
PUBLIC SUMMARY OF RISK MANAGEMENT PLAN
FLECAINIDE ORION 100 MG AND 200 MG PROLONGED-RELEASE CAPSULES, HARD
ORION CORPORATION
DATE: 02-07-2013, VERSION 1

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Electrical impulses mediated through specialized conducting system in the heart regulate synchronized contraction of the heart muscle. In cardiac arrhythmia, the function of this conduction system becomes disturbed leading to abnormal contraction of the heart and abnormalities in the heart rate. Heart rate may be too fast (so called tachycardia) or too slow (so called bradycardia) or the heartbeat may become irregular. Arrhythmia can originate primarily from the upper chambers of the heart, called atria, or from the lower chambers of the heart, called ventricles.

Fast cardiac arrhythmias originating from the atria are called supraventricular tachycardias. They are often characterized with episodes of fast heartbeat. Atrial fibrillation is the most common cardiac arrhythmia causing fast and irregular heartbeat. Approximately 1.5-2% of the general population in the developed countries experience atrial fibrillation, and the average age of patients with this condition is between 75 and 85 years.

Approximately 0.6-0.8% of adult population experiences other supraventricular arrhythmias. Supraventricular arrhythmias include several different type of conditions including tachycardias caused by re-entry of cardiac electrical impulses in accessory conducting pathways between atria and ventricles (e.g. Wolff-Parkinson-White syndrome) leading to episodes of rapid heartbeat.

Fast cardiac arrhythmias originating from the ventricles are called ventricular tachycardias. Ventricular tachycardia can also be seen in healthy heart, but it is often associated with other cardiac diseases or genetic predisposition.

VI.2.2 Summary of treatment benefits

Flecainide slows down conduction of cardiac electrical impulses both in atria and ventricles. It also has effects on cardiac impulse conduction in accessory conducting pathways e.g. in Wolff-Parkinson-White syndrome.

Atrial fibrillation is associated with a five-fold risk of stroke and a three-fold risk of heart failure, and higher mortality. Flecainide can be considered for the treatment of recurrent atrial fibrillation. Several studies have confirmed antiarrhythmic effect of flecainide in the prevention of recurrence episodes in drug resistant atrial fibrillation.

Supraventricular tachycardias are usually not life-threatening arrhythmias, but they cause frequent tachycardic episodes with need for emergency room visits. The efficacy of flecainide in the treatment of patients with supraventricular tachycardias caused by re-entry of cardiac electrical impulses in accessory conducting pathways (e.g. Wolff-Parkinson-White syndrome) has been shown in clinical studies.

Ventricular tachycardias include various clinical conditions varying from additional ventricular beats and short ventricular tachycardia episodes in normal subjects to sudden cardiac death due to ventricular tachycardia in heart diseases. Flecainide may be effective as adjunctive therapy in the management of arrhythmia-sensitive patients under special circumstances.

VI.2.3 Unknowns relating to treatment benefits

Currently, there are no data on the use of flecainide in paediatric patients.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
<p>Proarrhythmia During the treatment with antiarrhythmic drugs provocation or exacerbation of an arrhythmia that is different or more severe than the baseline arrhythmia is called proarrhythmia. Proarrhythmic adverse effects may occur with all antiarrhythmic drugs in use.</p>	<p>Flecainide most likely cause ventricular proarrhythmia in patients with structural heart disease, cardiac insufficiency, ventricular scar tissue (e.g. after myocardial infarction), electrolyte disturbances or inherited syndrome predisposing to ventricular arrhythmias and sudden death, called Brugada syndrome.</p>	<p>Flecainide Orion is contraindicated in patients with cardiogenic shock, heart failure, myocardial infarction with ventricular arrhythmias or Brugada syndrome. Flecainide Orion should be used in caution in patients with structural heart disease or abnormal function of the left ventricle. Electrolyte disorder (such as decreased or increased serum potassium concentrations) has to be corrected before use of Flecainide Orion.</p>
<p>Cardiac conduction disorders Impairment in electrical impulse conduction from the atria to the ventricles is called atrioventricular block. Atrioventricular block may vary in severity from slowed conduction to complete block. Impaired impulse conduction inside the ventricles may also occur.</p>	<p>Flecainide slows down conduction of the electrical impulses in the heart. This may lead to blockade of the impulse conduction from the atria to the ventricles or inside the ventricles. Slow heart beat is a typical symptom of cardiac conduction disorders.</p>	<p>In case of cardiac conduction disorders Flecainide Orion should be discontinued unless a ventricular pacemaker is in place. Flecainide should not be used in patients with pre-existing cardiac conduction abnormalities, such as sick sinus syndrome or atrioventricular block.</p>
<p>Increase in endocardial pacing threshold Endocardial pacing threshold refers to the sensitivity of cardiac cells to react on electrical impulses given by a pacemaker.</p>	<p>Flecainide is known to increase endocardial pacing thresholds, i.e. to decrease endocardial pacing sensitivity.</p>	<p>Flecainide Orion should be used with caution in all patients with permanent or temporary pacemakers.</p>
<p>Use in patients with impaired function of the liver</p>	<p>Because flecainide is extensively metabolized in liver, its elimination can be markedly slower in patients with severely impaired liver function.</p>	<p>Flecainide Orion should not be used in patients with severely impaired liver function unless the potential benefits clearly outweigh the risks. Frequent monitoring of flecainide plasma</p>

Risk	What is known	Preventability
		levels is required in these patients.
Use in patients with impaired function of the kidney	Flecainide is excreted mostly in urine and accumulates in patients with impaired function of the kidney.	Lower starting and maintenance dosages are used in patients with impaired function of the kidney. Frequent monitoring of flecainide plasma levels are recommended in these patients.
Interactions with other drugs	Flecainide has interactions with several other drugs. These include e.g. possible interactions with other anti-arrhythmic drugs where additive impulse conduction slowing effects may occur or interactions with drugs interfering with the metabolism of flecainide.	All medications, the patient is using have to be in attention of the treating physician. These include both prescription and non-prescription medicines or other supplemental products used.

Important potential risks

Risk	What is known
Use in elderly patients	Flecainide elimination from plasma may be reduced in elderly people. This should be taken into account when considering treatment of elderly patients.

Important missing information

Risk	What is known
Use in children	The safety and efficacy of flecainide has not been studied in paediatric patients under age of 12 years. Thus, the use of Flecainide Orion in children under age of 12 is not recommended.
Use during pregnancy	There is no clinical safety data on flecainide in human pregnancy. In New Zealand White rabbits high doses of flecainide caused some foetal abnormalities, but these effects were not seen in other rabbit strain or rats. The relevance of these animal findings to humans has not been established. Data have shown that flecainide crosses the placenta into the foetus. Flecainide Orion is not recommended for use during pregnancy unless the benefits are considered to clearly outweigh the possible risks to the foetus.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Flecainide Orion can be found on the website of Fimea www.fimea.fi.

This medicine has no additional risk minimisation measures.

VI.2.6 *Planned post authorisation development plan*

Not applicable.

VI.2.7 *Summary of changes to the Risk Management Plan over time*

Not applicable.