

Web Only Appendix: Drugs With Serious Safety Warnings and/or Withdrawn From the Market

Generic name	Brand name	Date of receipt of Notice Of Compliance	Date of first safety warning	Reason for warning	Date of withdrawal from the market	Reason for withdrawal
Abacavir	Ziagen	June 4, 1999	June 18, 2008	Risk of cardiac events		
Adalimumab	Humira	September 24, 2004	Feb. 2, 2005	Increased risk of hematologic events & increased risk infections when used with anakinra		
Alemtuzumab	Mabcampath	November 30, 2005	November 18, 2008	Infection related deaths		
Anakinra	Kineret	May 24, 2002	December 17, 2002	Higher incidence of serious infections when taken with etanercept		
Atomoxetine	Strattera	December 24, 2004	May 1, 2006	Cardiac related adverse events		
Belimumab	Benlysta	July 6, 2011	May 3, 2012	Severe and possibly fatal infusion and hypersensitivity reactions		

Bevacizumab	Avastin	September 9, 2005	October 24, 2006	Hypertensive encephalopathy & reversible posterior leukoencephalopathy syndrome		
Bupropion	Wellbutrin SR	April 28, 1998	July 3, 2001	Reduction in risk of seizures and drug interactions		
Ceftobiprole	Zeftera	June 26, 2008			April 16, 2010	Concerns re conduct trials
Celecoxib	Celebrex	April 14, 1999	May 13, 2002	Standard contraindications for NSAIDs added to Product Monograph		
Cerivastatin	Baycol	February 18, 1998	July 16, 2001	Rhabdomyolysis	August 8, 2001	Rhabdomyolysis
Citalopram	Celexa	February 5, 1999	May 26, 2004	Risk of self harm		
Clopidrogel	Plavix	Oct. 7, 1998	Aug. 14, 2009	Use with PPIs can decrease effectiveness of clopidrogel		

Dabigatran	Pradax	June 10, 2008	Mar. 16, 2012	Assess renal function before using & while using; don't use in patients with hemodynamically significant rheumatic valvular disease
Daclizumab	Zenaprax	January 4, 2000	November 6, 2003	Possible increase in mortality in cardiac transplant patients
Darbepoetin alpha	Aranesp	August 2, 2002	November 25, 2005	Antibody mediated pure red cell aplasia
Darunavir	Prezista	July 28, 2006	May 12, 2008	Hepatotoxicity
Dasatinib	Sprycell	March 26, 2007	August 26, 2011	Pulmonary artery hypertension
Deferasirox	Exjade	October 18, 2006	March 9, 2007	Acute renal failure & cytopenias
Denosumab	Prolia	Aug. 6, 2010	May 28, 2012	Risk of severe symptomatic hypocalcemia (warning issued for Xgeva)
Dexmethylphenidate	Attenade	August 12, 2003	May 1, 2006	Cardiac related adverse events

Dolastetron	Anzemet	May 21, 1997	June 23, 2006	Contraindicated in those under 18 for the prevention & treatment of post-operative nausea		
Doripenem	Doribax	Sept. 2, 2009	Jan. 26, 2012	Increased mortality compared to imipenem-cilastin		
Dronedarone	Multaq	August 11, 2009	March 10, 2011	Hepatocellular liver injury		
Drotrecogin Alfa	Xigris	January 31, 2003	January 31, 2005	Increased mortality in patients with single organ dysfunction & recent surgery	October 25, 2011	Failure to show benefit
Efalizumab	Raptiva	October 24, 2005	December 22, 2008	Progressive multifocal leukoencephalopathy	Feb. 22, 2009	Progressive multifocal leukoencephalopathy
Erlotinib	Tarceva	July 7, 2005	December 12, 2008	Increased risk of death in patients with moderate hepatic impairment & corneal perforation		
Etanercept	Enbrel	December 1, 2000	January 13, 2006	Risk of hepatitis B virus infection		

Etravirine	Intelence	March 27, 2008	October 15, 2009	Severe skin & hypersensitivity reactions		
Ezetimibe	Ezetrol	May 12, 2003	Feb. 1, 2005	Myalgia, rhabdomyolysis, hepatitis, pancreatitis & thrombocytopenia		
Formoterol	Foradil dry powder capsules	March 6, 1997	September 7, 2005	Increased risk of asthma-related deaths in patients who also used salmeterol		
Fosamprenavir	Telzir	December 10, 2004	July 17, 2009	Myocardial infarction		
Gadoversetamide	Optimark	December 11, 2000	January 8, 2010	Nephrogenic systemic fibrosis		
Galantamine	Reminyl	July 31, 2001	April 18, 2005	Increase in mortality in patients with mild cognitive impairment		
Gatifloxacin	Tequin	January 9, 2001	December 19, 2005	Serious hypoglycemia and hyperglycemia	June 29, 2006	Glucose metabolism disorders

Gefitinib	Iressa	December 17, 2003	August 26, 2005	Restricted use to patients whose tumours are EGFR expression status positive or unknown	
Grepafloxacin	Raxar	April 9, 1998			October 26, 1999
Ibritumomab	Zevalin	May 10, 2005	December 7, 2005	Severe mucocutaneous reactions	Cardiac arrhythmias
Imatinib	Gleevec	September 20, 2001	September 21, 2006	Significant decrease in left ventricular ejection failure and congestive heart failure	
Infliximab	Remicade	September 27, 2001	November 29, 2004	Risk of malignancies	
Infliximab	Remicade	June 6, 2001	November 29, 2004	Risk of malignancies	
Interferon Beta-1A	Rebif	February 5, 1998	December 4, 2003	Hepatotoxicity	
Irinotecan	Camptosar	July 4, 1997	May 11, 2001	Increased mortality in clinical trials	
Leflunomide	Arava	March 16, 2000	May 4, 2001	Hepatotoxicity	
Levofloxacin	Levaquin	Nov. 14, 1997	Mar. 9, 2012	Worsening of symptoms of myasthenia gravis	

