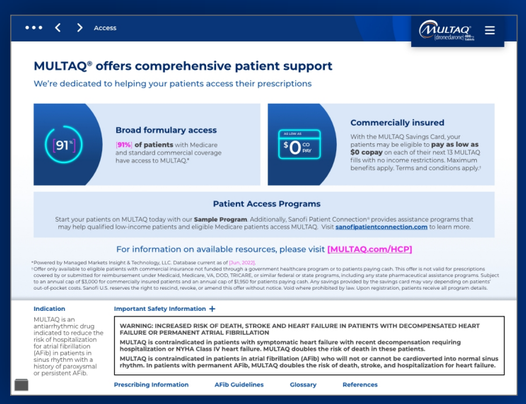


Dosing

Safety



Access



Summary

Prescribing Information

AFib Guidelines

Glossary

References

MULTAQ IS THE ONLY AAD STUDIED IN MULTIPLE, LARGE CLINICAL TRIALS[1]

WITH NEARLY 6000 PAROXYSMAL OR PERSISTENT AFib PATIENTS

Recommended as a 1st-line treatment option for sinus rhythm maintenance by AHA/ACC/HRS and ESC[2,3,*,†]

The only AAD proven to reduce the risk of AFib recurrence and CV-related hospitalization[1]

Evaluated in patients with CAD and HFpEF and in those with or without structural heart disease[4,5] (post hoc data)

*MULTAQ is a first-line recommendation for CAD patients and patients with nonstructural heart disease.
†MULTAQ is contraindicated in patients with NYHA Class IV heart failure, symptomatic heart failure with recent decompensation requiring hospitalization, or permanent AFib.[1]

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

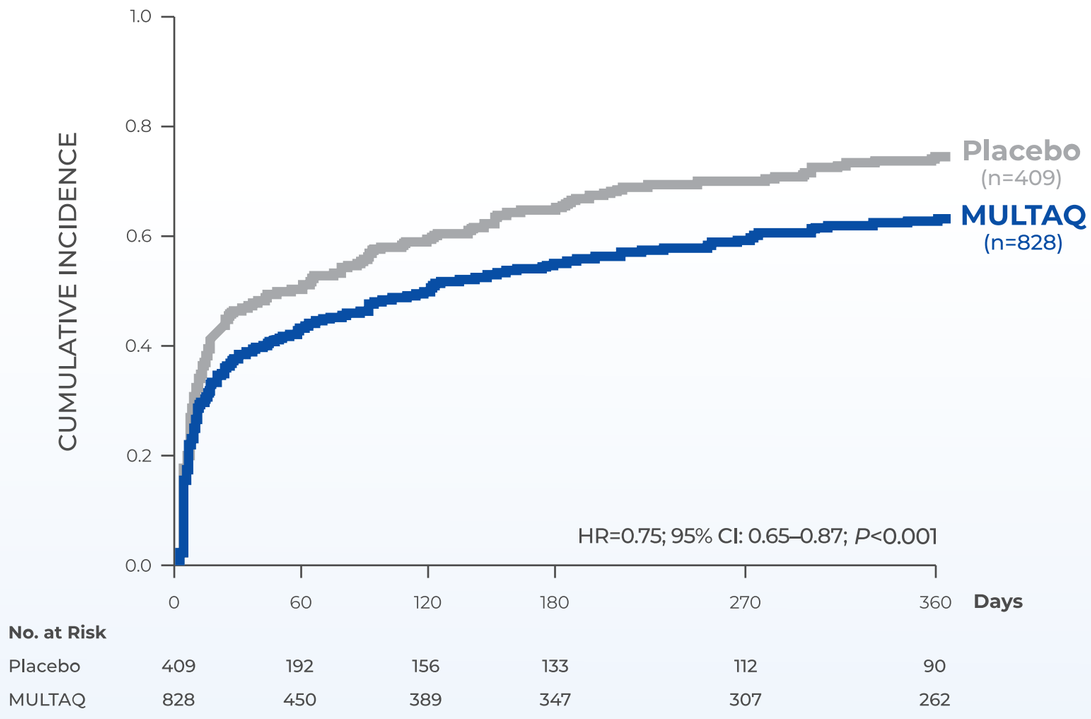
MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® helped deliver sustained sinus rhythm[1,6]

Patients experienced a significantly reduced risk of first AFib recurrence at Year 1[1]

Primary endpoint: Time to first AFib recurrence (N=1237)[6]



Primary endpoint: first documented recurrence of AFib/AFL, defined as an episode lasting for ≥10 minutes, and confirmed by 2 consecutive ECG recordings taken 10 minutes apart on ECG or transtelephonic monitoring (TTEM), within the 12-month period

25% RRR
11% ARR
NNT=9
P<0.001

Patients receiving MULTAQ remained in sinus rhythm 2.2x LONGER than patients receiving placebo (median time to recurrence: MULTAQ=116 days vs placebo=53 days).[6]

The majority of the first recurrences were symptomatic.[6]

EURIDIS/ADONIS study design +
Adverse reactions >
AFib symptoms data >
Cardioversion data >

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

EURIDIS/ADONIS study design[6]

- Double-blind, randomized, multicenter studies evaluating efficacy and safety of MULTAQ® in maintaining sinus rhythm in 1237 patients with nonpermanent AFib/AFL
- Patients with at least 1 episode of AFib/AFL observed on an ECG 3 months prior to study enrollment and in sinus rhythm for at least 1 hour prior to randomization were assigned to 400 mg MULTAQ (n=828) twice daily or placebo (n=409) for 12 months

Common CV comorbidities in patients in the MULTAQ EURIDIS/ADONIS trials

TYPICAL AFib PATIENTS
(N=1237)[1,6]

57% Hypertension
41% Structural heart disease
22% Coronary artery disease
17% CHF (NYHA Class I/II)

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, symptomatic heart failure with recent decompensation required hospitalization, and permanent AF.[1]

Common cardiovascular therapies treating patients in the MULTAQ and placebo arms[6]

TYPICAL AFib PATIENTS
(N=1237)[1,6]

70% Oral anticoagulant
56% Beta-blocker excluding sotalol
39% ACE inhibitor
32% Statin
18% Calcium channel blocker

Baseline characteristics of the study patients[6,*]

