

Table of Contents

Tab 1: Overview Memo

Bob Rappaport, MD; Director, Division of Anesthetic, Critical Care, and Addiction Drug Products

Tab 2: WHO Pharmaceuticals Newsletter; Nos. 7 & 8, July and August 1997;
relevant section only: Droperidol-revised data sheet: cardiac arrhythmias

Tab 3: 2001 MCA Statement: Important safety message:
Discontinuation of Droleptan tablets, suspension and injection (droperidol)

Tab 4: FDA Talk Paper; December 5, 2001:
FDA Strengthens Warning for Droperidol

Tab 5: Dear Healthcare Provider Letter; December 4, 2001:
Important Drug Warning

Tab 6: Droperidol Package Insert Prior to December, 2001

Tab 7: Droperidol Package Insert after December, 2001

Tab 8: American Society for Anesthesiologists (ASA) Newsletter:
FDA Alert: Current FDA Report on Droperidol Status and Basis for 'Black Box' Warning

Tab 9: ASA Update:
Update on Droperidol and the FDA

Tab 10: Meyer B. FDA "Black Box" Labeling. Ann Emerg Med. 2003 Apr; 41(4):559-60

Tab 11: Labeling Regulations 21 CFR § 201.57 (d & e)
Contraindications, Warnings

Tab 12: Committee for Proprietary Medicinal Products (CPMP) Points to Consider:
The Assessment of the Potential for QT Interval Prolongation by Non-Cardiovascular Medicinal Products

Tab 13: FDA Preliminary Concept Paper:
The Clinical Evaluation of QT/QTC Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs

Tab 14: ICH S7B: Draft Consensus Guideline:

“Safety Pharmacology Studies for Assessing the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals”

Tab 15: Literature

- Lischke V, et al. Droperidol causes a dose-dependent prolongation of the QT interval. Anesth Analg. 1994; 79:983-986
- Guy JM, et al. Torsades de pointes et allongement de la duree de l'intervalle QT apres injection de droperidol. An de Cardiologie et d'Angeiologie. 1991; 40:541-545
- Reilly et al. QTc-interval abnormalities and psychotropic drug therapy in psychiatric patients. Lancet 2000; 355:1048--52
- Lawrence & Nasraway, Pharmacotherapy 1997; 17(3): 531-7
- Frye et al. Continuous droperidol infusion for management of agitated delirium in an intensive care unit. Psychosomatics 1995; 36:301-5
- Drolet B et al. Droperidol lengthens cardiac repolarization due to block of the rapid component of the delayed rectifier potassium current. J Cardiovas Electrophys 1999; 10(12):1597--604
- Michalets et a. Torsade de pointes resulting from the addition of droperidol to an existing cytochrome P450 drug interaction. Ann Pharmacother 1998; 32(7-8):761-5
- Faigel et al. Torsade de pointes complicating the treatment of bleeding esophageal varices: association with neuroleptics, vasopressin, and electrolyte imbalance. Am J Gastroenterol 1995; 90(5):822-4
- Roden D. Acquired long QT syndromes and the risk of proarrhythmia. J Cardiovasc Electrophys 2000; 11:938-40
- Fenichel RR. Development of drugs that alter ventricular repolarization. Am J Ther 2002; 9(2):127-39
- Malik M and Camm AJ. Evaluation of drug-induced QT interval prolongation. Drug Safety 2001; 24(5):323-351
- Curran ME et al. Molecular mechanism of a serious adverse drug reaction: drug induced cardiac arrhythmias. Pharm Disc Development, 2002/03
- Keating MT and Sanguinetti MC. Molecular and cellular mechanisms of cardiac arrhythmias. Cell 2001; 104:569-80