

Excess medical costs of asthma compared to non-asthma and the role of comorbidity

Supplementary material

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S1. Data source.

A provincial health insurance program provides universal health care coverage to all legal residents of British Columbia (BC), Canada, one of the largest provinces, representing 13% of the Canadian population (4.4 million as of 2011) [1]. We retrieved data from the BC provincial health administrative databases for the period of January 1997 to December 2012 (16 years). These databases are linked at individual-level and provide information on health-care encounters of all legal residents of BC. We used registration files (capturing the status of insurance coverage of individuals) [2], vital statistics (capturing births and deaths) [3], the hospital discharge database (capturing inpatient encounters) [4], Medical Services Plan payment information (capturing outpatient encounters with physicians) [5] and PharmaNET (capturing all medication dispensations outside of hospital pharmacies, and regardless of any third-party insurance coverage) [6]. Previous analyses have showed a very low prevalence of missing data, under-reporting and misclassification in these databases [7, 8].

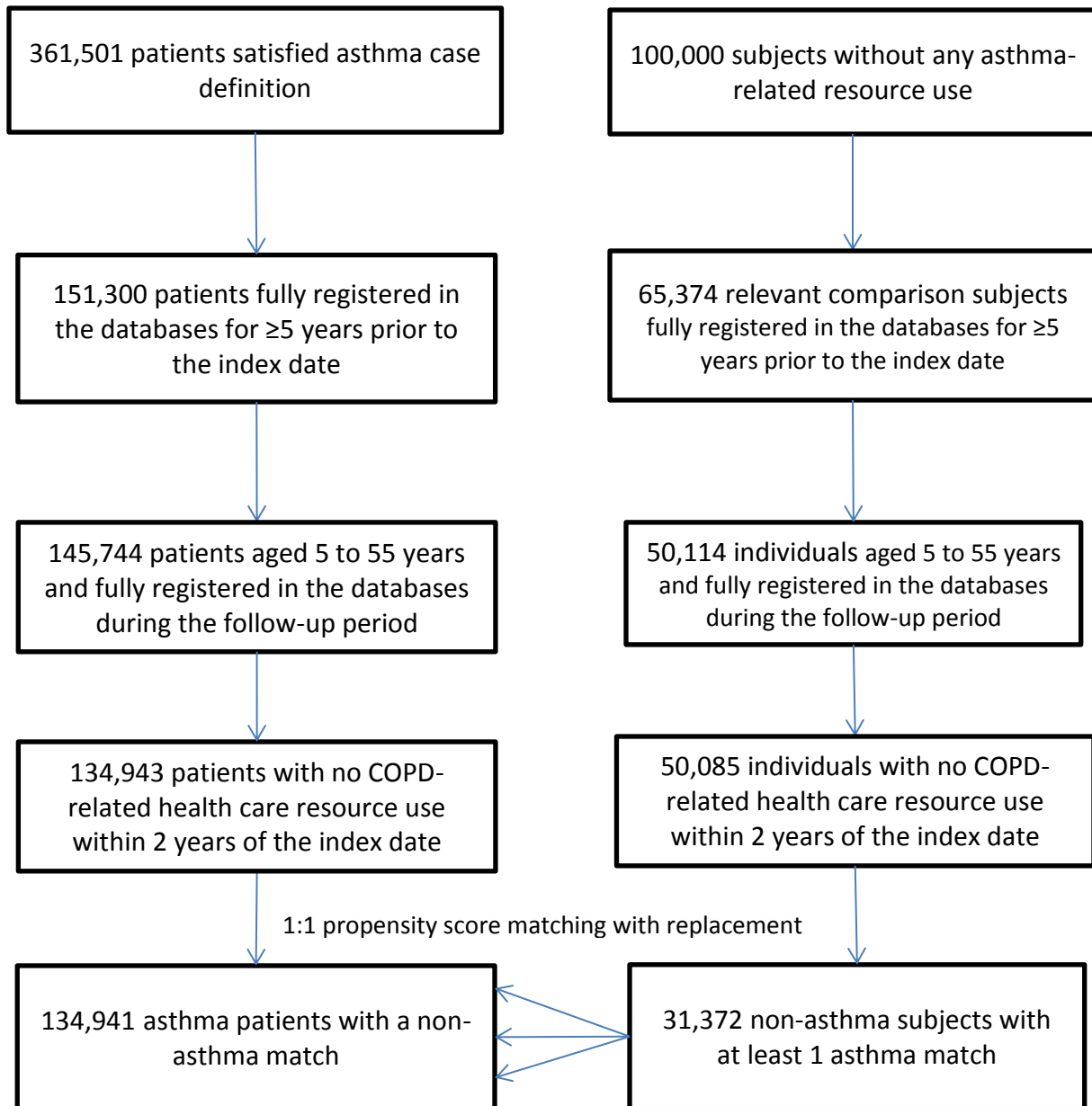
S2. List of asthma-related medications used for asthma case definition.