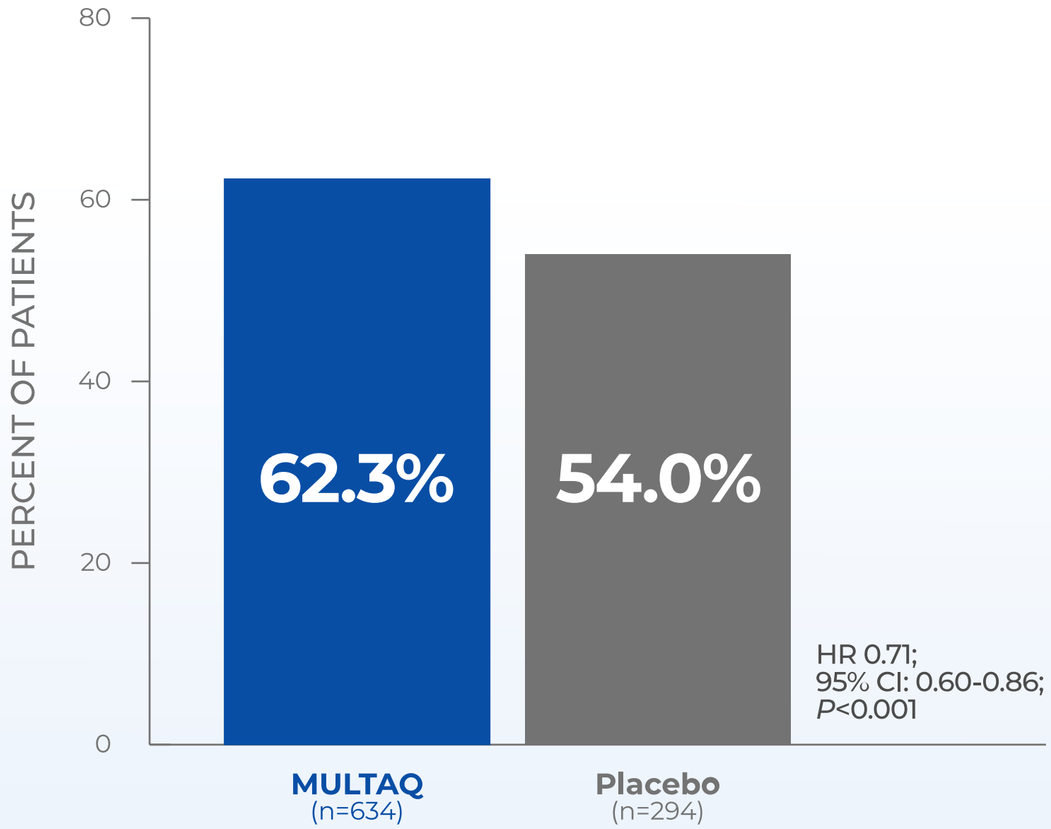
Characteristic	Placebo (n=409)	MULTAQ (n=828)
Sex—no. (%)		
Female	129 (31.5)	250 (30.2)
Male	280 (68.5)	578 (69.8)
Age—yr	62.2±11.1	63.5±10.7
Race—no. (%)†		
White	400 (97.8)	800 (96.6)
Black	3 (0.7)	9 (1.1)
Asian	0	6 (0.7)
Other	6 (1.5)	13 (1.6)
Body-mas index—no. (%)‡		
<30	273 (68.4)	538 (66.0)
≥30	126 (31.6)	277 (34.0)
Weight—kg	87.14±17.22	86.25±17.53
Cardiovascular history—no. (%)		
Structural heart disease§	159 (39.7)	348 (42.4)
Hypertension	205 (50.1)	497 (60.0)
Coronary artery disease‖	75 (18.3)	195 (23.6)
Cardiac valvular disease	61 (14.9)	136 (16.4)
Nonischemic cardiomyopathy	30 (7.3)	50 (6.0)
Implanted pacemaker	20 (4.9)	64 (7.7)
Implanted cardioverter-defibrillator	5 (1.2)	6 (0.7)
Rheumatic heart disease	14 (3.4)	25 (3.0)
Hypertrophic cardiomyopathy	12 (2.9)	23 (2.8)
Congenital heart disease	3 (0.7)	13 (1.6)
Left ventricular ejection fraction—%	58.5±10.98	58.75±10.77
Left atrial anteroposterior diameter—mm	42.4±6.8	42.6±7.0
Congestive heart failure—no. (%)¶		
Any disease	73 (17.8)	143 (17.3)
NYHA Class I	26 (6.4)	47 (5.7)
NYHA Class II	47 (11.5)	96 (11.6)
Symptoms of atrial fibrillation in the 3 months before randomization—no. (%)	355 (86.8)	726 (87.7)
Recent cardioversion (within 5 days before randomization) —no. (%)	121 (29.6)	243 (29.3)
Concomitant cardiovascular therapy—no. (%)		
Digoxin	95 (23.2)	145 (17.5)
Calcium-channel blocker (rate-lowering)	78 (19.1)	139 (16.8)
Beta-blocker (except sotalol)	238 (58.2)	453 (54.7)
Oral anticoagulant	291 (71.1)	571 (69.0)
Long-term antiplatelet therapy	152 (37.2)	326 (39.4)
Statin	131 (32.0)	263 (31.8)
ACE inhibitor	159 (38.9)	327 (39.5)
Previous antiarrhythmic treatment—no. (%)		
Class IA	40 (9.8)	82 (9.9)
Class IB	0	6 (0.7)
Class IC	108 (26.4)	190 (22.9)
Class II	67 (16.4)	159 (19.2)
Class III	27 (6.6)	86 (10.4)
Class IV	38 (9.3)	72 (8.7)
Amiodarone	126 (30.8)	243 (25.8)
Sotalol	112 (27.4)	214 (25.8)

*Plus–minus values are means ± SD.
†Race was determined by the investigators on the basis of hospital records.
‡The body-mass index was calculated as the weight in kilograms divided by the square of the height in meters. In the European trial, data were missing for 6 subjects in the placebo group and 6 in the MULTAQ group; in the non-European trial, data were missing for 4 subjects in the placebo group and 7 in the MULTAQ group.
§In the European trial, data were missing for 6 subjects in the placebo group and 1 in the MULTAQ group; in the non-European trial, data were missing for 2 subjects in the placebo group and 7 in the MULTAQ group.
‖The diagnosis of coronary artery disease was made on the basis of the clinical history and the results of investigational tests.
¶The diagnosis of congestive heart failure (NYHA Class I and II) was made on clinical grounds. Patients who were classified as having NYHA Class I congestive heart failure had received a diagnosis of the disease but had no symptoms.

MULTAQ® lowered AFib symptom recurrence[6]

62.3% of patients had no recurrence of AFib symptoms at Year 1[6]

Patients freed from symptomatic AFib at Year 1[6]



This preplanned analysis (n=928) was an assessment of the primary endpoint data that excluded patients who discontinued treatment or experienced recurrence of atrial fibrillation before reaching 5 days of study drug exposure. Patients with study-drug exposure of less than 5 days before the occurrence of the primary endpoint also were excluded from this analysis.[6]

Recurrence of AFib symptoms was defined as AFib symptoms during recordings of 12-lead ECG or transtelephonic monitoring and included 1 or more of the following symptom(s): palpitations, dizziness, fatigue, chest pain, and/or dyspnea.[6]

Post hoc analysis +

EURIDIS/ADONIS study design +

Adverse reactions >

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

EURIDIS/ADONIS post hoc analysis[6,7]

This post hoc analysis of EURIDIS/ADONIS studies evaluated treatment outcomes by baseline cardioversion status. Of the 1237 patients in the EURIDIS/ADONIS studies, 364 patients received cardioversion at study entry (MULTAQ: 243; placebo: 121) and 873 patients did not (MULTAQ: 585; placebo: 288).[6,7]

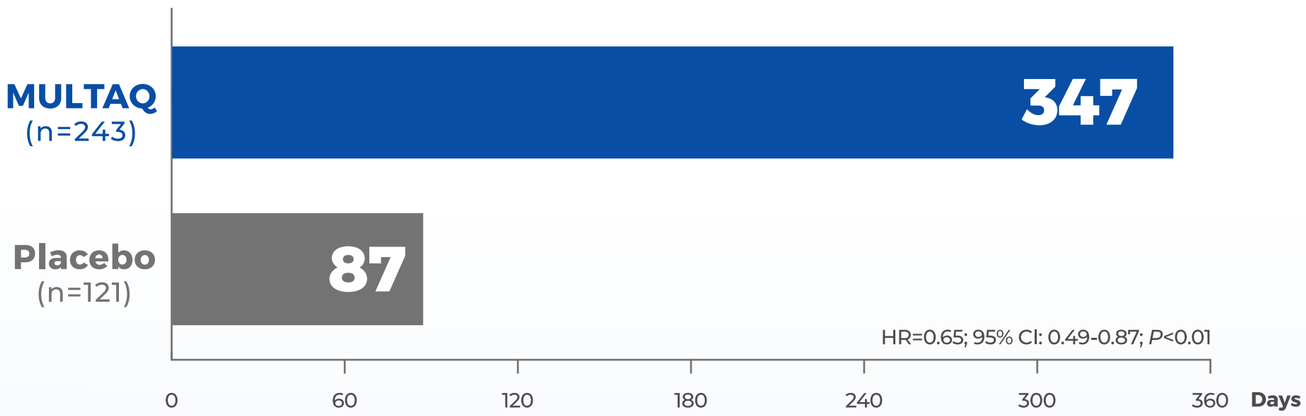
The median time to first symptomatic AFib recurrence in the non-cardioverted group was 288 days with MULTAQ and 120 days with placebo (HR 0.74; 95% CI: 0.62-0.90; P<0.01).[7,*]

The median time to documented AFib recurrence in the cardioverted group was 50 days with MULTAQ vs 15 days with placebo (HR 0.76; 95% CI: 0.59-0.97; *P*=0.02) and in the non-cardioverted group was 150 days with MULTAQ vs 77 days with placebo (HR 0.76; 95% CI: 0.64-0.90; *P*<0.01).[7]

