

Drug	Dose	WW Sales (billion \$) 2009*	Marketer	Molecular Target	Therapeutic Area	Indication(s)	Dosing (Chronic/Acute)	Was prototype discovered or invented?	Mechanism	Reversibility	Approval Date (FDA Drug DB)
amoxicillin	250-500	0.19 (2003)	generic	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	1-Dec-82
Augmentin/amoxicillin +clavulanic acid	250-500/125	1.04	GSK	PBP and beta-lactamase	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	06-Aug-1984
cefaclor/Ceclor	250-500	0.06	Lilly	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	20-Apr-88
cefprozil/cefzil	250-500	0.09 (2006)	generic	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	23-Dec-91
ceftriaxone/Rocephin	250-500	0.28	Roche	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	21-Dec-84
cefuroxime axetil/ceftin	250	0.30 (2006)	GSK	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	28-Dec-87
Cephalexin/keflex	250-500	0.01 (2008)	generic	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	1-Dec-86
D-cycloserine/seromycin	250 mg		generic	alanine racemase	ANTI-INFECTIVE	bacterial infection	A	discovered/anti-biotic screening	suicide		Approved Prior to Jan 1, 1982
fosfomicin/monurol	3000 mg	0.15 (2006)	Zambon/Merck	UDP-N-acetylglucosamine-3-enolpyruvyl-transferase	ANTI-INFECTIVE	anti-bacterial	A	discovered/anti-biotic screening	warhead intact		19-Dec-96
isoniazid			generic	enol-acyl carrier protein reductase	ANTI-INFECTIVE	tuberculosis	C	discovered/tuberculosis screening	suicide		14-Jul-82
meropenem	500 mg	1.18	AstraZeneca	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	21-Jun-1996
Omnicef/cefdinir/cefzon	125-300 mg	0.13	Abbott	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact		04-Dec-1997
penicillin V	250-500 mg		generic	PBP	ANTI-INFECTIVE	bacterial infection	A	discovered/pathogen screening	warhead intact	slow off	Approved Prior to Jan 1, 1982

## SUPPLEMENTARY INFORMATION

azacytidine/ azacitidine	100 mg	0.39		methyltransferase	CANCER	anticancer	A	invented/ mechanism based design	warhead intact		19-May-04
bortezomib/ Velcade	1.3 mg/m <sup>2</sup>	1.21	Millennium	proteasome	CANCER	anticancer	A	invented/ mechanism based design	warhead intact	slow off	13-May-03
decitabine/ azadC	50 mg	0.15	Eisai	methyltransferase	CANCER	anticancer	A	invented/ mechanism based design	warhead intact		2-May-06
dutasteride/ avodart	0.5 mg	0.83	GSK	5-alpha-reductase	CANCER	benign protactic hypertrophy	C	invented/ mechanism based design	suicide		20-Nov-2001
exemestane/ Aromasin		0.47 (2008)	Pfizer	aromatase	CANCER	breast cancer	A	discovered	suicide		21-Oct-99
floxuridine			Bedford/ APP Pharms/	thymidylate synthase	CANCER	anti-cancer (anti-metabolite)	A	invented/ mechanism based design	warhead intact		16-Apr-00
gemcitabine/ gemzar	200-1000 mg	1.72 (2008)	Teva/Lilly	ribonucleoside reductatase	CANCER	anti-cancer (anti-metabolite)	A	discovered	prodrug/ suicide		15-May-96
Proscar/ finasteride	5 mg	0.73	Merck	5-alpha-reductase	CANCER	benign protactic hypertrophy/hair growth stimulant	C	invented/ mechanism based design	suicide		19-Jun-1992
Plavix/ clopidogrel	75 mg	10.79	BMS/Sanofi	P2Y12, platelet purinergic receptor	CARDIO- VASCULAR	reduction of risk for stroke and heart attack	C	discovered/ ex vivo screen	prodrug		17-Nov-1997
warfarin	1-10 mg	0.2 (2007)	generic	vitamin K reductase	CARDIO- VASCULAR	anti-coagulant	A	discovered	suicide		17-Aug-82
rasagiline	1 mg	0.18 (2008)		MAO-B	CNS	Parkinson's disease	C	discovered	suicide		16-May-06
rivastigmine/ Exelon	topical/oral		Novartis	acetylcholinesterase	CNS	dementia/ Parkinson's disease	C	invented/ mechanism based design			
Selegiline	5 mg	0.006	Elan/Somerset/ DAVA and others/Valeant	MAO-B	CNS	Parkinson's disease	C	discovered	suicide		5-Jun-89
vigabatrin/sabril	500 mg			GABA- aminotransferase	CNS	anti-epileptic	A	invented/ mechanism based design	suicide		21-Aug-09