Medication categories	Medication type	Active ingredient(s)	ATC	DIN	Used in case definition?
Inhaled corticosteroids (ICS)	Controller	Beclomethasone	R03BA01	2242030, 2242029, 374407, 828521, 828548, 872334, 893633, 897353, 1949993, 1950002, 2079976, 2213710, 2213729, 2215039, 2215047, 2215055, 2216531	Y
		Budesonide	R03BA02	2229099, 1978918, 1978926, 852074, 851752, 851760	Y
		Fluticasone	R03BA05	2237247, 2237246, 2237245, 2237244, 2244293, 2244292, 2244291, 2174731, 2174758, 2174766, 2174774, 2213583, 2213591, 2213605, 2213613	Y
		Ciclesonide	R03BA08	2285614, 2285606, 2303671	Y
Short-acting beta-agonists (SABA)	Reliever	Salbutamol	R03AC02	790419, 812463, 832758, 832766, 851841, 860808, 867179, 897345, 1926934, 1938851, 1938878, 1945203, 1947222, 1986864, 2022125, 2046741, 2048760, 2069571, 2084333, 2148617, 2154412, 2173360, 2208229, 2208237, 2208245, 2212315, 2212323, 2213400, 2213419, 2213427, 2213478, 2213486, 2214997, 2215004, 2215616, 2215624, 2215632, 2216949, 2231430, 2231488, 2231678, 2231783, 2231784, 2232570, 2232987, 2236931, 2236932, 2236933, 2239365, 2239366, 2241497, 2243115, 2243828, 2244914, 2245669, 2259583, 2326450	Y
			R03CC02	620955, 620963, 874086, 894249, 894257, 1932691, 2035421, 2063689, 2091186, 2146843, 2146851, 2164434, 2164442, 2165368, 2165376, 2212390, 2213435, 2213443, 2213451, 2261324	Y
		Terbutaline	R03AC03	786616	Y
		Orciprenaline	R03CB03	249920, 3891, 2236783, 2229862, 2152568, 2192675	Y
Long-acting beta-agonists (LABA)	Controller	Salmeterol	R03AC12	2211742, 2214261, 2231129, 2136139, 2136147	Y
		Formoterol	R03AC13	2230898, 2237224, 2237225	Y
ICS and LABA in combination (ICS+LABA)	Controller	Budesonide, formoterol	R03AK07	2245385, 2245386	Y
		Fluticasone, salmeterol	R03AK06	2240835, 2245126, 2245127, 2240836, 2240837	Y
Leukotriene receptor antagonists (LTRA)	Controller	Montelukast	R03DC03	2247997, 2238217, 2243602, 2238216	Y
		Zafirlukast	R03DC01	2236606	Y
Anti-	Controller	Omalizumab	R03DX05	2260565	Y