*Documented AFib recurrence was confirmed by 2 consecutive 12-lead ECG or transtelephonic monitoring recordings taken at least 10 minutes apart.[7]

MULTAQ® was evaluated in recently cardioverted patients[7]

Secondary endpoint of a post hoc analysis:
Median time to first recurrence of AFib symptoms (N=364)[7]



MEDIAN TIME TO FIRST SYMPTOMATIC AFib RECURRENCE

Symptomatic AFib in patients cardioverted in the 5 days prior to randomization

AFib recurrence delayed by 4x
compared to placebo[7,*,†]

*Recurrence of AFib symptoms was defined as AFib symptoms during recordings of 12-lead ECG or transtelephonic monitoring and included 1 or more of the following symptom(s): palpitations, dizziness, fatigue, chest pain, and/or dyspnea.[7]

†Patients had to be in normal sinus rhythm to be eligible for the trial. This patient group was in sinus rhythm after undergoing cardioversion in the 5 days before initiating MULTAQ.[7]

Study limitations[7]

- Study considered exploratory
- Study not powered to evaluate efficacy and safety by cardioversion status
- Lack of multivariate analyses to identify factors associated with AFib/AFL
- Lack of characterization of AFib/AFL patient types

Post hoc analysis + **EURIDIS/ADONIS study design +**

Adverse reactions ›

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

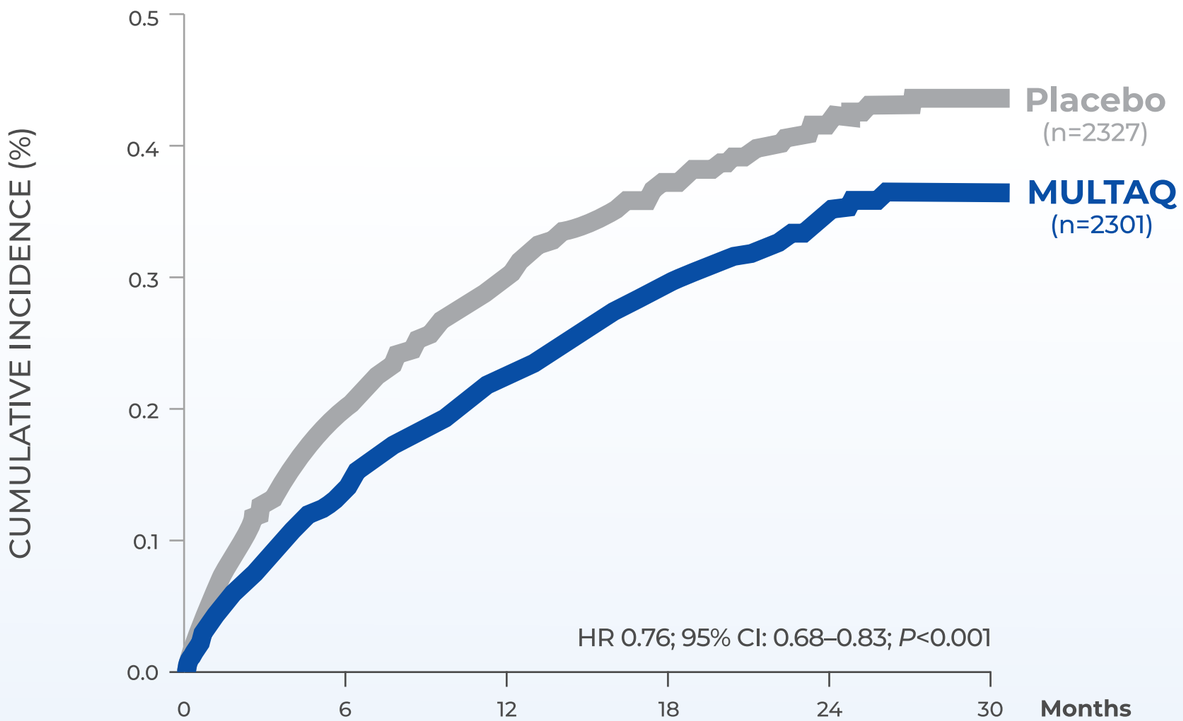
MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® significantly reduced CV hospitalization risk[1]

Patients experienced a 24% RRR of CV hospitalization or all-cause mortality with MULTAQ[1]

Primary composite endpoint: Time to first CV hospitalization or all-cause mortality (N=4628)[1]



No. at Risk						
Placebo	2327	1858	1625	1072	385	3
MULTAQ	2301	1963	1776	1177	403	2

24% RRR

7.6% ARR*

NNT=13

P<0.001

*Mean follow-up was 21±5 months.[1]

Composite endpoint analysis +

ATHENA study design +

Adverse reactions >

AFib hospitalization data >

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

ATHENA study design[4]

- Double-blind, multicenter, placebo-controlled study to evaluate efficacy and safety of MULTAQ® in 4628 patients ≥70 of age with **paroxysmal or persistent AFib/AFL** and an additional CV risk factor
- Patients who experienced AFib/AFL within 6 months, and were in sinus rhythm, were randomized 1:1 to receive 400 mg MULTAQ twice daily or placebo
- **Primary composite endpoint:** first hospitalization due to CV event or all-cause mortality
- ATHENA defined coronary artery disease as a documented history of either ischemic dilated cardiomyopathy, evidenced by clinically significant left ventricular dilatation secondary to coronary artery disease, or coronary artery disease, which was defined as acute myocardial infarction and/or the following: significant (≥70%) coronary artery stenosis, history of revascularization procedure (percutaneous transluminal coronary angioplasty, stent implantation in a coronary artery, coronary artery bypass grafting, etc), positive exercise test, and positive nuclear scan of cardiac perfusion

Common CV comorbidities in patients in the ATHENA trial

AFib PATIENTS WITH DEFINED ADDITIONAL RISK FACTORS (N=4628)[1,4]

86% Hypertension
60% Structural heart disease
30% Coronary artery disease
29% History of CHF (NYHA Class I to III)

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, symptomatic heart failure with recent decompensation required hospitalization, and permanent AFib.[1]

Common cardiovascular therapies treating patients in the MULTAQ and placebo arms[1,4]

AFib PATIENTS WITH DEFINED ADDITIONAL RISK FACTORS (N=4628)[1,4]

71% Beta-blocker
69% ACE inhibitor or ARB
60% Oral anticoagulant
39% Statin
14% Calcium antagonist

ATHENA included 196 patients (4.2%) who had undergone ablation for AFib/AFL prior to randomization.[8]

Baseline characteristics[4,*]

Characteristic	Placebo (n=2327)	MULTAQ (n=2301)
Age		
Mean ± SD—yr	71.7±9.0	71.6±8.9
<65 yr—no. (%)	442 (19.0)	431 (18.7)
65 to <75 yr—no. (%)	907 (39.0)	923 (40.1)
≥75 yr—no. (%)	978 (42.0)	947 (41.2)
Female sex—no. (%)	1038 (44.6)	1131 (49.2)
Atrial fibrillation or flutter—no. (%)	586 (25.2)	569 (24.7)
Structural heart disease—no. (%)†	1402 (60.9)	1330 (58.3
Hypertensions—no. (%)	1996 (85.8)	1999 (86.9)
Coronary heart disease—no. (%)	737 (31.7)	668 (29.0)
Valvular heart disease—no. (%)	380 (16.3)	379 (16.5)
Nonischemic cardiomyopathy—no. (%)	131 (5.6)	123 (5.3)
History Of HF, NYHA Class II Or III—no. (%)	515 (22.1)	464 (20.2)
LVEF—no. (%)‡		
<45%	285 (12.5)	255 (11.3)
<35%	87 (3.8)	92 (4.1)
Lone atrial fibrillation—no. (%)§	139 (6.0)	140 (6.1)
Pacemaker—no. (%)	243 (10.4)	214 (9.3)
Medications in use at baseline—no. (%)		
Beta-blocker	1641 (70.5)	1828 (70.8)
Calcium antagonists	307 (13.2)	139 (16.8)
Digoxin	308 (13.2)	321 (14.0)
ACE inhibitor or ARB	1602 (68.8)	1614 (70.1)
Statins	914 (39.2)	878 (38.2)
Vitamin K antagonists	1384 (59.5)	1403 (61.0)
Aspirin	1019 (43.8)	1018 (44.2)

*There were no significant differences between the 2 groups for any of the baseline characteristics, with the exception of the proportion of study patients who were women, which was significantly greater in the MULTAQ group (P=0.002).
† Complete data on structural heart disease were available for 2281 of the 2301 patients receiving MULTAQ, and for 2304 of the 2327 patients receiving placebo, for a total of 4585 patients.
‡ For left ventricular ejection fraction (LVEF), data were available for 2263 of the 2301 patients receiving MULTAQ, and for 2281 of the 2327 patients receiving placebo, for a total of 4544 patients. The category of LVEF less than 45% included the patients with LVEF of less than 35%.
§ Lone atrial fibrillation was defined as atrial fibrillation in the absence of cardiovascular disease and extracardiac precipitating causes of atrial fibrillation.

