



A REVIEW ON REGULATORY ASPECT OF ORPHAN DRUGS

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ABSTRACT

An orphan drug is defined as a medicine, vaccine or in vivo diagnostic agent intended to treat, prevent or diagnose a rare disease or not commercially viable to supply to treat, prevent or diagnose another disease or condition. This paper gives an idea about Innovation and the Orphan Drug Act which provides some incentives like grants funding, performance of clinical trials and credit of tax on clinical cost and create exclusive right of marketing. Prior research has been done on various aspects of the Orphan Drug Act. A few studies provided perspectives on the early implementation of the incentive. Some orphan drugs are enlisted in the paper designated by TGA. The EURORDIS Round Table of Companies (ERTC), FDA, TGA and Office of Orphan Product Development (OOPD) help to manage regulatory function of orphan drugs. They found that the drugs averaged about 8 years in clinical development (from Investigational New Drug [IND] to New Drug Application [NDA]) and approximately 1.8 years in FDA review.

KEYWORDS: orphan drugs, EURORDIS, clinical development.

INTRODUCTION

Orphan drugs are medicinal products intended for diagnosis, prevention or treatment of life-threatening or debilitating rare diseases. They are "orphans" because the pharmaceutical industry has little interest under normal market conditions in developing and marketing drugs intended for only a small number of patients suffering from very rare conditions. The growing number of rare diseases awaiting treatment is a public health issue. The scarcity of incentives for medicines manufacturers and the lack of documentation supporting the applications limit the number of new orphan medicines products. The first step in the development of any orphan medicinal product is to obtain designation as an Orphan Medicinal Product. EURORDIS plays an important role in the orphan drug development process through participation in the Committee for Orphan Medicinal Products at the European Medicines Agency. Patient advocates are actively involved in orphan medicines development and regulatory affairs. A good medication for rare disease patients is a medication that is both available in the country where they live and affordable. When a new medicine is being developed, patients want to know when it will be available. Not all patients can wait until the end of clinical trials and the evaluation of the marketing authorization application. Compassionate Use Programmes are designed to satisfy these needs. The EURORDIS Round Table of Companies (ERTC) brings together pharmaceutical companies with a common

interest in rare diseases and orphan medicinal product development. Before an application to register an orphan drug is made, a sponsor should first seek orphan drug designation. Designated orphan drugs are eligible for a waiver of their application and evaluation fees, but only if designation is received prior to submitting an application to register an orphan drug on the Australian Register of Therapeutic Goods (ARTG). Information on applications for orphan drug status can be found in the Applications for orphan drug designation. The quality, efficacy and safety of orphan drugs are assessed at the same standard as for other registered medicines.^[1] A social network of rare disease communities led by EURORDIS in partnership with leading disease-specific patient groups. Some rare diseases are as follows- Alkaptonuria, Alström Syndrome, Alternating Hemiplegia, Atypical Hemolytic Uremic Syndrome, Amyloidosis, Aortic Dissection, Apert Syndrome, Behcet's Syndrome, Brown-Vialetto-Van Laere syndrome, Castleman Disease, CDG, Choroideremia, Chromosome 18 abnormalities, CMT, Coats disease, Cobb Syndrome, Cone-rod dystrophies, Cryoglobulinemia, Cystinosis, Dravet Syndrome, DysNet, Dysmelia - Limb Differences, Ectodermal Dysplasia, EEC syndrome, Ehlers-Danlos Syndrome, Epidermolysis Bullosa, Erdheim-Chester Disease, Evans Syndrome, Familial Mediterranean Fever, Fetal AntiConvulsant Syndromes, Fibromuscular dysplasia, FOXP1, Glut1 DS, Hemiconvulsion-hemiplegia-epilepsy syndrome,

Hereditary Leiomyomatosis and Renal Cell Cancer, Hereditary Spastic Paraplegia, Idiopathic Pulmonary Fibrosis, Kallmann Syndrome, Leber hereditary optic neuropathy Leigh Syndrome, Lipodystrophy, Lipoprotein Lipase Deficiency, Lowe Syndrome, Mastocytosis, Multiple Myeloma, Multiple system atrophy, Moebius Syndrome, Moyamoya disease, Multiple Endocrine Neoplasia, Myasthenia Gravis, Narcolepsy, Neuroacanthocytosis, Neurofibromatosis type 1, Neurofibromatosis type 2 and Schwannomatosis, Niemann-Pick disease type C, Paraneoplastic Neurological Syndromes, Pemphigus and Pemphigoid,

Pitt Hopkins Syndrome, Pontine Tegmental Cap Dysplasia, Porphyria, Primary Orthostatic Tremor, Propionic Acidemia, Pseudomyxoma Peritonei, Pulmonary Hypertension, Rett Syndrome, Sanfilippo Syndrome (MPS III), Stargardt Disease, Stiff Person Syndrome, TRAPS, Trichorhinophalangeal syndrome, Trimethylaminuria, Undiagnosed brain disease, Vasculitis, Von Hippel-Lindau, Waldenstrom macroglobulinemia, Whim syndrome, Williams Syndrome etc. Drugs designated as orphan drugs by the TGA are shown in the table 1 and table 2.

Table 1: Drugs designated as orphan drugs by the TGA.

Sr.No	Drug	sponsor	Designation date
1	Adalimumab (Humira) solution for injection	AbbVie Pty Ltd	19/08/15
	For treatment of adult patients with non-infectious intermediate, posterior or panuveitis who have an inadequate response to corticosteroid therapy		
2	Adalimumab (HUMIRA) injection solution	AbbVie Pty Ltd	30/01/15
	For the treatment of paediatric Enthesitis-Related Arthritis (paediatric ERA)		
3	Adalimumab (HUMIRA) injection solution	Abbott Australasia Pty Ltd	16/01/12
	For active Paediatric Crohn's Disease Activity Index (PCDAI) score >30 in paediatric patients (6-17 years of age) having an inadequate response and intolerance to conventional therapy		
4	Adefovir dipivoxil	Gilead Sciences Pty Ltd	12/08/05
	In monotherapy/combination for recurrence of HBV infection in liver transplant recipients		
5	Adefovir dipivoxil 10mg oral tablets (HEPSERA)	Gilead Sciences Pty Ltd	30/10/08
	For the treatment of chronic hepatitis B in adolescent patients (12 to <18 years of age)		
6	Afamelanotide (SCENESSE) SC implant	Clinuvel PharmaLtd	08/11/10
	For the treatment of erythropoietic porphyrias		
7	Afatinib Tablets	Boehringer Ingelheim PtyLtd	01/06/12
	For the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with Epidermal Growth Factor Receptor (EGFR) mutation (s)		
8	Agalsidase alfa (REPLAGAL)	PPD Australia Pty Ltd	20/10/00
	For the long-term enzyme replacement therapy in patients with Fabry disease		
9	Agalsidase beta (FABRAZYME)	Genzyme Australia Pty Ltd	22/05/00
10	Aimspro (Goat Serum Derived Product)	Daval Australia Pty Ltd	22/08/05
	For treatment of Krabbe's Disease (Globoid Cell Leucodystrophy)		
11	Albutrepenonacog Alfa Injection	CSL Behring Australia Pty Ltd	27/10/14
	For prophylaxis of bleeding associated with congenital factor IX deficiency (haemophilia B)		
12	Aldesleukin (PROLEUKIN)	CSL Limited	16/10/98
	For the treatment of metastatic renal cell carcinoma and metastatic melanoma		
13	Alectinib Capsule	Roche Products Pty Ltd	27/10/15
	For the treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer		
14	Alglucosidase alfa (MYOZYME) infusion Powder	Genzyme Australia Pty Ltd	08/09/03
	For the treatment of Pompe disease (glycogen storage disease type II)		
15	α -1-proteinase inhibitor for IV injection	Baxter Healthcare Pt Ltd	03/07/12
	For chronic augmentation in adults with emphysema incongenital deficiency of α -1-antitrypsin		
16	5-aminolevulinic acid hydrochloride (Gliolan) Powder for oral solution	Specialized Therapeutics Australia Pty Ltd	30/03/12
	For photodynamic diagnosis of glioblastoma multiforme (GBM) (malignant) on preoperative imaging and intended for gross macroscopic resection of all visible tumors		
17	5-azacytidine	Pharmion PtyLtd	02/09/04
	For the treatment of myelodysplastic syndrome		
18	6-chloro-2, 3, 4, 9-tetrahydro-1H-carboxamide	Siena Biotech Italy	11/03/11
	For the treatment of Huntington's Disease		
19	Beclometasone dipropionate (ORBEC) Oral capsules 1 mg immediate release beclometasone dipropionate tab, enteric-coated beclometasone dipropionate tablet	Orphan Australia Pty Ltd	31/10/08