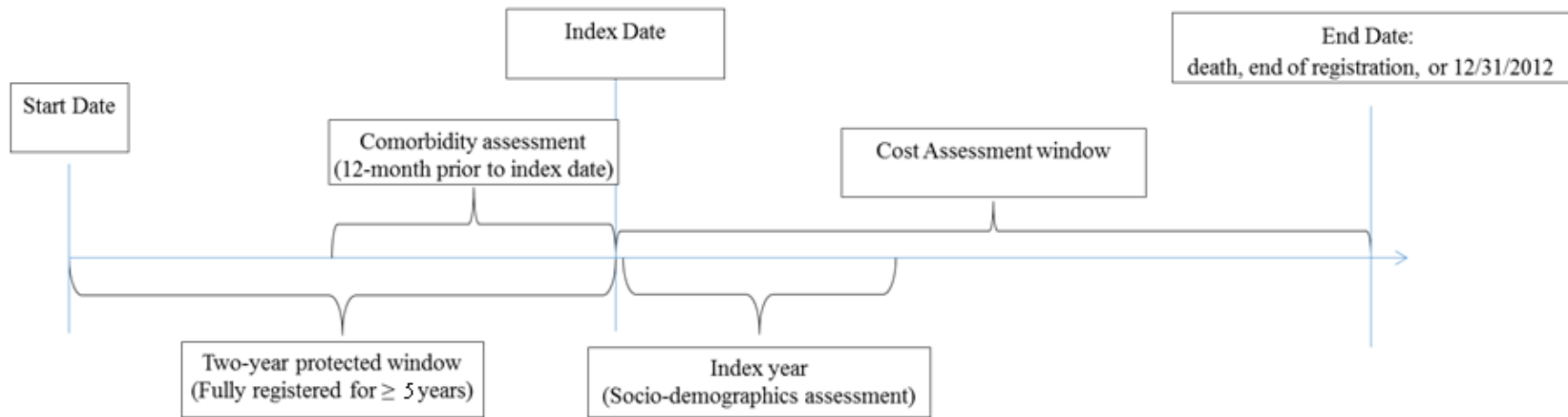
immunoglobulin E monoclonal antibody					
Inhaled mast cell stabilizers	Controller	Cromoglicic acid (cromolyn)	R03BC01	2231431, 2231671, 2046113, 534609, 555649, 261238, 638641, 2049082, 2219468	Y
Theophylline	Controller	Choline theophyllinate	R03DA02	346071, 405310, 441724, 441732, 451282, 458708, 458716, 476366, 476390, 476412, 503436, 511692, 536709, 565377, 589942, 589950, 792934	Y
		Theophylline	R03DA04	156701, 261203, 460982, 460990, 461008, 466409, 488070, 532223, 556742, 575151, 599905, 627410, 631698, 631701, 692689, 692697, 692700, 722065, 1926586, 1926594, 1926608, 1926616, 1926640, 1966219, 1966227, 1966235, 1966243, 1966251, 1966278, 1966286, 2014165, 2014181, 2230085, 2230086, 2230087	Y
		Aminophylline	R03DA05	14923, 178497, 497193, 497193, 497207, 582654, 582662, 868450, 2014270, 2014289	Y
Inhaled anticholinergics	Reliever	Ipratropium bromide	R01AX03	2246084, 2246083, 2163705, 2163713, 2240508, 2240072	N
			R03BB01	2126222, 2243827, 2231494, 731439, 576158, 2247686, 824216, 2026759, 1950681, 2239131, 2216221, 2210479, 2231785, 2236934, 2236935, 2237134, 2237135, 2239627, 2231135, 2231136, 2231245, 2231244, 2097141, 2097176, 2097168	N
		Ipratropium bromide, fenoterol	R03AK03	02148633	N
		Tiotropium bromide	R03BB04	02246793	N
Other beta-agonists	Reliever	Epinephrine	R03AA01	2017555, 466417, 525103, 1927582	N
		Ephedrine	R03CA02	2237085, 2229698, 2100231, 2100258, 2243148, 2236722, 2229678, 2219743, 2012111, 2229711, 38121, 2242961, 876534, 893323, 893331, 438847, 2242639, 2126419, 2126400	N
		Isoprenaline	R03AB02	2017652	N
		Orciprenaline	R03AB03	1923870, 1928449, 2017660, 254134, 3859	N
Other corticosteroids	Controller	Cortisone	H02AB10	280437, 16241, 16446, 16438	N
		Triamcinolone	H02AB08	2194090, 15016, 15024, 2194082	N
		Prednisone	H02AB07	610623, 598194, 550957, 312770, 252417, 210188, 868426, 868434, 868442, 21695, 232378, 607517, 508586, 156876, 271373, 271381	N
		Prednisolone	H02AB06	21679, 2230619, 2152541, 2245532	N
		Methylprednisolone	H02AB04	1934325, 1934333, 1934341, 30759, 30767, 36129, 30988, 2245406, 2245400, 2245408, 2245407, 2241229, 2231893, 2231894, 2231895,	N