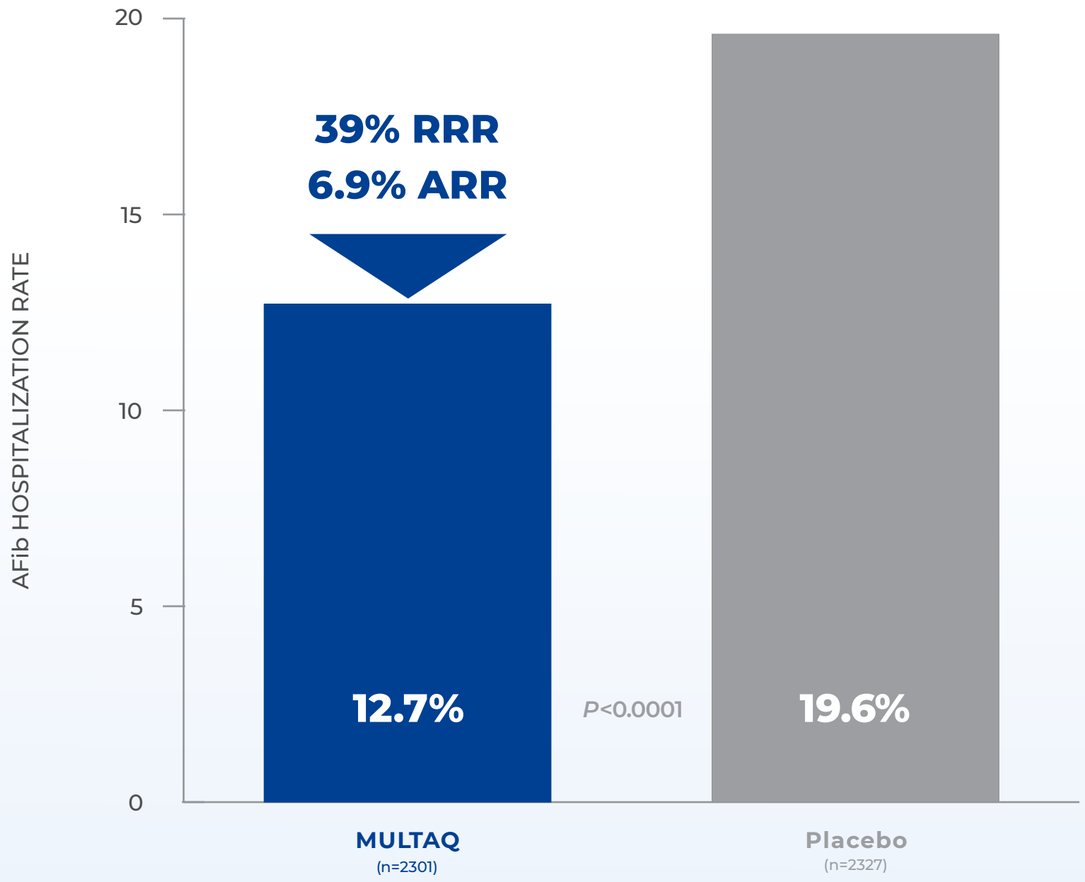
Composite endpoint analysis

Relative risk reduction in the primary composite endpoint was entirely attributable to reduction in CV hospitalization.[1]

Rates of the primary composite endpoint of CV hospitalization or all-cause mortality were 31.6% with MULTAQ vs. 39.2% with placebo.[1]

MULTAQ® significantly reduced AFib hospitalization risk[1,*]

Patients experienced a 39% RRR of AFib hospitalization[1]



39%

RRR in AFib-related hospitalization[1]

(ARR=19.6-12.7=6.9%; HR=0.61; 95% CI: 0.53-0.71; *P*<0.0001)

*Hospitalization due to AFib and other supraventricular rhythm disorders was a component of the secondary endpoint of CV hospitalization.[1]

ATHENA study design + **Adverse reactions ›**

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

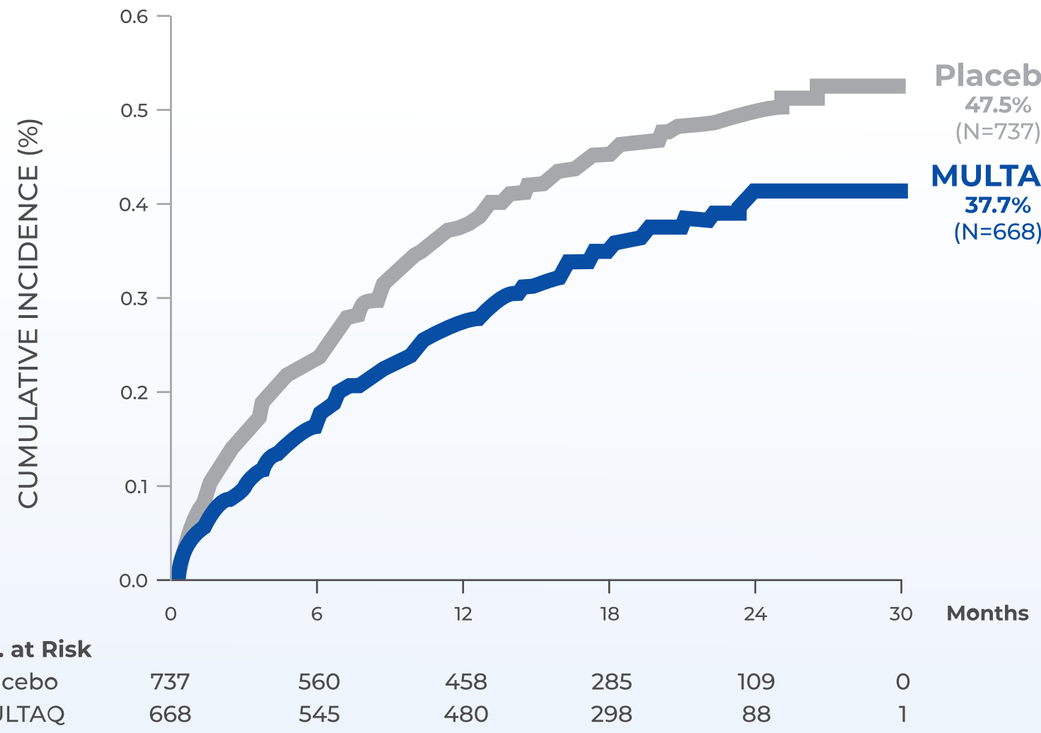
MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® was evaluated in patients with AFib and CAD[4,9]

In a post hoc analysis of trial data, patients experienced a RRR in CV hospitalization and all-cause mortality[4,9]

Post hoc analysis primary composite endpoint: time to first CV hospitalization or all-cause mortality (n=1405)[9]



No. at Risk						
Placebo	737	560	458	285	109	0
MULTAQ	668	545	480	298	88	1

27% RRR

9.8% ARR

Study limitations[9]