	For gastrointestinal Graft-Versus-Host-Disease (GVHD), allergenic haematopoietic cell transplantation with an induction course of high-dose prednisone/methylprednisolone		
20	Bevacizumab (AVASTIN) conc.solution for injection 100mg in 4 mLs and 400 mg in 16 mLs	Roche Products Pty Ltd	13/01/09
	For the treatment of malignant glioma		
21	Bevacizumab (AVASTIN) Injection conc.	Roche Products Pty Ltd	21/03/14
	For the treatment of persistent, recurrent of Stage IV carcinoma of the cervix		
22	BicaVera sterile peritoneal dialysis soln	Fresenius Medical Care Australia Pty Ltd	29/10/02
	For peritoneal dialysis solution in management of end stage renal disease & acute renal failure		
23	Blinatumomab	Amgen Australia Pty Ltd	20/11/13
	For the treatment of B-precursor acute lymphoblastic leukemia		
24	Bortezomib (VELCADE) Powder for Inj.	Janssen-Cilag Pty Ltd	22/10/03
	For the treatment of resistant or relapsed multiple myeloma and mantle cell lymphoma		
25	Bosentan	Omnicare Clinical Research	12/02/01
	For the treatment of primary and secondary pulmonary hypertension in patients meeting WHO criteria for inclusion in functional class III-IV pulmonary hypertension		
26	Bosentan Film coated tablet	Actelion Pharmaceuticals Australia Pty Ltd	02/12/14
	For the treatment of Pulmonary Arterial Hypertension		
27	Bosentan (TRACLEER) 62.5, 125 mg Tab	Actelion Pharmaceuticals Australia Pty Ltd	27/08/10
	For the treatment of digital ulcers in patients with systemic sclerosis		
28	Bosutinib Tablets	Pfizer Australia Pty Ltd	13/08/12
	For the second or third line treatment of chronic myeloid leukaemia		
29	Brentuximab vedotin (ADCETRIS) infusion Powder	Nycomed Pty Ltd	17/09/12
	For relapsed or refractory Hodgkin lymphoma, systemic anaplastic large cell lymphoma		
30	Busulfan (BUSULFEX)	Orphan Australia Pty Ltd	12/10/05
	For use in combination with other chemotherapeutic agents and/or radiotherapy as a conditioning regimen prior to haematopoietic progenitor cell transplantation		
31	C1 esterase inhibitor (BERINERT P) Powder for injection	CSL Limited	10/04/07
	For the treatment of hereditary angioedema		
32	C1 esterase inhibitor (CINRYZE) Powder for reconstitution for IV administration	Cedarglen Investments Pty Ltd	15/10/10
	For the treatment, routine prevention and pre-procedure prevention of angioedema attacks in adults, adolescents, and children from 6 years of age with C1 inhibitor deficiency		
33	Caffeine citrate injection, 40 mg/2mL, oral solution 25mg/5mL	Ophthalmic Laboratories Pty Limited	02/08/07
	For short term treatment of apnoea of prematurity of gestational age 28 to less than 33 weeks		
34	Canakinumab (ILARIS) injection Powder	Novartis Pharmaceuticals Australia	01/05/13
	For active Systemic Juvenile Idiopathic Arthritis (sJIA) in patients aged 2 years and older		
35	Canakinumab (ILARIS) injection powder	Novartis Pharmaceuticals Australia	30/01/09
	For Cryopyrin Associated Syndromes (CAPS) in adults and children aged 4 years and older, Muckle-Wells Syndrome (MWS), Familial Cold-induced Autoinflammatory Syndrome (FCAS)/Familial Cold Urticaria (FCU), Neonatal-Onset Multisystem Inflammatory Disease, (NOMID)/Chronic Infantile Neurological Cutaneous Articular Syndrome		
36	Caprine hyperimmune injection for HIV lysate (AIMSPRO) 4.5mg total protein/ml subcutaneous	Daval Australia Pty Ltd	15/05/09
	For the treatment of amyotrophic lateral sclerosis		
37	Carboprost as the tromethamine (HEMABATE)	Pharmacia & Upjohn	16/10/98
	For the treatment of post-partum haemorrhage due to uterine atony		
38	Carglumic acid (CARBAGLU™) Dispersible tablet	Emerge Health Pty Ltd	13/03/12
	For hyperammonaemia due to N-acetylglutamate synthase primary deficiency, hyperammonaemia due to isovaleric acidemia, hyperammonaemia due to methylmalonic acidemia and hyperammonaemia due to propionic acidemia		
39	Carmustine (GLIADEL)	Orphan Australia Pty Ltd	25/09/03
	For use as an adjunct to surgery to prolong survival in patients with malignant glioma		
40	Carmustine implants (GLIADEL wafers)	Rhone-Poulenc Rorer Australia	16/10/98
	For use as an adjunct to surgery to prolong survival in patients with recurrent glioblastoma multiforme for whom surgical resection is indicated		
41	Catridecacog Powder for injection	Novo Nordisk Pharmaceuticals Pty Ltd	22/11/11