				2232750, 2232748, 2063727, 2063697, 2063719, 2063700, 36137, 2230210, 2230211, 30678, 30651, 30643	
		Betamethasone	H02AB01	2237835, 36366, 2063190, 176834, 28096, 28185	N
		Hydrocortisone	H02AB09	888222, 888230, 888206, 888214, 30910, 30929, 872520, 872539, 878618, 878626, 30635, 30600, 30619, 30627	N
		Dexamathasone	H02AB02	2261081, 2250055, 213624, 16462, 354309, 716715, 874582, 1977547, 664227, 2204274, 2204266, 295094, 285471, 489158, 2239534, 732893, 732885, 2260301, 2237044, 2260298, 2237046, 2237045, 1946897, 1964976, 1964968, 1964070, 2279363, 783900, 751863, 2311267, 2240687, 2240685, 2240684	N
Other xanthines	Controller	Theophylline, combination	R03DA54	545090, 476374, 334510, 356123, 792942, 721301, 317225, 828718, 640093, 828726, 828742, 307548	N
Other anti-allergic agents	Anti-allergic	Levocabastine	R01AC02	2020017	N
		Ketotifen	R06AX17	2221330, 2176084, 2230730, 2218305, 2231680, 2231679, 600784, 577308	N

S3. Flowchart of study cohort selection.



S4. Schematic presentation of study design



S5. Mapping the American Hospital Formulary Service (AHFS) medication categories to ICD-10 disease categories.

Disease category	ICD 10 code	AHFS Category Level 1	AHFS level 1 code	AHFS Category Level 2	AHFS level 2 code
Certain infectious and parasitic diseases	A00-B99	ANTI-INFECTIVE AGENTS	8	ANTHELMINTICS	808
				ANTIBACTERIALS	812
				ANTIFUNGAL (SYSTEMIC)	814
				ANTIMYCOBACTERIALS	816
				ANTIPROTOZOALS	830
				ANTIVIRALS (SYSTEMIC)	818
				URINARY ANTI-INFECTIVES	836
Neoplasmse	C00-D48	ANTINEOPLASTIC AGENTS	10	ANTINEOPLASTIC AGENTS	1000
Diseases of the blood and blood-forming origin	D50-D89	NA	NA	NA	NA
Endocrine, nutritional and metabolic diseases	E00-E90	HORMONES AND SYNTHETIC SUBSTITUTES	68	ADRENALS	6804
				ANDROGENS	6808
				ANTIDIABETIC AGENTS	6820
				ANTIHYPOLYCEMIC AGENTS	6822
				CONTRACEPTIVES	6812
				ESTROGENS AND ANTIESTROGENS	6816
				GONADOTROPINS	6818
				PARATHYROID	6824
				PITUITARY	6828
				PROGESTINS	6832
				SOMATOSTATIN AGONISTS AND ANTAGONISTS	6829
SOMATOTROPIN AGONISTS AND ANTAGONISTS	6830				
THYROID AND ANTITHYROID AGENTS	6836				
Mental and behavioural disorders	F00-F99	CENTRAL NERVOUS SYSTEM AGENTS	28	ANTICONVULSANTS	2812

				PSYCHOTHERAPEUTIC AGENTS	2816
Diseases of the nervous system	G00-G99	CENTRAL NERVOUS SYSTEM AGENTS	28	ANALGESICS AND ANTIPIRETTICS	2808
				ANOREXIGENICS;RESPIRATORY,CNS STIMULANTS	2820
				ANTIMANIC AGENTS	2828
				ANTIMIGRAINE AGENTS	2832
				ANTIPARKINSONIAN AGENTS (CNS)	2836
				ANXIOLYTICS, SEDATIVES AND HYPNOTICS	2824
				CENTRAL NERVOUS SYSTEM AGENTS, MISC.	2892
				GENERAL ANESTHETICS	2804
				OPIATE ANTAGONISTS	2810
Diseases of the eye and adnexa; Diseases of the ear and mastoid process (Combined into one category: diseases of the eye, ear and nose)	H00-H59 H60-H95	EYE, EAR, NOSE AND THROAT (EENT) PREPS.	52	ANTI-INFECTIVES (EENT)	5204
				ANTI-INFLAMMATORY AGENTS (EENT)	5208
				ANTIALLERGIC AGENTS	5202
				ANTIGLAUCOMA AGENTS	5240
				CONTACT LENS SOLUTIONS	5212
				EENT DRUGS, MISCELLANEOUS	5292
				LOCAL ANESTHETICS (EENT)	5216
				MOUHWASHES AND GARGLES	5228
				MYDRIATICS	5224
				VASOCONSTRICTORS	5232
Diseases of the circulatory system	I00-I99	BLOOD FORMATION,COAGULATION + THROMBOSIS	20	ANTIANEMIA DRUGS	2004
				ANTIHEMORRHAGIC AGENTS	2028
				ANTITHROMBOTIC AGENTS	2012
				HEMATOPOIETIC AGENTS	2016
				HEMORRHEOLOGIC AGENTS	2024
Diseases of the circulatory system	I00-I99	CARDIOVASCULAR DRUGS	24	ALPHA-ADRENERGIC BLOCKING AGENTS	2420
				ANTILIPEMIC AGENTS	2406
				BETA-ADRENERGIC BLOCKING AGENTS	2424
				CALCIUM-CHANNEL BLOCKING AGENTS	2428