- Post hoc analysis where potential bias could be introduced, given that patients were randomized based on CAD status. The analysis was retrospective, exploratory, and based on a much smaller population than the full randomized population in the ATHENA trial
- In patients who had a history of CAD, patients receiving MULTAQ had similar rates of any TEAEs and serious TEAEs as patients receiving placebo, but had significantly higher rates of bradycardia, QT interval prolongation, gastrointestinal events, and increases in serum creatinine

Post hoc analysis + ATHENA study design + Adverse reactions >

AFib + HFpEF >

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

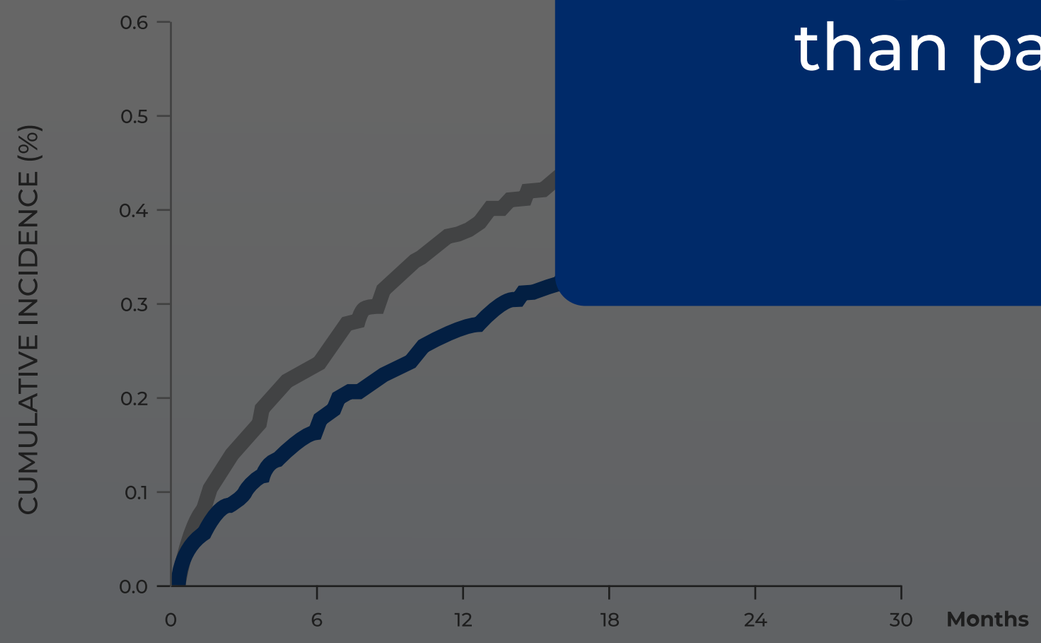
MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® was eval

In a post hoc analysis of trial
and all-cause mortality[4,9]

**Post hoc analysis primary compos
hospitalization or all-caus**



No. at Risk						
Placebo	737	560	458	285	109	0
MULTAQ	668	545	480	298	88	1

Patients with AFib and CAD have a **20% greater risk of hospitalization** than patients with AFib alone.[10]

retrospective, exploratory, and based on a much smaller population than the full randomized population in the ATHENA trial

- In patients who had a history of CAD, patients receiving MULTAQ had similar rates of any TEAEs and serious TEAEs as patients receiving placebo, but had significantly higher rates of bradycardia, QT interval prolongation, gastrointestinal events, and increases in serum creatinine

Post hoc analysis + ATHENA study design + Adverse reactions >

AFib + HFpEF >

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

ATHENA post hoc analysis

Results in the primary composite endpoint were consistent in patients with or without CAD.[9]

This post hoc analysis assessed safety and cardiovascular outcomes of MULTAQ in a total of 1405 patients with CAD from the ATHENA study.[9]

In the ATHENA study (N=4628), MULTAQ significantly reduced the primary composite endpoint with a 24% RRR, 7.6% ARR, and NNT=13 (HR=0.76; 95% CI: 0.68–0.83; *P*<0.0001).[1]

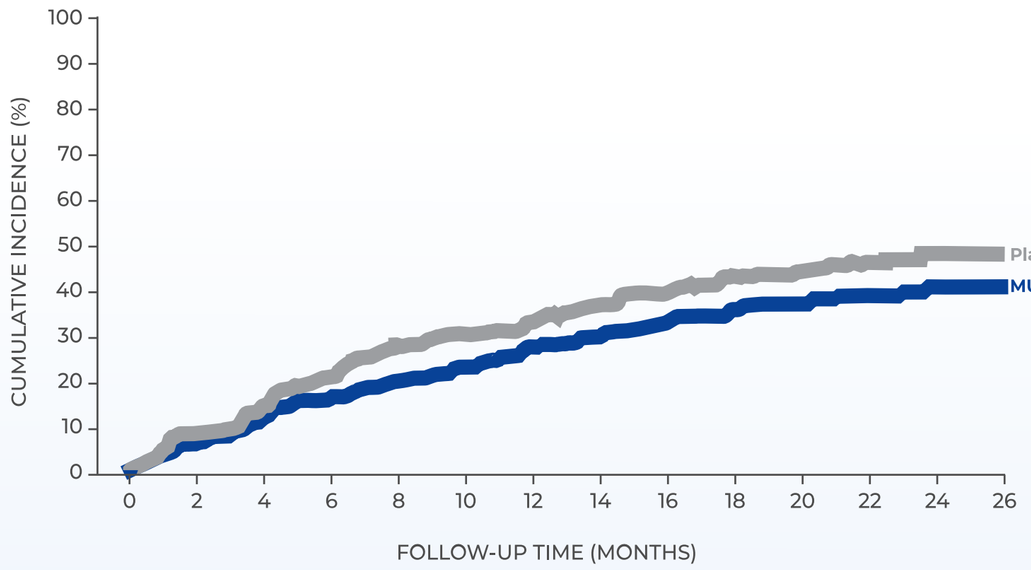
This post hoc analysis assessed safety and cardiovascular outcomes of MULTAQ in a total of 534 patients with HFpEF/HFmrEF from the ATHENA study (N=4628).[5]

MULTAQ® was evaluated in patients with AFib + HFpEF or HFmrEF[5]

Post hoc analysis: Risk of CV hospitalization or all-cause mortality[5]

Post hoc analysis primary composite endpoint: CV hospitalization or all-cause mortality (n=534)[5]

Heart Failure with Preserved and Mildly Reduced Ejection Fraction



No. at Risk														
Placebo	268	243	227	211	193	185	178	154	132	113	92	72	35	11
MULTAQ	266	248	233	221	211	204	192	174	150	128	111	80	48	23

Risk of death or CV hospitalization for patients with AFib + HFpEF or HFmrEF

- Placebo: 57 per 100 patient-years (incidence rate)
- MULTAQ: 44 per 100 patient-years (incidence rate)

Rates of death, CV hospitalization, and HF hospitalization each directionally favored MULTAQ vs placebo in HFpEF/HFmrEF, but these treatment effects were not statistically significant.