	Routine prophylaxis for bleeding in patients with congenital Factor XIII A subunit deficiency		
42	Catumaxomab (REMOVAB) Conc. infusion	Biotech Regulatory Solutions	15/09/10
	For the treatment of patients with malignant ascites due to EpCAM-positive carcinomas		
43	Celecoxib (CELEBREX)	Searle	10/04/00
	To reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP), as an adjunct to usual care (eg endoscopic surveillance, surgery)		
44	Ceritinib (ZYKADIA) Hard capsule	Novartis P'ceuticals Australia Pty Ltd	01/09/14
	For non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive		
45	Chlormethine (VALCHLOR) Topical gel	Actelion P'ceuticals Australia Pty Ltd	25/03/15
	For the treatment of cutaneous T cell lymphoma		
46	Cholic acid oral capsules 50 mg, 250 mg	Orpharma Pty Ltd	25/07/13
	For treatment of inborn errors of bile acid synthesis responsive to treatment with cholic acid		
47	Cholic acid (ORPHACOL) Capsule	Emerge Health	04/09/14
	For treatment of inborn errors of primary bile acid synthesis due to 3 β -hydroxy- Δ 5-C27-steroid oxidoreductase (3 β -HSD) / Δ 4-3-oxosteroid 5 β -reductase (Δ 4-3-oxoR) deficiency		
48	Cladribine (LITAK)	Orphan Australia Pty Ltd	23/01/03
	For hairy cell leukaemia, lymphoplasmacytic lymphoma (Waldenstrom's macroglobulinaemia)		
49	Clobazam (FRISIUM) Tablet	Sanofi-Aventis Australia Pty Ltd	14/09/09
	For the treatment of paediatric refractory epilepsy		
50	Clofarabine (EVOLTRA) con infusion soln	Hospira Australia Pty Ltd	02/10/07
	For acute myeloid leukaemia in adults 60 years and over, for acute lymphoblastic leukaemia in paediatric patients who have relapsed or refractory after receiving at least two prior regimens		
51	Colistimethate sodium Sterile lyophilised powder 1MIU and 2MIU (colistimethate base) in single use vials for nebulisation	Phebra Pty Ltd	31/10/08
	For treatment of pseudomonas aeruginosa infections in patients with cystic fibrosis		
52	Combivir Tablets (lamivudine 150 mg & zidovudine 300 mg)	GlaxoSmithKline Australia Pty Ltd	10/07/07
	For antiretroviral combination therapy for HIV infected children under 12 years of age		
53	Crizotinib (XALKORI) 200, 250mg capsules	Pfizer Australia Pty Ltd	05/09/11
	For anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC)		
54	Cyclosporin	Delpharm Consultants Pty Ltd	17/11/04
	For the prevention of graft rejection of lung transplants		
55	Cytarabine intrathecal injection	Orphan Australia Pty Ltd	07/01/04
	For the treatment of symptomatic neoplastic meningitis		
56	Dabrafenib Capsules	GlaxoSmithKline Australia Pty Ltd	30/05/12
	For BRAF V600 mutation positive unresectable or metastatic (Stage IV) melanoma		
57	Darunavir (75, 150, 300, 600 mg tablet)	Janssen-Cilag Pty Ltd	22/08/08
	For HIV infection in paediatric patients (children and adolescents aged 6 to <18 years)		
58	Dasatinib (SPRYCEL) Tab	Bristol-Myers Squibb P'ceuticals Pty Ltd	12/10/05
	For chronic myeloid leukaemia in resistant of imatinib, Philadelphia+ acute lymphoblastic leukaemia		
59	Decitabine (DACOGEN) Injection	Janssen-Cilag Pty Ltd	16/10/12
	For adult patient's $\geq$ 65 years with newly diagnosed or secondary acute myeloid leukaemia		
60	Defactinib Tablet	Plunkett Consulting Pty Ltd	24/11/14
	For the treatment of malignant mesothelioma		
61	Deferasirox (EXJADE) Dispersible tab	Novartis P'ceuticals Australia Pty Ltd	24/09/04
	For the treatment of chronic iron overload in patients with transfusion-dependent anaemias		
62	Deferiprone (FERRIPROX)	Orphan Australia Pty Ltd	22/05/01
	For iron overload in patients with thalassaemia major/ unable to take desferrioxamine therapy		
63	Defibrotide Concentrate infusion solution	Link Healthcare	12/11/13
	For the treatment of hepatic veno-occlusive disease (VOD)		
64	Denosumab (XGEVA) Solution for injection	Amgen Australia Pty Ltd	27/06/14
	For the treatment of hypercalcaemia of malignancy that is refractory to IV bisphosphonates		
65	Denosumab (XGEVA) Injection	Amgen Australia Pty Ltd	03/10/12
	For the treatment of patients with giant cell tumours of the bone		
66	DEXPRAMIPEXOLE Tablets	Biogen Idec Australia Pty Ltd	25/10/11
	For the treatment of amyotrophic lateral sclerosis (ALS)		
67	Digoxin-Specific Antibody Fragment F(Ab) (Ovine) Powder for injection	Phebra Pty Ltd	19/05/11

	For patients with life-threatening or potentially life-threatening digoxin toxicity or overdose		
68	Dornase alpha (PULMOZYME)	Roche Products Pty Ltd	28/04/04
	For demonstrated respiratory complications in cystic fibrosis in children under 5 yrs.		
69	Drisapersen Solution for injection	GlaxoSmithKline Australia Pty Ltd	10/12/13
	For the treatment of patients with Duchenne muscular dystrophy (DMD) bearing certain mutations that are amenable to treatment with exon 51 skipping.		
70	Duodopa (LEVODOPA / CARBIDOPA) 20 & 5mg/mL intestinal gel	Abbott Products Pty Ltd	16/12/10
	For advanced idiopathic Parkinson's disease with severe fluctuations and no oral response		
71	Ecaltantide (KALBITOR) injection Solution	Link Medical Products Pty Ltd	13/05/11
	For the treatment of patients with hereditary angioedema		
72	Ecuzimab (SOLIRIS) Solution for IV infusion 300mg in 30 mL vial	Alexion Pharmaceuticals Australasia Pty Ltd	05/09/11
	For the treatment of atypical haemolytic uraemic syndrome (aHUS)		
73	Ecuzimab (SOLIRIS) Concentrated solution for IV infusion vial	Alexion Pharmaceuticals Australasia Pty Ltd	26/10/12
	For the treatment of infection - associated haemolytic uraemic syndrome		
74	Ecuzimab (SOLIRIS) solution for injection	Cedarglen Investments Pty Ltd	10/04/07
	For the treatment of paroxysmal nocturnal haemoglobinuria		
75	Efavirenz (STOCRIN)	Merck Sharp & Dohme (Australia) Pty Ltd	31/10/00
	For the treatment of HIV-1 infection in children and adolescents over the age of 3 years		
76	ELAPRASE idursulfase-rhu IV Infusion vial	Genzyme Australasia Pty Ltd	30/06/06
	For the long treatment of patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II)		
77	Eliglustat Capsules	Sanofi-Aventis Australia Pty Ltd	02/08/13
	The indication is for long term treatment of adult patients with Gaucher disease type 1 (GD1)		
78	Elosulfase-Alpha infusion Solution	BioMarin Pharmaceutical Australia Pty Ltd	05/07/13
	For the treatment of mucopolysaccharidosis IV type A (Morquio A syndrome, MPS IVA)		
79	Eltrombopag Powder for oral liquid	GlaxoSmithKline Australia Pty Ltd	29/10/14
	For the treatment of chronic idiopathic thrombocytopenic purpura (ITP)		
80	Eltrombopag olamine Tablet (REVOLADE)	GlaxoSmithKline Australia Pty Ltd	17/07/08
	For the treatment of idiopathic thrombocytopenic purpura (ITP)		
81	Emtricitabine (EMTRIVA) Tablets	Gilead Sciences Pty Ltd	23/03/12
	For the treatment of HIV-1 Infection in paediatric patients aged 12 to 17 years inclusive		
82	Epoprostenol Lyophilized powder	Actelion P'ceuticals Australia Pty Ltd	17/01/12
	Treatment of pulmonary arterial hypertension		
83	Epoprostenol sodium (FLOLAN)	Glaxo Wellcome Australia Ltd	06/12/99
	For the long term treatment of primary pulmonary hypertension in New York Heart Association (NYHA) Class III and IV patients		
84	Epoprostenol sodium (FLOLAN)	GlaxoSmithKline Australia Pty Ltd	05/04/06
	For the treatment of Pulmonary Arterial Hypertension (PAH) associated with collagen vascular diseases, in New York Heart Association functional class III and class IV patients		
85	Eptacog alfa (NOVOSEVEN)	Novo Nordisk Pharmaceuticals Pty Ltd	14/01/05
	For bleeding episodes with congenital Factor VII deficiency/ Glanzmann's Thrombasthenia		
86	Ecaltantide Solution for Injection	Link Medical Products Pty Ltd	13/05/11
	For the treatment of patients with hereditary angioedema		
87	Ecuzimab (rmc) (SOLIRIS) Solution for intravenous infusion 300mg in 30 mL vial	Alexion Pharmaceuticals Australasia Pty Ltd	05/09/11 & 26/10/12
	For atypical haemolytic uraemic and infection - associated haemolytic uraemic syndrome		
88	Ecuzimab (SOLIRIS) solution for injection E	Cedarglen Investments Pty Ltd	10/04/07
	For the treatment of paroxysmal nocturnal haemoglobinuria		
89	Efavirenz (STOCRIN)	Merck Sharp & Dohme (Australia) Pty Ltd	31/10/00
	For the treatment of HIV-1 infection in children and adolescents over the age of 3 years		
90	ELAPRASE idursulfase-rhu IV Infusion vial	Genzyme Australasia Pty Ltd	30/06/06
	For treatment of patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II)		
91	Eliglustat Capsules	Sanofi-Aventis Australia Pty Ltd	02/08/13
	The indication is for long term treatment of adult patients with Gaucher disease type 1 (GD1)		
92	Elosulfase-Alpha infusin Solution	BioMarin P'ceutical Australia Pty Ltd	05/07/13
	For the treatment of mucopolysaccharidosis IV type A (Morquio A syndrome, MPS IVA)		