				CARDIAC DRUGS	2404
				HYPOTENSIVE AGENTS	2408
				RENIN-ANGIOTENSIN-ALDOSTERONE SYS. INHIB	2432
				SCLEROSING AGENTS	2416
				VASODILATING AGENTS	2412
Diseases of the respiratory system	J00-J99	RESPIRATORY TRACT AGENTS	48	ANTI-INFLAMMATORY AGENTS (RESPIRATORY)	4810
				ANTITUSSIVES	4808
				CYSTIC FIBROSIS (CFTR) MODULATORS	4814
				EXPECTORANTS	4816
				MUCOLYTIC AGENTS	4824
				PHOSPHODIESTERASE TYPE 4 INHIBITORS	4832
				PULMONARY SURFACTANTS	4836
				RESPIRATORY TRACT AGENTS, MISCELLANEOUS	4892
Diseases of the digestive system	K00-K93	GASTROINTESTINAL DRUGS	56	ANTACIDS AND ADSORBENTS	5604
				ANTI-INFLAMMATORY AGENTS (GI DRUGS)	5636
				ANTIDIARRHEA AGENTS	5608
				ANTIEMETICS	5622
				ANTIFLATULENTS	5610
				ANTIULCER AGENTS AND ACID SUPPRESSANTS	5628
				CATHARTICS AND LAXATIVES	5612
				CHOLELITHOLYTIC AGENTS	5614
				DIGESTANTS	5616
				EMETICS	5620
				GI DRUGS, MISCELLANEOUS	5692
				LIPOTROPIC AGENTS	5624
				PROKINETIC AGENTS	5632
Diseases of the skin and subcutaneous tis	L00-L99	SKIN AND MUCOUS MEMBRANE AGENTS	84	ANTI-INFECTIVES (SKIN + MUCOUS MEMBRANE)	8404

				ANTI-INFLAMMATORY AGENTS (SKIN + MUCOUS)	8406
				ANTIPRURITICS AND LOCAL ANESTHETICS	8408
				ASTRINGENTS	8412
				CELL STIMULANTS AND PROLIFERANTS	8416
				DEPIGMENTING AND PIGMENTING AGENTS	8450
				DETERGENTS	8420
				EMOLLIENTS, DEMULCENTS, AND PROTECTANTS	8424
				KERATOLYTIC AGENTS	8428
				KERATOPLASTIC AGENTS	8432
				SKIN AND MUCOUS MEMBRANE AGENTS, MISC.	8492
				SUNSCREEN AGENTS	8480
Diseases of the musculoskeletal system an	M00-M99	NA	NA	NA	NA
Diseases of the genitourinary system	N00-N99	NA	NA	NA	NA
Pregnancy, childbirth and the puerperium	O00-O99	NA	NA	NA	NA
Certain conditions originating in the per	P00-P96	NA	NA	NA	NA
Congenital malformations, deformations, a	Q00-Q99	NA	NA	NA	NA
Symptoms, signs and abnormal clinical and	R00-R99	Not included	NA	NA	NA
Injury, poisoning and certain other conse	S00-T98	Not included	NA	NA	NA
Provisional codes for research and tempor	U00-U99	Not included	NA	NA	NA
External causes of morbidity and mortalit	V01-Y98	Not included	NA	NA	NA
Factors influencing health status and con	Z01-Z99	Not included	NA	NA	NA
NA	MIS	ANTIHISTAMINE DRUGS	4	FIRST GENERATION ANTIHISTAMINES	404
				OTHER ANTIHISTAMINES	492
				SECOND GENERATION ANTIHISTAMINES	408