Study limitations[5]

- This exploratory subgroup analysis was not designed or powered to detect differences between treatment groups
- Elements that are useful in affirming HFpEF diagnoses including natriuretic peptide levels, detailed physical examination signs or symptom reporting, and prior HF hospitalization status were not available
- Angiotensin receptor–neprilysin inhibitors or sodium–glucose cotransporter 2 inhibitors were not used

Post hoc analysis + ATHENA study design + Adverse reactions >

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

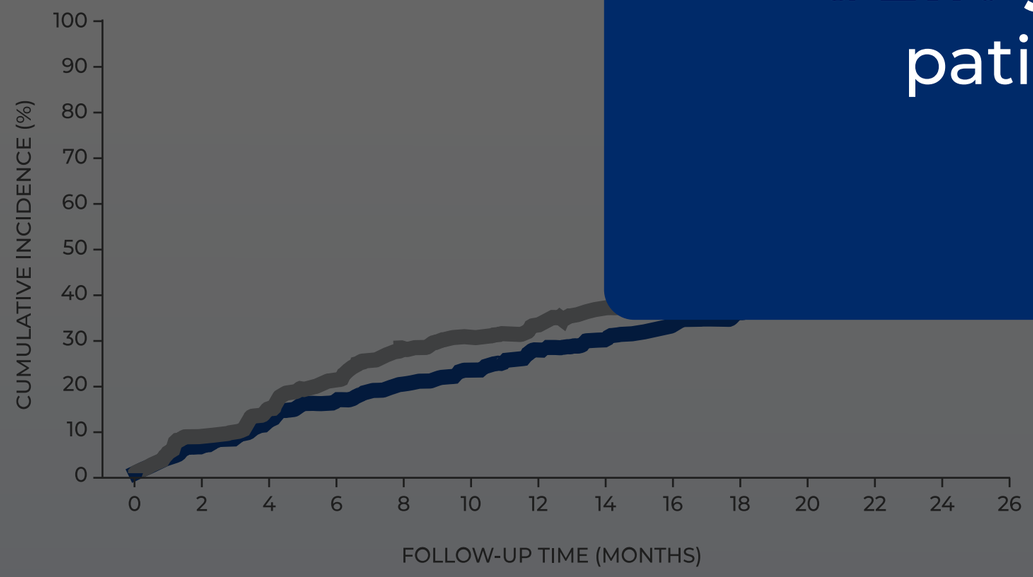
MULTAQ® (dronedarone) 400 mg Tablets

MULTAQ® was eval

Post hoc analysis: Risk of CV

Post hoc analysis primary
CV hospitalization or all-ca

Heart Failure with Preserved and Mil



No. at Risk

Placebo	268	243	227	211	193	185	178	154	132	113	92	72	35	11
MULTAQ	266	248	233	221	211	204	192	174	150	128	111	80	48	23

Patients with AFib and HFpEF have a **21% greater risk of death** than patients with HFpEF alone.[11]

detect differences between treatment groups

- Elements that are useful in affirming HFpEF diagnoses including natriuretic peptide levels, detailed physical examination signs or symptom reporting, and prior HF hospitalization status were not available
- Angiotensin receptor–neprilysin inhibitors or sodium–glucose cotransporter 2 inhibitors were not used

Post hoc analysis + **ATHENA study design +** **Adverse reactions >**

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® features outpatient initiation with no need for continuous ECG monitoring

1 MULTAQ tablet (400 mg)
2x daily with full meals[1,*]

- **Out-of-hospital initiation[1]**
- **No need for continuous ECG monitoring[1]**
- **No need for loading dose or titration[1]**
- **No dose titration for renal impairment[1]**
- **No specific assessment of thyroid function required[1]**

*After repeated administration, steady state is reached within 4 to 8 days.[1]

Monitoring considerations[1]

- Patients treated with MULTAQ should undergo monitoring of cardiac rhythm at least every 3 months
- Consider obtaining periodic hepatic serum enzymes, especially during first 6 months of treatment
- Monitor renal function periodically
- Monitor INR after initiating MULTAQ in patients taking warfarin

Bioavailability +

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

Bioavailability

Recommended administration considerations for your patients with paroxysmal or persistent AFib who are taking MULTAQ[1]

Taking MULTAQ with a full, high-fat meal increases the absolute bioavailability by as much as 4x[1]

Patients should avoid grapefruit juice while taking MULTAQ, as grapefruit juice significantly increases exposure to MULTAQ[1]

MULTAQ® has a well-established safety profile[1]

Studied across 5 clinical trials in more than 6000 patients with paroxysmal or persistent AFib[1]

ADVERSE REACTIONS (AR): POOLED DATA | ADVERSE REACTIONS: EURIDIS/ADONIS | ADVERSE REACTIONS: ATHENA

Adverse drug reactions that occurred in at least 1% of patients and were more frequent than placebo in 5 placebo-controlled trials (pooled data)[1]

	Placebo (n=2875)	MULTAQ (n=3282)
Gastrointestinal disorders		
Diarrhea	6%	9%
Nausea	3%	5%
Abdominal Pain	3%	4%
Vomiting	1%	2%
Dyspeptic signs and symptoms	1%	2%
General disorders		

Discontinuation rates were generally similar between MULTAQ and placebo[1]

(11.8% and 7.7%, respectively). The most common reasons for discontinuation were GI disorders (3.2%) and QT prolongation (1.5%).[1]

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® has a well-established safety profile[1]

Studied across 5 clinical trials in more than 6000 patients with paroxysmal or persistent AFib[1]

ADVERSE REACTIONS (AR): POOLED DATA | ADVERSE REACTIONS: EURIDIS/ADONIS | ADVERSE REACTIONS: ATHENA

Adverse drug reactions that occurred in at least 1% of patients and were more frequent than placebo in 5 placebo-controlled trials (pooled data)[1]

	Placebo (n=2875)	MULTAQ (n=3282)
Gastrointestinal disorders		
Diarrhea	6%	9%
Nausea	3%	5%
Abdominal Pain	3%	4%
Vomiting	1%	2%
Dyspeptic signs and symptoms	1%	2%
General disorders		
Asthenic conditions	5%	7%
Cardiac disorders		
Bradycardia	1%	3%
Skin and subcutaneous-tissue disorders		
Including rashes (generalized, macular, maculopapular, erythematous), pruritus, eczema, dermatitis allergic	3%	5%

Discontinuation rates were generally similar between MULTAQ and placebo[1]

(11.8% and 7.7%, respectively). The most common reasons for discontinuation were GI disorders (3.2%) and QT prolongation (1.5%).[1]

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® has a well-established safety profile[1]

Studied across 5 clinical trials in more than 6000 patients with paroxysmal or persistent AFib[1]

ADVERSE REACTIONS (AR): POOLED DATA | **ADVERSE REACTIONS: EURIDIS/ADONIS** | ADVERSE REACTIONS: ATHENA

Selected ARs and laboratory abnormalities from the EURIDIS/ADONIS trials[6]

Event	Placebo (n=409)	MULTAQ (n=828)	*P*-Value
Death n (%)			
Any cause	3 (0.7)	8 (1.0)	1.00
Sudden death	1 (0.2)	4 (0.5)	1.00
Stroke n (%)			
	3 (0.7)	4 (0.5)	0.69
Pulmonary event n (%)			
Cough	7 (1.7)	19 (2.3)	0.67

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® has a well-established safety profile[1]

Studied across 5 clinical trials in more than 6000 patients with paroxysmal or persistent AFib[1]

ADVERSE REACTIONS (AR): POOLED DATA | **ADVERSE REACTIONS: EURIDIS/ADONIS** | ADVERSE REACTIONS: ATHENA

Selected ARs and laboratory abnormalities from the EURIDIS/ADONIS trials[6]

Event	Placebo (n=409)	MULTAQ (n=828)	*P*-Value
Death n (%)			
Any cause	3 (0.7)	8 (1.0)	1.00
Sudden death	1 (0.2)	4 (0.5)	1.00
Stroke n (%)			
	3 (0.7)	4 (0.5)	0.69
Pulmonary event n (%)			
Cough	7 (1.7)	19 (2.3)	0.67
Dyspnea	15 (3.7)	27 (3.3)	0.74
Endocrine event n (%)			
Hyperthyroidism	56/396 (14.1)	67/801 (8.4)	0.002
Hypothyroidism	14/396 (3.5)	44/801 (5.5)	0.15
Cardiac event n (%)			
Bradycardia or conduction block			
Any event	8 (2.0)	22 (2.7)	0.56
Serious event	3 (0.7)	8 (1.0)	1.00
Heart failure or shock			
Any event	4 (1.0)	20 (2.4)	0.12
Serious event	3 (0.7)	13 (1.6)	0.29
Ventricular arrhythmia	2 (0.5)	6 (0.7)	1.00
Neurological event n (%)			
Insomnia or other sleep disorder	6 (1.5)	12 (1.4)	1.00
Memory impairment	0	1 (0.1)	1.00
Peripheral neuropathy	1 (0.2)	0	0.33
Paresthesia	4 (1.0)	11 (1.3)	0.78
Tremor	2 (0.5)	6 (0.7)	1.00
Gastrointestinal or hepatic event			
Diarrhea n (%)	20 (4.9)	59 (7.1)	0.14
Nausea n (%)	14 (3.4)	36 (4.3)	0.54
Abnormality of liver function n/total n (%)	55/405 (13.6)	100/822 (12.2)	0.52
Dermatologic event n (%)			
Photosensitivity or skin discoloration	1 (0.2)	6 (0.7)	0.44
Other			
Elevation of serum creatinine n (%)	1 (0.2)	20 (2.4)	0.004

