

**Pharmacovigilance Working Party Public Assessment Report on  
Neuroleptics and Cardiac safety, in particular QT prolongation, cardiac arrhythmias,  
ventricular tachycardia and torsades de pointes**

The drugs were differentiated into three categories depending on the degree of documentation supportive of the potential for cardiotoxicity:

**Insufficient:** no data or insufficient data to assess cardiac risk

**Intermediate:** Some documentation from at least one data source suggesting potential for cardiotoxic risk

**Good:** Evidence from one or more data sources of a clinically significant prolongation of the QT interval and/or of the occurrence of serious cardiac arrhythmias associated with treatment).

The PhVWP agreed on the classification of neuroleptics as shown in Table 1, and on the core SPC wording as outlined in Table 2.”

**Table 1** Classification of neuroleptic drugs by level of documentation supportive of cardiotoxic risk

<b>Insufficient</b>	<b>Intermediate</b>	<b>Good</b>
Loxapine	Amisulpride	Haloperidol
Oxypertine	Benperidol	Pimozide
Perphenazine	Chlorpromazine	Sertindole
Pipiothiazine	Clozapine	Ziprasidone
Prochlorperazine	Fluphenazine	
Promazine	Flupenthixol	
Remoxipiride	Levomepromazine	
	Olanzapine	
	Quetiapine	
	Sulpiride	
	Trifluoperazine	
	Zotepine	
	Zuclopenthoxol	

**Table 2** Key principles of SPC wording proposed by the PhVWP

<b>Level of Risk</b>	<b>Insufficient / intermediate</b>	<b>Good</b>
Section 4.3		<ul style="list-style-type: none"> <li>• Clinically significant cardiac disorders (eg recent acute myocardial infarction, uncompensated heart failure, arrhythmias treated with class IA and III antiarrhythmic medicinal products)</li> <li>• QTc interval prolongation</li> <li>• History of ventricular arrhythmia or torsades de pointes</li> <li>• Uncorrected hypokalaemia</li> <li>• Other QT prolonging drugs</li> </ul>

Section 4.4	<ul style="list-style-type: none"> <li>• Caution in patients with cardiovascular disease or family history of QT prolongation</li> <li>• Avoid concomitant neuroleptics</li> </ul>	<ul style="list-style-type: none"> <li>• Caution in patients with cardiovascular disease or family history of QT prolongation</li> <li>• Baseline ECG prior to treatment (see section 4.3)</li> <li>• During therapy, the need for ECG monitoring should be assessed on an individual patient basis</li> <li>• Whilst on therapy, reduce dose if QT is prolonged and discontinue if QTc is &gt;500ms</li> <li>• Periodic electrolyte monitoring recommended</li> <li>• Avoid concomitant neuroleptics</li> </ul>
Section 4.5	<ul style="list-style-type: none"> <li>• Concomitant QT prolonging drugs</li> <li>• Drugs causing electrolyte imbalance</li> <li>• Metabolic inhibitors (CYP....) where known</li> </ul>	<ul style="list-style-type: none"> <li>• Concomitant QT prolonging drugs **</li> <li>• Drugs causing electrolyte imbalance</li> <li>• Metabolic inhibitors (CYP....) where known</li> </ul>
Section 4.8*	<ul style="list-style-type: none"> <li>• QT prolongation</li> <li>• Ventricular arrhythmias - VF, VT (rare)</li> <li>• Sudden unexplained death</li> <li>• Cardiac arrest</li> <li>• Torsades de pointes</li> </ul>	<ul style="list-style-type: none"> <li>• QT prolongation</li> <li>• Ventricular arrhythmias - VF, VT (rare)</li> <li>• Sudden unexplained death</li> <li>• Cardiac arrest</li> <li>• Torsades de pointes</li> </ul>

\*For those products for which no data are available the wording in section 4.8 of the SPC should be accompanied by a statement that these adverse effects are class effects of neuroleptics.

\*\* A list of drugs should be included - eg Class IA and III antiarrhythmics, arsenic trioxide, halofantrine, levomethadyl acetate, mesoridazine, thioridazine, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, dolansetron mesylate, mefloquine, sertindole or cisapride. The list may have to be amended on a national basis depending on the marketing status of different products.