

e-Appendix 1: Products withdrawn from the Canadian market because of safety concerns between 1963 and 2004

Drug	Class/indication	Reason for withdrawal*	Date of Notice of Compliance/ year first listed in <i>CPS</i>	Date withdrawn/ year last listed in <i>CPS</i>	Source of information about withdrawal	Listed in Drug Product Database† as discontinued
Aminopyrine	Analgesic	Bone marrow suppression, agranulocytosis	1960	1963	Withdrawn from US and/or UK markets	No
Astemizole	Antihistamine	Cardiac arrhythmias	1985	Sept. 1999	Health Canada	Yes
Benoxaprofen‡	Analgesic, anti-inflammatory	Hepatotoxicity	Feb. 1982		Withdrawn from US and/or UK markets	No
Bithionol§	Antipruritic/antiseptic	Photosensitivity	1960	Apr. 4, 1968	Health Canada	No
Bunamiodyl	Cholecystographic medium for cholecystography	Nephropathy	1963	1963	Withdrawn from US and/or UK markets	No
Cerivastatin	Cholesterol lowering	Rhabdomyolysis	Feb. 18, 1998	Aug. 8, 2001	Rawson and Kaitin ⁷	Yes
Chlormezanone	Muscle relaxant, tranquilizer, anxiolytic	Severe cutaneous reactions (e.g., toxic epidermal necrolysis)	1960	1991	Withdrawn from US and/or UK markets	No
Cisapride	Gastrointestinal dysmotility	Cardiac arrhythmias, sudden cardiac deaths	Aug. 15, 1991	Aug. 7, 2000	Rawson and Kaitin ⁷	Yes
Clioquinol	Antidiarrheal	Neurotoxicity	1960	1983	Withdrawn from US and/or UK markets; confirmed by company	No (topical creams, ointments, vaginal tablets listed as discontinued)
Danthron	Laxative	Genotoxicity	1963	1998	Withdrawn from US and/or UK markets	Yes
Dexfenfluramine	Appetite suppressant	Cardiac valve disease	July 1996	Sept. 15, 1997	Health Canada	No
Dipyrrone	Analgesic	Agranulocytosis	1960	1963	Withdrawn from US and/or UK markets	No for human use (veterinary injectable listed as discontinued)
Etretinate	Keratinization disorder therapy	Teratogenicity	1985	1995	Withdrawn from US and/or UK markets	No
Fenfluramine	Appetite suppressant	Cardiac valve disease	Oct. 22, 1970	Sept. 15, 1997	Health Canada	Yes
Grepafloxacin	Antibiotic	Cardiac arrhythmias	Apr. 9, 1998	Oct. 26, 1999	Rawson and Kaitin ⁷	Yes
Iproniazid	Antidepressant	Interactions with food products containing tyrosine	1960	July 1964	Health Canada	No
Methapyrilene	Antihistamine	Carcinogenicity (in rats)	1960	July 11, 1979	Health Canada	No (veterinary ear liquid listed as discontinued)
Nefazodone	Antidepressant	Hepatotoxicity	1994	Nov. 27, 2003	Health Canada	Yes
Neomycin (injectable)	Antimicrobial	Nephropathy, neurotoxicity (nerve deafness)	1967	1989	Withdrawn from US and/or UK markets; not confirmed by company	No
Nialamide	Antidepressant	Interactions with food products containing tyrosine	1960	1963	Withdrawn from US and/or UK markets	No

Nomifensine	Antidepressant	Hemolytic anemia	May 1983	Jan. 20, 1986	Withdrawn from US and/or UK markets; confirmed by company	No
Oxeladin	Antitussive	Carcinogenicity	1967	1976	Withdrawn from US and/or UK markets	No
Oxyphenbutazone	Anti-inflammatory	Bone marrow suppression	1961	Mar. 29, 1985	Material from company	No
Oxyphenisatin	Laxative	Hepatotoxicity	1967	July 1, 1978	Health Canada	No
Pemoline	Central nervous system stimulant	Hepatotoxicity	Mar. 3, 1977	Sept. 30, 1999	Health Canada	No (ointment listed as discontinued)
Phenacetin	Analgesic	Nephropathy	1960	June 1973	In UN Consolidated List	No
Phenformin	Oral hypoglycemic	Lactic acidosis	1960	1977	In UN Consolidated List	No
Phenolphthalein	Laxative	Carcinogenicity	1967	Sept. 30, 1997	In UN Consolidated List	Yes
Phenylpropanolamine	Decongestant	Hemorrhagic stroke	1960	May 30, 2001	Health Canada	Yes
Potassium chloride (enteric coated)	Potassium replacement	Small-bowel ulceration	1960	1963	Withdrawn from US and/or UK markets	No
Prenylamine	Antianginal	Cardiac arrhythmias	July 1965	Oct 1988	Withdrawn from US and/or UK markets	No
Remoxipride	Antipsychotic	Aplastic anemia	July 26, 1993	Mar. 14, 1994	Rawson and Kaitin ⁷	No
Sulfamethoxy-pyridazine	Antimicrobial	Bone marrow suppression, severe cutaneous reactions, nephrotoxicity	1960	1978	Withdrawn from US and/or UK markets	No
Terfenadine	Antihistamine	Cardiac arrhythmias	May 1983	June 1, 1998	Health Canada	Yes
Thenalidine	Allergic and pruritic conditions	Neutropenia	1960	1963	Withdrawn from US and/or UK markets; company unable to find any information about reason for withdrawal from Canada	No
Tolcapone	Parkinson's disease	Hepatotoxicity	Late 1997	Nov. 20, 1998	Health Canada	Yes
Tranlycypromine and trifluoroperazine¶	Depression	Combination used in some situations that were not of sufficient gravity to justify the risk	1960	July 24, 1964	Health Canada	No
Troglitazone**	Oral hypoglycemic	Hepatotoxicity	May 9, 1997		Rawson and Kaitin ⁷	No
Trovafloxacin	Antibiotic	Hepatotoxicity	Dec. 4, 1998	Nov. 22, 2001	Rawson and Kaitin ⁷	Yes
Urethane	Leukemia	Carcinogenicity, mutagenicity	1960	1963	Withdrawn from US and/or UK markets	No
Zomepirac	Analgesic	Anaphylaxis	1981	1983	Withdrawn from US and/or UK markets	No

Note: CPS = Compendium of Pharmaceuticals and Specialties.

*Information is from Health Canada where available. Otherwise it is from the United States, the United Kingdom or the following United Nations publication: Department of Economic and Social Affairs. Consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by government. Eighth issue: Pharmaceuticals. New York: United Nations; 2003.¹²

†Maintained by Health Canada on its Web site (www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_drugs_dpd_e.html).

‡Never marketed due to recognition of adverse drug reactions in the United Kingdom and the United States.

§Combination product (Actamer) withdrawn because of this component.

¶Combination withdrawn. Individual drugs remained on the market.

**Never sold because of a dispute between the company and the Patented Medicine Prices Review Board about the introductory price.