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® has a well-established safety profile[1]

Studied across 5 clinical trials in more than 6000 patients with paroxysmal or persistent AFib[1]

ADVERSE REACTIONS (AR): POOLED DATA | ADVERSE REACTIONS: EURIDIS/ADONIS | **ADVERSE REACTIONS: ATHENA**

Selected ARs and laboratory abnormalities from the ATHENA trial[4]

Event	Placebo (n=2313)	MULTAQ (n=2291)	*P*-Value
Any TEAE n (%)	1603 (69.3)	1649 (72.0)	0.048
Cardiac Events			
Any	221 (9.6)	260 (11.3)	1.00
Bradycardia	28 (1.2)	81 (3.5)	0.69
QT-Interval Prolongation	14 (0.6)	40 (1.7)	<0.001
Respiratory Events	337 (14.6)	332 (14.5)	0.97
Cough	83 (3.6)	83 (3.6)	1.00

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® has a well-established safety profile[1]

Studied across 5 clinical trials in more than 6000 patients with paroxysmal or persistent AFib[1]

ADVERSE REACTIONS (AR): POOLED DATA | ADVERSE REACTIONS: EURIDIS/ADONIS | **ADVERSE REACTIONS: ATHENA**

Selected ARs and laboratory abnormalities from the ATHENA trial[4]

Event	Placebo (n=2313)	MULTAQ (n=2291)	*P*-Value
Any TEAE n (%)	1603 (69.3)	1649 (72.0)	0.048
Cardiac Events			
Any	221 (9.6)	260 (11.3)	1.00
Bradycardia	28 (1.2)	81 (3.5)	0.69
QT-Interval Prolongation	14 (0.6)	40 (1.7)	<0.001
Respiratory Events	337 (14.6)	332 (14.5)	0.97
Cough	83 (3.6)	83 (3.6)	1.00
Dyspnea	97 (4.2)	120 (5.2)	0.10
Interstitial lung disease	5 (0.2)	5 (0.2)	1.00
Gastrointestinal Events	508 (22.0)	600 (26.2)	<0.001
Diarrhea	144 (6.2)	223 (9.7)	<0.001
Nausea	72 (3.1)	122 (5.3)	<0.001
Abnormal liver-function test	14 (0.6)	12 (0.5)	0.84
Endocrine Events	25 (1.1)	25 (1.1)	1.00
Hyperthyroidism	6 (0.3)	11 (0.5)	0.23
Hypothyroidism	7 (0.3)	6 (0.3)	1.00
Neurologic Events	381 (16.5)	373 (16.3)	0.87
Dizziness	152 (6.6)	169 (7.4)	0.30
Headache	87 (3.8)	70 (3.1)	0.19
Skin-related Events	176 (7.6)	237 (10.3)	0.001
Rash	47 (2.0)	77 (3.4)	0.006
Urticaria	9 (0.4)	11 (0.5)	0.66
Serum Creatinine Increase	31 (1.3)	108 (4.7)	<0.001
Any serious TEAE n (%)	489 (21.1)	456 (19.9)	0.31
Cardiac Events	15 (0.6)	15 (0.7)	1.00
Respiratory Events	45 (1.9)	41 (1.8)	0.74
Gastrointestinal Events	68 (2.9)	81 (3.5)	0.28
Endocrine Events	5 (0.2)	4 (0.2)	1.00
Neurologic Events	27 (1.2)	21 (0.9)	0.47
Skin-related Events	6 (0.3)	7 (0.3)	0.79
Increase in Serum Creatinine	1 (<0.1)	5 (0.2)	0.12
Premature discontinuation of study drug because of an adverse event n (%)	187 (8.1)	290 (12.7)	<0.001

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® offers comprehensive patient support

We're dedicated to helping your patients access their prescriptions

Broad formulary access

[**91%**] **of patients** with Medicare and standard commercial coverage have access to MULTAQ.*

Commercially insured

With the MULTAQ Savings Card, your patients may be eligible to **pay as low as $0 copay** on each of their next 13 MULTAQ fills with no income restrictions. Maximum benefits apply. Terms and conditions apply.†

Patient Access Programs

Start your patients on MULTAQ today with our **Sample Program**. Additionally, Sanofi Patient Connection® provides assistance programs that may help qualified low-income patients and eligible Medicare patients access MULTAQ. Visit **sanofipatientconnection.com** to learn more.

For information on available resources, please visit [MULTAQ.com/HCP]

*Powered by Managed Markets Insight & Technology, LLC. Database current as of [Jun, 2022].

†Offer only available to eligible patients with commercial insurance not funded through a government healthcare program or to patients paying cash. This offer is not valid for prescriptions covered by or submitted for reimbursement under Medicaid, Medicare, VA, DOD, TRICARE, or similar federal or state programs, including any state pharmaceutical assistance programs. Subject to an annual cap of $3,000 for commercially insured patients and an annual cap of $1,950 for patients paying cash. Any savings provided by the savings card may vary depending on patients' out-of-pocket costs. Sanofi U.S. reserves the right to rescind, revoke, or amend this offer without notice. Void where prohibited by law. Upon registration, patients receive all program details.

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

IN THE TREATMENT OF PAROXYSMAL OR PERSISTENT AFib

MULTAQ HELPS KEEP PATIENTS IN SINUS RHYTHM & OUT OF THE HOSPITAL

Studied across 5 clinical trials with more than 6000 patients

Significantly reduced the risk of first AFib recurrence at Year 1[1,6]

25% RRR

P<0.001

Significantly reduced the risk of CV hospitalization or all-cause mortality[1,*]
(primary composite endpoint)

24% RRR

P<0.001

*Entirely attributable to reduction in CV hospitalization.

MULTAQ was evaluated in a wide range of patients with AFib[1]

Including patients with CAD and HFpEF and those with or without structural heart disease.[4,5]

MULTAQ has broad formulary access

91% of patients with Medicare and standard commercial coverage have access to MULTAQ.†

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, symptomatic heart failure with recent decompensation requiring hospitalization, or permanent AFib.[1]

†Powered by Managed Markets Insight & Technology, LLC. Database current as of [Jun, 2022].

Please see Important Safety Information, below, and full Prescribing Information page, including **boxed WARNING.**

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ® (dronedarone) 400mg Tablets

IN THE TREATMENT OF PAROXYSMAL OR PERSISTENT AFib

MULTAQ HELPS KEEP PATIENTS IN SINUS RHYTHM & OUT OF THE HOSPITAL

Studied across 5 clinical trials with more than 6000 patients

Significantly reduced the risk of first AFib recurrence at Year 1[1,6]

25% RRR

P<0.001

Significantly reduced the risk of CV hospitalization or all-cause mortality[1,*]

(primary composite endpoint)

24% RRR

P<0.001

*Entirely attributable to reduction in CV hospitalization.

MULTAQ was evaluated in a wide range of patients with AFib[1]

Including patients with CAD and HFpEF and those with or without structural heart disease.[4,5]

MULTAQ has broad formulary access

91% of patients with Medicare and standard commercial coverage have access to MULTAQ.†

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, symptomatic heart failure with recent decompensation requiring hospitalization, or permanent AFib.[1]

†Powered by Managed Markets Insight & Technology, LLC. Database current as of [Jun, 2022].