93	Eltrombopag Powder for oral liquid	GlaxoSmithKline Australia Pty Ltd	29/10/14
	For the treatment of chronic idiopathic thrombocytopenic purpura (ITP)		
94	Eltrombopag olamine Tablet (REVOLADE)	GlaxoSmithKline Australia Pty Ltd	17/07/08
	For the treatment of idiopathic thrombocytopenic purpura (ITP)		
95	Emtricitabine Tablets	Gilead Sciences Pty Ltd	23/03/12
	For the treatment of HIV-Infection in paediatric patients aged 12 to 17 years inclusive		
96	Epoprostenol Lyophilized powder	Actelion P'ceuticals Australia Pty Ltd	17/01/12
	Treatment of pulmonary arterial hypertension		
97	Epoprostenol sodium (FLOLAN)	Glaxo Wellcome Australia Ltd	06/12/99
	For the long term treatment of primary pulmonary hypertension in New York Heart Association (NYHA) Class III and IV patients		
98	Epoprostenol sodium (FLOLAN)	GlaxoSmithKline Australia Pty Ltd	05/04/06
	For the treatment of Pulmonary Arterial Hypertension (PAH) associated with collagen vascular diseases, in New York Heart Association functional class III and class IV patients		
99	Eptacog alfa (NOVOSEVEN)	Novo Nordisk Pharmaceuticals Pty Ltd	14/01/05
	For bleeding episodes with congenital Factor VII deficiency/ Glanzmann's Thrombasthenia		
100	Equine Antithymocyte Immunoglobulin (ATGAM) Injection solution	Pfizer Australia Pty Ltd	08/10/15
	For the treatment of aplastic anaemia		
101	Erlotinib Tablets (TARCEVA)	Roche Products Pty Ltd	14/04/11
	For the treatment of advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer (NSCLC) with activating EGFR mutations		
102	Ethyl eicosapentaenoate	Orphan Australia Pty Ltd	15/07/04
	For the treatment of Huntington's Disease		
103	Everolimus (AFINITOR) 5 , 10 mg tab	Novartis P'ceuticals Australia Pty Ltd	17/07/08
	For the treatment of advanced renal cell carcinoma (RCC)		
104	Everolimus (AFINITOR) 5 , 10 mg tab	Novartis P'ceuticals Australia Pty Ltd	26/07/10
	For tuberous sclerosis complex, SEGA, angiomyolipoma and lymphangiomyomatosis		
105	Everolimus Capsules (AFINITOR)	Novartis Pharmaceuticals Australia Pty Ltd	19/07/12
	For the treatment of pancreatic neuroendocrine tumours		
106	Ex vivo cultured adult human mesenchymal stem cells (PROCHYMAL) Solution for IV infusion	Delpharm Consultants Pty Ltd	08/11/10
	For acute Graft versus Host Disease (aGvHD) with Haematopoietic Stem Cell Transplantation		
107	Extraneal brand of icodextrin 7.5% w/v dialysis soln	Baxter Healthcare Pty Ltd	26/09/01
	For alternative in dialysis solutions for long dwell exchange in patients with peritoneal dialysis		
108	Factor eight inhibitor bypassing activity (FEIBA VH)	Baxter Healthcare Pty Ltd	20/05/04
	For haemophilia A patients (Factor VIII inhibitor), haemophilia B (Factor IX inhibitor)		
109	Factor VIII[rDNA], (KOGENATE FS, SF, HELIXATE FS, SF)	Bayer Australia Limited	17/06/99
	For prophylaxis of bleeding in haemophilia A (congenital factor VIII deficiency) in previously treated and untreated patients, in patients with Factor VIII inhibitors (neutralising antibodies) who continue to respond to Kogenate FS (ie in whom haemostasis is achieved) [Kogenate FS does not contain von Willebrand's Factor and is not indicated in von Willebrand's disease]		
110	Factor XI Concentrate (human coagulation factor XI) Powder for injection	CSL Behring (Australia) Pty Ltd	12/12/14
	For patient bleeding with either congenital factor XI deficiency/ acquired factor XI inhibitors		
111	Fedratinib Capsules	Sanofi-Aventis Australia Pty Ltd	
	For primary myelofibrosis, of post-polycythaemia vera myelofibrosis and of post-essential thrombocythaemia myelofibrosis		
112	FEIBA NF factor 8 inhibitor bypassing fraction 500U powder For injection vial with diluent vial	Baxter Healthcare Pty Ltd	22/06/04
	For second line therapy of spontaneous bleeding episodes and in haemophilia A or B surgery with inhibitors, for whom recombinant human factor VIIa has failed, is contraindicated or has been associated with unacceptable adverse effects		
113	Fingolimod (GILENYA, FILOSIR & FYNEFTA) Capsule	Novartis Pharmaceuticals Australia Pty Ltd	24/11/14
	For Primary Progressive Multiple Sclerosis to delay the progression of physical disability		
114	Fluocinolone acetonide intravitreal implant	Bausch & Lomb (Australia) Pty Ltd	12/12/05

	For treatment of chronic, non-infectious uveitis affecting the posterior segment of the eye		
115	Fomepizole (TBA) Injection	AFT Pharmaceuticals Pty Ltd	06/01/15
	For the treatment of ethylene glycol and methanol poisonings		
116	Fomivirsen sodium (VITRAVENE)	Ciba Vision Australia Pty Ltd	01/04/99
	For the local treatment of cytomegalovirus (CMV) retinitis in patients with AIDS		
117	Forodesine (FOSODINE) 100mg tablets and 5 mg/mL solution for injection	Mundipharma Pty Ltd	24/03/09
	For the treatment of cutaneous T-cell lymphoma (CTCL)		
118	Factor eight inhibitor bypassing activity (FEIBA VH)	Baxter Healthcare Pty Ltd	20/05/04
	For haemophilia A patients, Factor VIII inhibitor and haemophilia B, Factor IX inhibitor		
119	G17 DT Immunogen IM injection	Orion Clinical Services (Australia) Ptd Ltd	29/11/02
	For the treatment of gastric and pancreatic cancers		
120	G17DT (IMMUNOGEN)	Kendle R & D Pty Ltd	20/11/03
	For the treatment of gastric and pancreatic cancers		
121	Galsulfase rch (NAGLAZYME) injection soln	Cedarglen Investments Pty Ltd	18/01/06
	For long-term enzyme replacement therapy with mucopolysaccharidosis type VI (MPS VI)		
122	Gemtuzumab ozogamicin (MYLOTARG)	Wyeth Australia Pty Ltd	25/10/00
	For the treatment of acute myeloid leukaemia		
123	GENOTROPIN brand of somatropin (rbe) Powder for injection	Pfizer Australia Pty Ltd	09/02/07
	For the treatment of growth disturbance in children with chronic renal insufficiency		
124	Histamine dihydrochloride	FH Faulding and Co Limited	25/10/00
	For the treatment of metastatic melanoma (stage IV)		
125	Human fibrinogen (RIASTAP) Powder for injection IV infusion	CSL Limited	15/05/09
	For the treatment of congenital fibrinogen deficiency		
126	Human hepatitis B immunoglobulin (HEPATECT CP) Solution for intravenous infusion	Bioregulatory Consulting	03/06/10
	For re-infection of a transplanted liver who carry the surface antigen of the hepatitis B virus		
127	Human hepatitis B Ig (HEPATECT CP)	Link Medical Products Pty Ltd	27/08/09
	Prophylaxis of re-infection of a transplanted liver having surface antigen of hepatitis B virus		
128	Human plasma-derived protein C (CEPROTIN)	Baxter Healthcare Pty Ltd	23/01/03
	For the treatment of severe congenital protein C deficiency		
129	Humatrope brands of somatropin powder SC/IM Inj	Eli Lilly Australia Pty Ltd	13/06/02
	For the treatment of growth failure in children born small for gestational age		
130	Ibuprofen (PEDEA) Solution for Injection	Emerge Health Pty Ltd	29/05/13
	For the treatment of haemodynamically significant patent ductus arteriosus in preterm newborn infants less than 34 weeks of gestational age		
131	Icatibant (FIRAZYR) Solution for injection	Shire Australia Pty Ltd	10/10/13
	Treatment of angiotensin-converting-enzyme inhibitor (ACE-1) induced angioedema		
132	Icatibant (FIRAZYR) 30mg/3mL pre-filled syringe	Shire Australia Pty Ltd	12/02/09
	For the treatment of acute attacks of hereditary angioedema		
133	Icodextrin 7.5% extraneal peritoneal dialysis soln	Baxter Healthcare Pty Ltd	16/10/98
	For life threatening, End Stage Renal Disease, for those patients who have been identified as requiring the specialised treatment of peritoneal dialysis, and who have subsequently demonstrated significantly reduced ultrafiltration with intraperitoneal hyperosmolar glucose		
134	Iloprost trometamol (ILOMEDIN)	Schering P/L	13/10/00
	For the treatment of primary pulmonary hypertension		
135	Imatinib mesylate (GLIVEC) Tablets and capsules	Novartis Australia Pty Ltd	12/05/11
	For the treatment of pulmonary arterial hypertension		
136	Imatinib mesylate (GLIVEC)	Novartis Pharmaceuticals Australia Pty Limited	12/08/02
	For the treatment of chronic myeloid leukaemia		
137	Imatinib mesylate (GLIVEC)	Novartis Pharmaceuticals Australia Pty Limited	10/12/01
	For the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumours		
138	Imatinib mesylate (GLIVEC) 5 mg & 100 mg capsules and 100 mg & 400 mg tablets	Novartis Pharmaceuticals Australia Pty Limited	01/10/08
	For use as adjuvant therapy For gastrointestinal stromal tumour (GIST)		
139	Imatinib mesylate (GLIVEC)	Novartis Pharmaceuticals Australia Pty Limited	03/05/06
	For Philadelphia-positive acute lymphoblastic leukaemia, Dermatofibrosarcoma protuberans (DFSP)		