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Nexium/ esomeprazole	20 mg	4.96	AstraZeneca	H+/K+ ATPase	GASTRO- INTESTINAL	esophageal reflux and heartburn	C	discovered/ animal screen	prodrug		20-Feb-2001
orlistat/Xenical/ Alli	60 mg	0.68	Roche/GSK	lipase	GASTRO- INTESTINAL	hyperlipidemia	C	discovered/ enzyme screen	warhead intact		23-Apr-99
Prevacid/ lansoprazole	15 mg	3.40	TAP	H+/K+ ATPase	GASTRO- INTESTINAL	esophageal reflux and heartburn	C	discovered	prodrug		10-May-1995
Prilosec/ omeprazole	20 mg	1.00	AstraZeneca	H+/K+ ATPase	GASTRO- INTESTINAL	esophageal reflux and heartburn	C	discovered	prodrug		14-Sep-1989
Protonix/ pantoprazole	20-40 mg	2.36 (2008)	Wyeth/Pfizer	H+/K+ ATPase	GASTRO- INTESTINAL	esophageal reflux and heartburn	C	discovered	prodrug		02-Feb-2000
Aciphex/ rabeprazole	20 mg	0.996(US)	Eisai/ Janssen-Cilag	H+/K+ ATPase	GASTRO- INTESTINAL	esophageal reflux and heartburn	C		prodrug		
aspirin	81 mg	0.99	Bayer	cyclooxygenase	INFLAMMA- TION	inflammation and stroke prevention	A and C	discovered	warhead intact		26-May-82
disulfiram/ antabuse	250-500 mg			aldehyde dehydrogenase	OTHER	alcoholism	C	discovered	warhead intact		5-Aug-83
eflornithine	topical		Sanofi-Aventis/ SKINMEDICA	ornithine decarboxylase	OTHER	facial hair retardant and anti- trypanosomiasis	A	invented/ mechanism based design	suicide		28-Nov-90
propylthiouracil/ procasil	50 mg		Dava/Westward	thyroxine-5- deiodinase	OTHER	hyperthyroidism	A	discovered/ animal screening	warhead intact		Approved Prior to Jan 1, 1982
saxagliptin/ Onglyza	2.5-5 mg	0.02	BMS	DPP-IV	OTHER	diabetes		invented/ mechanism based design	warhead intact	slow off	31-Jul-09
vildagliptin/ Eugreas	50 mg	0.18	Novartis	DPP-IV	OTHER	diabetes	C	invented/ mechanism based design	warhead intact	slow off	withdrawn July 2008
phenoxy- benzamine hydrochloride	10 mg		Wellspring Pharm	alpha adrenoceptor	CARDIO- VASCULAR	pheochromo- cytoma	A		warhead intact		Approved Prior to Jan 1, 1982
mercaptopurine/ purinethol	50 mg		Teva Pharmaceuticals	purine nucleotide synthesis	CANCER	acute lymphatic leukemia	A	discovered			Approved Prior to Jan 1, 1982
carbidopa/ lodosyn				DOPA decarboxylase	CNS	Parkinson's disease	C	invented/ mechanism based design	warhead intact		Approved Prior to Jan 1, 1982

#Total Sales in 2009 (or 2007 or 2008 if 2009 data not available)

33.962#

The first 39 compounds were used in the generation of Figure 1

\*Source: Integrity Database (<https://integrity.thomson-pharma.com/integrity>)