Please see Important Safety Information, below, and full Prescribing Information page, including **boxed WARNING.**

Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information +

WARNING: INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

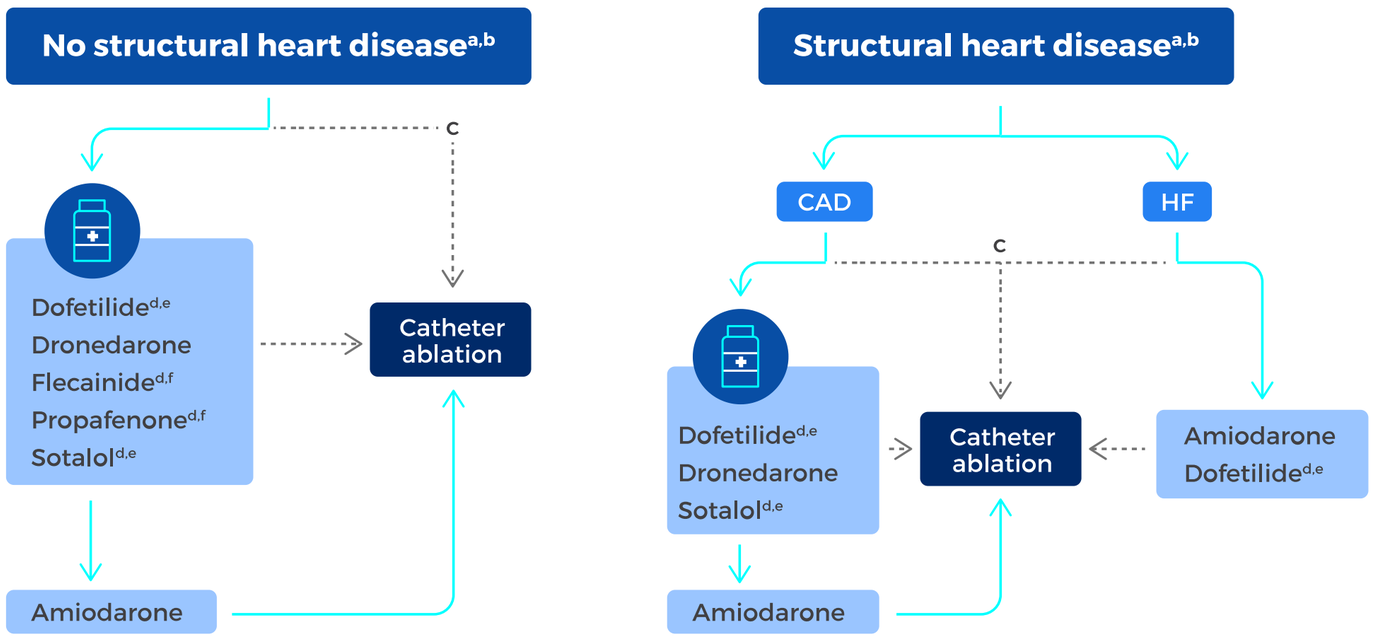
MULTAQ® is a recommended 1st-line treatment option for sinus rhythm maintenance[3]

AHA/ACC/HRS | ESC

From the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation: Executive Summary[2]

- When a rhythm-control strategy is desired, AAD therapy may be selected based on patient characteristics[2]
- Risks of AAD therapy should be considered before initiating therapy[2]
- Strategies for drug and procedure selection can be guided by the presence or absence of structural heart disease
- MULTAQ is recommended for patients with AFib to maintain sinus rhythm, depending on underlying heart disease and comorbidities (Class 1A)[2]
  - Before initiating AAD therapy, treatment of precipitating or reversible causes of AFib is recommended

Recommended strategies for rhythm control in patients with paroxysmal and persistent AF[2]:



Graphic created by Sanofi and adapted from guidelines. The above are excerpts only.

[a]Catheter ablation is only recommended as first-line therapy for patients with paroxysmal AF (class IIa recommendation).
[b]Drugs are listed alphabetically.
[c]Depending on patient preference when performed in experienced centers.
[d]Not recommended with severe LVH (wall thickness >1.5 cm).
[e]Should be used with caution in patients at risk for torsades de pointes ventricular tachycardia.
[f]Should be combined with atrioventricular nodal-blocking agents.

MULTAQ® is a recommended 1st-line treatment option for sinus rhythm maintenance[3]

AHA/ACC/HRS | **ESC**

From the 2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed in Collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)[3]

- Strategies for drug and procedure selection can be based on the underlying disease*:

Recommended strategies for long-term rhythm control therapy:

The above are excerpts only.

Glossary

RRR (relative risk reduction) is a proportional measure of how much the treatment reduced the risk of bad outcomes relative to the control group who did not receive treatment.

- RRR < 1 (or <100%) means the treatment reduced the risk of a bad outcome

AAR (absolute risk reduction) is the absolute difference of risk in the control arm vs the treatment arm.

- ARR= event rate in the control arm – event rate in the treatment arm

NNT (number needed to treat) is the number of patients that need to be treated to prevent 1 additional bad outcome.

- NNT = 1/ARR

AAD=antiarrhythmic drug

ACC=American College of Cardiology

ACE=angiotensin-converting enzyme

ADONIS=American–Australian–African Trial With Dronedarone in Patients With Atrial Fibrillation or Atrial Flutter Patients for the Maintenance of Sinus Rhythm

AE=adverse event

AFib=atrial fibrillation

AFL=atrial flutter

ARB=angiotensin receptor blocker

ARR=absolute risk reduction

ATHENA=A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg bid for the Prevention of Cardiovascular Hospitalization or Death from any Cause in Patients with Atrial Fibrillation/Atrial Flutter

CAD=coronary artery disease

CHF=congestive heart failure

CI=confidence interval

CV=cardiovascular

ECG=electrocardiogram

ESC=European Society of Cardiology

EURIDIS=European Trial in Atrial Fibrillation or Flutter Patients Receiving Dronedarone for the Maintenance of Sinus Rhythm

GI=gastrointestinal

HF=heart failure

HFmrEF=heart failure with mildly reduced ejection fraction

HFpEF=heart failure with preserved ejection fraction

HR=hazard ratio

HRS=Heart Rhythm Society

INR=international normalized ratio

LVEF=left ventricular ejection fraction

NNT=number needed to treat

NYHA=New York Heart Association

RRR=relative risk reduction

SD=standard deviation

TEAE=treatment-emergent adverse event

References

1. MULTAQ [package insert]. Bridgewater, NJ. sanofi-aventis U.S. LLC; 2017. USPI - NOV-2020 (v2.0).
2. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. *J Am Coll Cardiol*. 2014;64(21):e1-e76.
3. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2020;42(5):373-498.
4. Hohnloser SH, Crijns HJ, van Eickels M, et al. Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med*. 2009;360(7):668-678.
5. Vaduganathan M, Piccini J, Camm AJ, et al. Dronedarone for the treatment of atrial fibrillation with concomitant heart failure with preserved and mildly reduced ejection fraction: post-hoc analysis of the ATHENA Trial. *Eur J Heart Fail*. 2022 Mar 15. doi: 10.1002/ejhf.2487.
6. Singh BN, Connolly SJ, Crijns HJ, et al. Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. N *Engl J Med*. 2007;357(10):987-999.
7. Thind M, Crijns HJ, Naccarelli GV, et al. Dronedarone treatment following cardioversion in patients with atrial fibrillation/flutter: a post hoc analysis of the EURIDIS and ADONIS trials. *J Cardiovasc Electrophysiol*. 2020;31(5):1022-1030.
8. Vamos M, Calking H, Kowey PR, et al. P1034 Impact of ablation status on the efficacy and safety of dronedarone in patients with atrial fibrillation/flutter: a post hoc analysis of the ATHENA trial. Poster presentation at: European Society of Cardiology Congress 2019; August 31–September 4, 2019; Paris, France.
9. Pisters R, Hohnloser S, Connolly SJ, et al. Effect of dronedarone on clinical end points in patients with atrial fibrillation and coronary heart disease: insights from the ATHENA trial. *Eurospace*. 2014;16(2):174-181.
10. Chamberlain AM, Alonso A, Gersh BJ, et al. Multimorbidity and the risk of hospitalization and death in atrial fibrillation: a population-based study. *Am Heart J*. 2017;185:74-84.
11. Cheng M, Lu X, Huang J, et al. The prognostic significance of atrial fibrillation in heart failure with a preserved and reduced left ventricular function: insights from a meta-analysis. *Eur J Heart Fail*. 2014;16(12):1317-1322.

sanofi

MAT-US-2204576-v1.0-06/2022

June 2022