	Myelodysplastic / myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements Idiopathic hypereosinophilic syndrome including acute and chronic eosinophilic leukaemia Systemic mastocytosis without the D816V c-kit mutation		
140	Imiglucerase (CEREZYME)	Genzyme Australasia Pty Ltd	16/10/98
	For enzyme replacement for patients with a confirmed diagnosis of Gaucher's disease		
141	Immunoglobulin - antithymocyte (rabbit) (ATG-Fresenius) Solution for IV injection	Dutec Diagnostics Pty Ltd	18/06/10
	For the prevention of graft versus host disease in allogeneic haematopoietic stem cell transplantation		
142	Indinavir sulfate (CRIXIVAN)	Merck Sharp & Dohme (Australia) Pty Ltd	3/10/00
	For the treatment of HIV-1 infection in children and adolescents over the age of 3 years.		
143	Infliximab	Schering-Plough Pty Ltd	12/10/05
	For reducing the signs and symptoms in patients with moderately to severely active polyarticular-course juvenile rheumatoid arthritis (JRA) who have had an inadequate response to methotrexate		
144	Ivacaftor (KALYDECO) Tablets	Vertex Pharmaceuticals Australia Pty Ltd	14/08/14
	For the treatment of cystic fibrosis (CF) in patients who have a CFTR mRNA Splice Site (Class V) mutation or a residual function CFTR mutation in the CFTR gene.		
145	Ivacaftor (KALYDECO) film coated 150mg tablet	Vertex Pharmaceuticals Australia Pty Ltd	14/03/12
	For cystic fibrosis (CF) in patients who have a gating or an R117H mutation in the CFTR gene		
146	Ivacaftor (KALYDECO) Granules	Vertex Pharmaceuticals (Australia) Pty Ltd	24/11/14
	For the treatment of cystic fibrosis (CF) in patients aged 2 to 5 years old who have a gating (class III) or R117H, Residual or mRNA Splice Site (Class V) mutation in the CFTR gene		
147	Ivacaftor (VX-770) Tablets	Vertex Pharmaceuticals Australia Pty Ltd	22/09/14
	In combination with Lumacaftor (VX-809) for cystic fibrosis in patients who are homozygous for F508del mutation in the cystic fibrosis transmembrane conductance regulator gene		
148	Lamivudine (ZEFFIX 3TCTM)	Glaxo Wellcome Australia Ltd	11/01/01
	For use in combination with other antiretroviral agents for HIV infection in children		
149	Lamivudine (ZEFFIX)	GlaxoSmithKline Australia Pty Ltd	19/06/02
	For children (2 years & above), adolescents with chronic hepatitis B and evidence of hepatitis B virus (HBV) replication. This indication is based on changes in serological and histological markers in clinical studies up to 18 months duration in patients with compensated liver disease		
150	Lanreotide (SOMATULINE AUTOGEL)	Ipsen Pty Ltd	19/03/04
	For carcinoid syndrome associated with carcinoid tumours and the symptoms of VIPomas		
151	Laronidase (ALDURAZYME)	Genzyme Australasia Pty Ltd	08/08/01
	For the treatment of mucopolysaccharidosis		
152	Leflunomide	Aventis Pharma Pty Ltd	08/04/04
	For treatment of polyarticular course juvenile rheumatoid arthritis in patient 3-17 years of age		
153	Lenalidomide (REVLIMID) Capsule	Celgene Pty Ltd	28/01/15
	For the treatment of patients with mantle cell lymphoma		
154	Lenalidomide (REVLIMID) Capsules	Celgene Pty Ltd	06/09/06
	For previously treated multiple myeloma patients in combination with dexamethasone & patients of transfusion-dependent anaemia due to low/ intermediate-1 risk myelodysplastic syndromes with a deletion 5q cytogenetic abnormality with/without cytogenetic abnormalities		
155	Lenvatinib Mesilate Capsules	Eisai Australia Pty Ltd	27/11/14
	For the patients with progressive, radioiodine - refractory differentiated thyroid cancer		
156	Lepirudin (REFLUDAN) 50mg powder for injection	Celgene Pty Ltd	09/10/08
	For the treatment of acute heparin associated thrombocytopenia (HAT) type II patients with thrombocytopenia or thromboembolic complications and for the prophylaxis of thrombocytopenia or new thromboembolic events in patients with a history of HAT type II and a need for effective antithrombotic measures (e.g. during open heart surgery)		
157	Lamivudine (ZEFFIX 3TCTM)	Glaxo Wellcome Australia Ltd	11/01/01
	For combination with other antiretroviral agents for the treatment of HIV infection in children		
158	Leuprorelin Acetate (LUCRIN) Injection	AbbVie Pty Ltd	19/12/12
	For the treatment of Central Precocious Puberty (CPP)		
159	Leuprorelin Acetate (LUCRIN) Injection	Abbott Australasia Pty Ltd	22/07/11
	For Central Precocious Puberty		
160	Linezolid (ZYVOX)	Pharmacia Australia Pty Ltd	09/01/03
	For the treatment of children, from birth to less than 18 years, with suspected or proven infections due to		