		AUTONOMIC DRUGS	12	ANTICHOLINERGIC AGENTS	1208
				AUTONOMIC DRUGS, MISCELLANEOUS	1292
				PARASYMPATHOMIMETIC (CHOLINERGIC AGENTS)	1204
				SKELETAL MUSCLE RELAXANTS	1220
				SYMPATHOLYTIC ADRENERGIC BLOCKING AGENTS	1216
				SYMPATHOMIMETIC (ADRENERGIC) AGENTS	1212
		BLOOD DERIVATIVES	16	BLOOD DERIVATIVES	1600
		DENTAL AGENTS	34	DENTAL AGENTS	3400
		DEVICES	94	DEVICES	9400
		DIAGNOSTIC AGENTS	36	ADRENOCORTICAL INSUFFICIENCY	3604
				DIAGNOSTIC AGENTS	3600
				DIPHThERIA	3628
				DRUG HYPERSENSITIVITY	3630
				FUNGI	3632
				GALLBLADDER FUNCTION	3634
				GASTRIC FUNCTION	3636
				INTESTINAL ABSORPTION	3638
				KIDNEY FUNCTION	3640
				LIVER FUNCTION	3644
				MUMPS	3652
MYASTHENIA GRAVIS	3656				
OCULAR DISORDERS	3658				
PANCREATIC FUNCTION	3661				
PITUITARY FUNCTION	3666				
ROENTGENOGRAPHY	3668				
THYROID FUNCTION	3660				
TUBERCULOSIS	3684				
URINE AND FECES CONTENTS	3688				

		DISINFECTANTS (FOR NON- DERMATOLOGIC USE)	38	DISINFECTANTS (FOR NON- DERMATOLOGIC USE)	3800
		ELECTROLYTIC, CALORIC, AND WATER BALANCE	40	ACIDIFYING AGENTS	4004
				ALKALINIZING AGENTS	4008
				AMMONIA DETOXICANTS	4010
				CALORIC AGENTS	4020
				DIURETICS	4028
				ION-REMOVING AGENTS	4018
				IRRIGATING SOLUTIONS	4036
				REPLACEMENT PREPARATIONS	4012
				SALT AND SUGAR SUBSTITUTES	4024
				URICOSURIC AGENTS	4040
		ENZYMES	44	ENZYMES	4400
		GOLD COMPOUNDS	60	GOLD COMPOUNDS	6000
		HEAVY METAL ANTAGONISTS	64	HEAVY METAL ANTAGONISTS	6400
		LOCAL ANESTHETICS (PARENTERAL)	72	LOCAL ANESTHETICS (PARENTERAL)	7200
		MISCELLANEOUS THERAPEUTIC AGENTS	92	5-ALPHA-REDUCTASE INHIBITORS	9208
				ALCOHOL DETERRENTS	9204
				ANTIDOTES	9212
				ANTIGOUT AGENTS	9216
				BONE RESORPTION INHIBITORS	9224
				CARIOSTATIC AGENTS	9228
				COMPLEMENT INHIBITORS	9232
				DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	9236
				GONADOTROPIN-RELEASING HORMONE ANTAGNTS	9240
				IMMUNOMODULATORY AGENTS	9220
				IMMUNOSUPPRESSIVE AGENTS	9244
				OTHER MISCELLANEOUS THERAPEUTIC AGENTS	9292

			PROTECTIVE AGENTS	9256	
		OXYTOCICS	76	OXYTOCICS	7600
		PHARMACEUTICAL AIDS	96	PHARMACEUTICAL AIDS	9600
		SMOOTH MUSCLE RELAXANTS	86	GENITOURINARY SMOOTH MUSCLE RELAXANTS	8612
				RESPIRATORY SMOOTH MUSCLE RELAXANTS	8616
		VITAMINS	88	MULTIVITAMIN PREPARATIONS	8828
				VITAMIN A	8804
				VITAMIN B COMPLEX	8808
				VITAMIN C	8812
				VITAMIN D	8816
				VITAMIN E	8820
		VITAMIN K ACTIVITY	8824		
		CONTRACEPTIVES (E.G. FOAMS, DEVICES)	32	CONTRACEPTIVES (E.G. FOAMS, DEVICES)	3200
		SERUMS, TOXOIDS, AND VACCINES	80	SERUMS	8004
				TOXOIDS	8008
				VACCINES	8012

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