Lumiracoxib	Prexige	November 2, 2006			October 3, 2007	Hepatotoxicity
Methylnatrexone	Relistor	March 28, 2008	July 28, 2010	Gastrointestinal perforation		
Mirtazapine	Remeron	May 18, 2001	May 26, 2004	Risk of self harm		
Modafinil	Alertec	February 26, 1999	December 18, 2007	Serious rash, allergic reactions & mental problems		
Moroctocog alpha	Refacto	May 28, 2002	September 15, 2003	Lack of effect		
Moxifloxacin	Avelox	Oct. 19, 2000	Mar. 9, 2012	Worsening of symptoms of myasthenia gravis		
Natalizumab	Tysabri	September 28, 2006	June 2, 2008	Liver injury & hypersensitivity		
Nevirapine	Viramune	September 4, 1998	November 10, 2000	Severe life-threatening & fatal hepatotoxicity		
Norelgestromin/ethinyl estradiol	Evra	August 20, 2002	November 21, 2006	Increased risk of venous thromboembolism		
Oxcarbazepine	Trileptal	April 13, 2000	April 27, 2005	Life-threatening dermatological reactions & multi-organ hypersensitivity		

Pegaptanib	Macugen	May 2, 2005	January 12, 2006	Hypersensitivity reaction		
Pegvisomant	Somavert	October 17, 2005	June 2, 2008	Marked hepatic enzyme elevations (>10 times normal) with pegvisomant & somatostatin analogue		
Pioglitazone	Actos	August 17, 2000	April 18, 2007	Increased incidence of fractures in women		
Raloxifene	Evista	November 6, 1998	May 18, 2006	Increased mortality due to stroke		
Repaglinide	Gluconorm	April 6, 1999	July 17, 2003	Should not be used in combination with gemfibrozil risk of severe and prolonged hypoglycemia		
Rituximab	Rituxan	March 17, 2000	July 27, 2004	Hepatitis B reactivation		
Rofecoxib	Vioxx	October 25, 1999	April 15, 2002	Increase in cardiovascular risk	September 30, 2004	Increased cardiovascular events
Rosiglitazone	Avandia	March 21, 2000	November 9, 2010	Restrictions on use due to cardiac safety		
Rosuvastatin	Crestor	February 18, 2003	June 15, 2004	Rhabdomyolysis		

Sibutramine	Meridia	December 28, 2000			October 8, 2010	Serious cardiovascular events
Sildenafil	Viagra	March 8, 1999	June 19, 2006	Serious visual disturbances		
Sirolimus	Rapamune	January 5, 2001	May 14, 2002	Increase in mortality, graft loss & hepatic artery thrombosis when used in conjunction with tacrolimus		
Sitaxsentan	Thelin	May 30, 2007	July 9, 2007	Hepatotoxicity, risks to fetus & important drug-drug interactions	December 15, 2010	Hepatotoxicity
Tadalafil	Cialis	September 17, 2003	June 19, 2006	Serious visual disturbances		
Tegaserod	Zelnorm	March 12, 2002	April 28, 2004	Diarrhoea & ischemic colitis	March 30, 2007	Cardiovascular events
Telbivudine	Sebivo	November 28, 2006	March 7, 2008	Risk of peripheral neuropathy with telbivudine & interferon		
Telithromycin	Ketek	May 28, 2003	September 29, 2006	Hepatic events, aggravation of myasthenia gravis & syncope		

Temsirolimus	Torisel	December 21, 2007	August 6, 2008	Hypersensitivity/infusion reactions		
Tenofovir	Viread	Mar. 18, 2003	June 9, 2005	Co-administration with didanosine and either efavirenz or nevirapine can lead to high rate of virological failure		
Tipranavir	Aptivus	November 21, 2005	June 29, 2006	Intracranial hemorrhage		
Tocilizumab	Actemra	April 30, 2010	September 13, 2010	Fatal anaphylaxis		
Tolcapone	Tasmar	October 8, 1997			November 20, 1998	Hepatotoxicity
Topiramate	Topamax	March 6, 1997	September 13, 2001	Acute myopia & secondary angle closure glaucoma		
Trastuzumab	Herceptin	Aug. 13, 1999	Apr. 21, 2009	Oligohydramnios		
Troglitazone	Rezulin	May 9, 1997			March 15, 2000	Hepatotoxicity
Trovafloxacin	Trovan (tablets)	December 4, 1998			November 22, 2001	Hepatotoxicity
Valdecoxib	Bextra	December 11, 2002	December 31, 2002	Serious skin reactions	April 21, 2005	Skin reactions

Vandetanib	Caprelsa	Jan. 12, 2012	Feb. 13, 2012	QTc prolongation,Torsade de Pointes & sudden death
Vardenafil	Levitra	March 17, 2004	June 19, 2006	Serious visual disturbances
Varenicline	Champix	January 24, 2007	June 13, 2008	Serious neuropsychiatric adverse events
Zafirlukast	Accolate	October 21, 1997	October 7, 2002	Hepatotoxicity
Zoledronic acid	Zometa	August 21, 2000	August 9, 2005	Clinically significant deterioration in renal function