	organisms resistant to multiple classes of antibiotics, including methicillin resistant Staphylococcus species and vancomycin resistant Enterococcus species		
161	Lonoctocog Alfa Powder for reconstitution and injection	CSL Behring Australia	26/11/15
	For the treatment in adults and children with haemophilia A (congenital FVIII deficiency)		
162	Lumacaftor (VX-809) Tablets	Vertex Pharmaceuticals (Australia) Pty Ltd	22/09/14
	In combination with Ivacaftor for cystic fibrosis (CF) in patients who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene		
163	Lenalidomide (REVLIMID) Capsule	Celgene Pty Ltd	28/01/15
	For the treatment of patients with mantle cell lymphoma		
164	M-iodobenzyl [123I] guanidine injection (MIBGEN)	Australian Nuclear Science and Technology Organisation (ANSTO)	15/08/02
	For diagnostics of tumours originating embryologically stems from the neural crest like neuroblastomas, pheochromocytomas, paragangliomas, chemodectomas and ganglioneuromas. Detection, staging and follow-up on therapy of neuroblastomas. Diagnosis of neural crest tumours, arising from the adrenal medulla, by evaluation of the uptake of iobenguane		
165	Macitentan Film coated tablets	Actelion Pharmaceuticals Australia Pty Ltd	13/07/12
	For the treatment of pulmonary arterial hypertension		
166	Mannitol (BRONCHITOL) 40mg powder for inhalation	Pharmaxis Ltd	16/04/09
	For the cystic fibrosis to improve lung function and reduce pulmonary exacerbations		
167	Mecasermin [rhIGF-1] injection (INCRELEX) 10mg/ml in 40 mg vial Solution for subcutaneous injection	Ipsen Pty Ltd	01/07/08
	For the long-term treatment of growth failure in children and adolescents with severe primary insulin-like growth factor-1 deficiency (severe primary IGFD)		
168	Melphalan (ALKERAN INJECTION)	Glaxo Wellcome Australia Ltd	22/03/99
	For the treatment of multiple myeloma in patients For whom oral therapy is inappropriate.		
169	Mepolizumab injection powder	GlaxoSmithKline Australia Pty Ltd	17/03/08
	For the treatment of patients with hypereosinophilic syndrome		
170	Mercaptamine Hydrochloride (Cystadrops) eye drops	Emerge Health Pty Ltd	17/07/15
	For the corneal cystine deposits in cystinosis in adults/ children over 2 years of age		
171	Mercaptopurine Oral suspension	Ballia Holdings Pty Ltd	14/12/12
	For the treatment of Acute Lymphoblastic Leukaemia in Children		
172	Mercaptopurine (XALUPRINE) Oral Susp ⁿ	Link Medical Products Pty Ltd	15/08/12
	For the treatment of Acute Lymphoblastic Leukaemia in paediatric patients		
173	Methotrexate Oral suspension	Ballia Holdings Pty Ltd	14/12/12
	For the treatment of Acute Lymphoblastic Leukaemia in Children		
174	Methoxsalen (UVADEX) Injection solution	Terumo BCT Australia Pty Limited	15/09/15
	For the treatment of Cutaneous T- cell lymphomas (CTCL)		
175	Methoxsalen (UVADEX) Injection solution	Terumo BCT Australia Pty Ltd	01/10/15
	For the treatment of Graft-versus-host disease following allogeneic HSC transplantation		
176	Midazolam (MIDAZOLAM BUCCAL LIQUID) 10mg in 1mL liquid via an oral syringe into the buccal cavity	Phebra Pty Ltd	01/06/09
	For the treatment of status epilepticus in children and adolescents aged 0 to 19 years		
177	Miglustat (ZAVESCA) Capsules	Actelion Pharmaceuticals Australia Pty Ltd	11/07/05
	For the treatment of mild to moderate type 1 Gaucher disease		
178	Miglustat (ZAVESCA) Capsules	Actelion Pharmaceuticals Australia Pty Ltd	08/07/08
	For the treatment of Niemann-Pick disease Type C		
179	Mometasone furoate	RhinoScience Pty Ltd	14/09/11
	For the treatment of persistent post-surgical eosinophilic polypoid chronic rhinosinusitis		

Table.2 some others orphan drugs (continue from table 1)

180	MultiBic	Fresenius Medical Care Australia Pty Ltd	16/08/04
	For the treatment of acute renal failure in intensive care units		
181	Mycophenolic acid 180 mg, 360 mg enteric coated tablets	Novartis Pharmaceuticals Australia Pty Limited	11/01/10
	For induction and maintenance treatment of lupus nephritis.		
182	Nandrolone decanoate (DECA-DURABOLIN 100)	Organon	30/12/99

	For patients who proven HIV infection who have lost at least 5% of their usual body weight		
183	Nanoparticle albumin-bound paclitaxel Powder for injection (ABRAXANE)	Abraxis BioScience Australia Pty Ltd	01/12/09
	For treatment of pancreatic cancer		
184	Natalizumab (TYSABRI) Concentrated injection solution	Nitecs Pty Limited	01/07/14
	For the treatment of relapsing-remitting multiple sclerosis in children aged 10-17 years		
185	Nevirapine (VIRAMUNE)	Boehringer Ingelheim Pty Limited	11/03/03
	For the prevention of mother to child transmission of HIV-1 in pregnant women who are not taking antiretroviral therapy at time of labour		
186	Nilotinib (TASIGNA) 200mg capsules blister packs	Novartis Pharmaceuticals Australia Pty Limited	09/06/06
	For treatment of patients with chronic myeloid leukaemia		
187	Nitazoxanide (CRYPTAZ)	Tri-Med Distributors	13/10/99
	For the treatment of patients with AIDS who are positive for a stool test for cryptosporidiosis		
188	Nitisinone (ORFADIN) 2mg, 5mg and 10mg capsules	Orphan Australia Pty Ltd	30/10/08
	For the treatment of hereditary tyrosinaemia type 1		
189	Nitric oxide (INOMax) 800 ppm medicinal gas	Delpharm Consultants Pty Ltd	11/05/06
	For the treatment of Persistent Pulmonary Hypertension (PPH) in neonates		
190	Nitric Oxide (INOMax)	Ikaria Australia Pty Ltd	11/09/13
	It is indicated, in conjunction with ventilator support as part of the treatment of peri-and post-operative pulmonary hypertension in newborn infants, infants and toddlers, children and adolescents, ages 0-17 years in conjunction with heart surgery, in order to selectively decrease pulmonary arterial pressure and improve right ventricular function and oxygenation.		
191	Normal immunoglobulin (human) IV injection	Baxter Healthcare Pty Ltd	29/11/12
	For the treatment of immunomodulatory therapy in multifocal motor neuropathy (MMN)		
192	Normal immunoglobulin (INTRAGLOBIN F)	Medical Dynamics Australia Pharma	27/02/01
	For Primary Immune Deficiency Syndromes Kawasaki disease Paediatric HIV infection / Congenital Allogeneic Bone Marrow Transplantation Idiopathic Thrombocytopaenic Purpura		
193	NOVOSEVEN brand of eptacog alfa Inj Powder	Novo Nordisk Pharmaceuticals Pty Ltd	30/01/07
	For postpartum haemorrhage in patients unresponsive to standard obstetrical management, oxytocic drugs and standard blood component therapy prior to major invasive therapy		
194	NSC-631570 (UKRAIN)	Mrs Aleksandra Harasemcuk	08/06/04
	For the treatment of pancreatic cancer		
195	Oblimersen (GENASENSE)	Aventis Pharma Pty Ltd	25/09/03
	For the treatment of patients with stage IV malignant melanoma.		
196	Oblimersen (GENASENSE) Solution for infusion	ICON Clinical Research	10/01/08
	For the treatment of patients with stage IV malignant melanoma.		
197	Oblimersen (GENASENSE)	Kendle R & D Pty Ltd	24/11/06
	For the treatment of patients with stage IV malignant melanoma.		
198	Octocog alfa rch (ADVATE) IV inj	Baxter Healthcare Pty Ltd	19/02/07
	Is indicated for use in haemophilia A for prevention and control of haemorrhagic episodes.		
199	Octocog alfa rch (ADVATE) powder for injection vials with diluent	Baxter Healthcare Pty Ltd	10/03/04
	Is indicated for use in haemophilia A for prevention and control of haemorrhagic episodes		
200	Octreotide (SANDOSTATIN / SANDOSTATIN LAR) 500µg/1mL, 50µg/1mL, 100µg/1mL, injection ampoule	Novartis Pharmaceuticals Australia Pty Limited	15/05/09
	For patients with functional gastro-entero-pancreatic neuroendocrine tumours (GEP/NETs), Glucagonomas, Gastrinomas/Zollinger-Ellison syndrome, Insulinomas, for pre-operative control of hypoglycaemia and for maintenance therapy, GRFomas		
201	Octreotide (SANDOSTATIN LAR) 10, 20 and 30 mg prefilled syringe composite packs	Novartis Pharmaceuticals Australia Pty Limited	15/09/10
	For the treatment of patients with advanced neuroendocrine tumours of the midgut or unknown primary tumour location.		
202	Olaparib Capsule	AstraZeneca Pty Ltd	15/01/14
	monotherapy for treatment of adult patients with platinum-sensitive relapse BRCA-mutated ovarian, fallopian tube/ primary peritoneal cancer, response to platinum-based chemotherapy		

203	Oprelvekin (IL-11) (NEUMEGA)	Wyeth Australia Pty Ltd	07/04/99
	For the prevention of severe chemotherapy-induced thrombocytopenia with non-myeloid malignancies who are judged by their physician to be at risk of severe thrombocytopenia		
204	Ovine anti-colchicine polyclonal antibody fragments Ampoules	Microfarm Limited	04/07/11
	As an antidote in cases of acute colchicine toxicity		
205	Panobinostat (FARYDAK) Capsule	Novartis Pharmaceuticals Australia Pty Ltd	21/01/14
	For relapsed multiple myeloma (MM), or relapsed-and-refractory MM treatment		
206	Panobinostat (TBA) Capsule	Novartis Pharmaceuticals Australia Pty Limited	24/03/09
	For the treatment of cutaneous T-cell lymphoma (CTCL)		
207	Para-aminosalicylic acid (PASER) Enteric coated granules	Link Medical Products Pty Ltd	11/02/15
	For use as part of an appropriate combination therapy for multi-drug resistant tuberculosis		
208	Pasireotide (SIGNIFOR LAR) Modified release injection	Novartis Pharmaceuticals Australia Pty Limited	29/10/13
	For the treatment of patients with Acromegaly for whom medical therapy is appropriate		
209	Pasireotide (SIGNIFOR) Inj Solution	Novartis Pharmaceuticals Australia Pty Ltd	03/08/11
	For the treatment of patients with Cushing's disease for whom medical therapy is appropriate		
210	Pazopanib (PATORMA) 200mg and 400mg film coated tablets	GlaxoSmithKline Australia Pty Ltd	24/03/09
	For the treatment of advanced and/or metastatic renal cell carcinoma (RCC)		
211	Pazopanib (VOTRIENT) Tablets	GlaxoSmithKline Australia Pty Ltd	13/05/11
	For the treatment of advanced (unresectable and/or metastatic) soft tissue sarcoma		
212	PEDITRACE and ADDAMEL N brands of trace element IV soln	Fresenius Medical Care Australia Pty Ltd	08/11/01
	For the supply of basal trace element requirements in infants/children and adults, respectively		
213	Pegaspargase (ONCASPAR) Inj	Link Medical Products	24/04/15
	For the treatment of patients with acute lymphoblastic leukaemia (ALL)		
214	Pegaspargase (PEGASPAR)	Rhone-Poulenc Rorer Australia	20/01/99
	For the treatment of acute lymphoblastic leukaemia who require L-asparaginase in their treatment regimen, but have developed hypersensitivity to the native forms of L-asparaginase		
215	Peginterferon alfa-2a and ribavirin (PEGASYS RBV) Injection	Roche Products Pty Ltd	15/06/12
	For the treatment of chronic hepatitis C in treatment-naïve children and adolescents 5 years of age and older with compensated liver disease		
216	Peginterferon alfa-2b and ribavirin (PEGATRON COMBINATION THERAPY) Peginterferon alfa-2b; 50, 80, 100, 120 and 150 microgram powder for injection and ribavirin 200 mg capsule.	Schering-Plough Pty Ltd	15/01/10
	For the treatment of chronic hepatitis C in children = 27 kg with compensated liver disease and who have not received previous interferon treatment		
217	Pegvisomant (rbe) (SOMAVERT) Powder for injection with diluent	Pharmacia Australia Pty Ltd	09/10/03
	For the treatment of patients with acromegaly		
218	Pegylated liposomal doxorubicin (CAELYX) Injection vial 20 ml/10mL and 50mg/25mL	Schering-Plough Pty Ltd	05/07/07
	In combination for progressive multiple myeloma in patients who have received at least one prior therapy and who have undergone or are unsuitable for bone marrow transplantation		
219	Pegylated liposomal doxorubicin hydrochloride (CAELYX)	Schering-Plough Pty Ltd	28/02/00
	For advanced ovarian cancer in first-line platinum-based chemotherapy failed women		
220	Pentostatin (NIPENT) 10mg powder for injection and powder for solution for infusion	Hospira Australia Pty Ltd	15/05/09
	For the treatment of Hairy Cell Leukaemia (HCL)		
221	Peritoneal dialysis solution (GAMBROSOL BIO)	Gambro	23/12/99
	For the treatment of patients receiving peritoneal dialysis who may need to change from peritoneal dialysis because of decreased ultrafiltration or infusion pain.		
222	Peritoneal dialysis solution with 1.1% amino acids	Baxter Healthcare Pty Ltd	04/03/99

	(Nutrineal-PD4)		
	For the treatment of protein malnutrition in patients with End Stage Renal Disease (ESRD) who are maintained by peritoneal dialysis		
223	Pertuzumab Concentrate for IV infusion	Roche Products Pty Ltd	19/01/12
	For the treatment of HER-2 positive metastatic (Stage IV) or locally recurrent breast cancer		
224	PHYSIONEAL 40 brand of peritoneal dialysis solutions containing 13.6mg/mL, 22.7mg/mL or 38.7mg/mL glucose	Baxter Healthcare Pty Ltd	08/05/02
	For peritoneal dialysis		
225	Piracetam (NOOTROPIL)	UCB Pharma	04/05/00
	as "add-on" treatment of cortical myoclonus		
226	Plerixafor (MOZOBIL) Injection	Genzyme Australasia Pty Ltd	20/10/08
	For the mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent transplantation		
227	Pomalidomide Capsules	Celgene Pty Ltd	17/10/12
	For the treatment of multiple myeloma in patients who have failed two or more prior therapies		
228	Ponatinib (tradename TBA) 15mg and 45mg immediate film coated tab	ARIAD Pharmaceutical (Australia) Pty Ltd	14/05/13
	For the treatment of acute lymphoblastic leukaemia and adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) that is resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy		
229	Poractant alfa (CUROSURF)	Douglas Pharmaceuticals Australia Ltd	11/04/03
	For the treatment of Respiratory Distress Syndrome (RDS) in preterm infants and for prophylactic use in preterm infants at risk for RDS		
230	Pralatrexate (FOLOTYN) Solution for Injection	Mundipharma Pty Ltd	05/09/11
	For the treatment of adult patients with relapsed or refractory peripheral T-cell lymphoma (nodal, extranodal and leukaemic/disseminated)		
231	Pralidoxime chloride	Ophthalmic Laboratories Pty Ltd (T/A Pharmalab)	03/05/06
	For the treatment of poisoning due to those pesticides and chemicals of the organophosphate class which have anticholinesterase activity and the control of overdosage of the anticholinesterase drugs used in the treatment of myasthenia gravis		
232	Propranolol hydrochloride Oral soln	Pierre Fabre Medicament Australia Pty Ltd	03/10/12
	For the treatment of proliferating infantile hemangiomas requiring systemic therapy		
233	Rabies immunoglobulin Pasteurised (IMOGAM RAGE)	CSL Limited	16/10/98
	To treat subjects who are thought to have been exposed to rabies virus, especially cases of major exposure, in accordance with WHO recommendations		
234	Raltegravir (ISENTRRESS) Tablet	Merck Sharp & Dohme (Australia) Pty Ltd	05/09/11
	Treatment of HIV-1 infection in children and adolescents from 2 to 18 years of age		
235	Ramucirumab (Cyramza) Solution for infusion	Eli Lilly Australia Pty Ltd	17/09/13
	The indication is for the treatment of patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma after prior chemotherapy		
236	Ranpirinase (ONCONASE)	Delpharm Consultants Pty Ltd	22/03/05
	For the treatment of malignant mesothelioma		
237	Rasburicase (FASTURTEC)	Sanofi-Synthelabo Aust Pty Ltd	23/03/01
	For the treatment and prophylaxis of acute hyperuricaemia in patients with haematological malignancy at risk of a rapid tumour lysis		
238	Recombinant factor IX (BENEFIX)	Wyeth Australia Pty Ltd	16/10/98
	For the prevention of haemorrhagic episodes and for routine and surgical prophylaxis in patients with haemophilia B (congenital factor IX deficiency or Christmas disease)		
239	Recombinant factor IX (FIXTERA) IV injection	Baxter Healthcare Pty Ltd	03/10/12
	For control and prevention of haemorrhagic episodes and for routine and surgical prophylaxis in patients with haemophilia B (congenital factor IX deficiency or Christmas disease)		
240	Recombinant factor VIII (ADVATE)	Baxter Healthcare Pty Ltd	10/03/03
	For prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)		
241	Recombinant factor VIII (rDNA)(cho) (REFACTO)	Wyeth Australia Pty Ltd	18/01/99
	For the control of haemorrhagic episodes and for routine and surgical prophylaxis in patients with haemophilia A (congenital factor VIII deficiency or classical haemophilia)		
242	Recombinant human coagulation factor IX Fc fusion protein (rFIXFc) Lyophilised powder for IV inj	Biogen Idec Australia Pty Ltd	20/09/12

	For the treatment of the control and prevention of haemorrhagic episodes in patients with haemophilia B (congenital factor IX deficiency or Christmas disease), including the control and prevention of bleeding in surgical settings		
243	Recombinant human coagulation factor VIII Fc fusion protein Lyophilized powder for reconstitution IV injection	Biogen Idec Australia Pty Ltd	22/02/13
	For the treatment of control and prevention (including routine prophylaxis) of bleeding episodes in adults and children with haemophilia A		
244	Recombinant human iduronate-2-sulfatase	Genzyme Australasia Pty Ltd	18/01/06
	For long-term treatment of patients with Hunter syndrome		
245	Retroviral γ c cDNA-containing vector (IMMUGENE)	AVAX Australia Pty Ltd	21/08/02
	For the treatment of severe combined immunodeficiency X1 (SCID X1). Status: The orphan drug designation for this product was withdrawn on 2 October 2002		
246	RidaForolimus Gastro resistant tablet	Merck Sharp & Dohme Pty Ltd	14/09/11
	Treatment of metastatic soft tissue sarcoma or bone sarcoma.		
247	Rifaximin (XIFAXAN) Tablets	Norgine Pty Ltd	24/02/11
	For the prevention of the recurrence of Hepatic Encephalopathy in adults		
248	Riluzole (RILUTEK)	Aventis Pharma Pty Ltd	03/05/01
	For the treatment of amyotrophic lateral sclerosis (ALS)		
249	Riociguat Immediate - release tablets	Bayer Australia Limited	16/10/12
	For the treatment of Pulmonary Arterial Hypertension (PAH) and Chronic Thromboembolic Pulmonary Hypertension (CTEPH)		
250	Rituximab Intravenous infusion (MabThera)	Roche Products Pty Ltd	13/10/11
	Induction of remission in patients with severely active anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis		
251	Romidepsin (ISTODAX) 10 mg powder for injection	Celgene Pty Ltd	27/08/10
	For the treatment of patients with peripheral T-cell lymphoma (PTCL) who have received at least one prior systemic therapy; and patients with cutaneous T-cell lymphoma (CTCL) who have received at least one prior systemic therapy		
252	Ruxolitinib (JAKAVI) Tablet	Novartis Pharmaceuticals Australia Pty Ltd	16/10/14
	For the treatment of polycythaemia vera who are resistant to or intolerant of hydroxyurea		
253	Ruxolitinib Tablet (JAKAVI)	Novartis Pharmaceuticals Australia Pty Limited	23/04/12
	For the treatment of primary myelofibrosis, post-polycythaemia vera myelofibrosis and post-essential thrombocythaemia myelofibrosis		
254	Sapropterin dihydrochloride Tablet	Serono Pty Ltd	30/08/06
	For treatment of patients with hyperphenylalaninemia		
255	Sebelipase Alfa Injection solution	Alexion Pharmaceuticals Australasia Pty Ltd	14/11/15
	For the treatment of lysosomal acid lipase (LAL) deficiency		
256	Selexipag Tablet	Actelion Pharmaceuticals Australia Pty Ltd	25/09/14
	For the treatment of pulmonary arterial hypertension		
257	Siltuximab (Sylvant) Powder for infusion	Janssen-Cilag Pty Ltd	14/08/14
	Treatment of adults with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpes virus-8 (HHV-8) negative		
258	Sirolimus Tablets 1 mg, 2 mg and 5 mg and oral solution (1 mg/mL, 60 mL)	Wyeth Australia Pty Ltd	26/03/07
	For the prevention of coronary allograft vasculopathy		
259	Sodium phenylbutrate Granules (PHEBURANE)	Orpharma Pty Ltd	13/08/14
	Treatment of urea cycle disorders		
260	Somatropin (HUMATROPE PENFIL)	Aza Research	10/06/99
	For control of growth retardation in pre-pubertal children with chronic renal insufficiency		
261	Somatropin (rbe) (GENOTROPIN)	Pharmacia & Upjohn	08/05/00
	For improvement of body composition and treatment of Prader-Wili syndrome.		
262	Somatropin (rbe) (NORDITROPIN SIMPLEXX and NORDITROPIN NORDIFLEX) Injection-solution multidose cartridges	Novo Nordisk Pharmaceuticals Pty Ltd	08/05/09
	For the treatment of prader-willi syndrome, for improvement of growth and body composition		
263	Somatropin rbe human growth hormone	Pharmacia Australia Pty Ltd	28/11/01
	For treatment of growth disturbance in pre-pubertal children with chronic renal insufficiency		
264	Somatropin rbe human growth hormone	Pharmacia Australia Pty Ltd	02/11/01

	For treatment of growth failure children born small for gestational age		
265	Somatropin (rbe) recombinant human growth hormone	Novo Nordisk P'ceuticals	22/05/02
	For severe growth failure due to intrauterine growth retardation in children 2 years of age		
266	Somatropin (SAIZEN)	Merck Serono Australia Pty Ltd	05/09/11
	Growth disturbance in pre-pubertal children with chronic renal insufficiency		
267	Sorafenib Tablet (NEXAVAR)	Bayer Australia Limited	04/03/13
	For refractory, locally, advanced treatment of metastatic differentiated thyroid cancer (DTC)		
268	Stay and seep Safe Balance sterile soln	Fresenius Medical Care Australia Pty Ltd	21/08/02
	For the management of end stage renal disease and acute renal failure		
269	Sunitinib malate (SUTENT) capsules	Pfizer Australia Pty Ltd	04/05/10
	For the treatment of pancreatic neuroendocrine tumours (pNET)		
270	Susoctocog alfa Powder for injection	Baxter Healthcare Pty Ltd	03/07/14
	For the prevention of serious bleeding episodes in patients with acquired haemophilia A		
271	Tacrolimus (PROGRAF)	Janssen-Cilag Pty Ltd	22/10/03
	For use as an immunosuppressant in lung transplantation		
272	Tacrolimus (PROGRAF) intravenous infusion	Janssen-Cilag Pty Ltd	06/09/06
	For use as an immunosuppressant in heart transplantation		
273	Tadalafil (ADCIRCA) 20mg tablets	Eli Lilly Australia Pty Ltd	21/04/10
	For pulmonary arterial hypertension (WHO Group I) to improve exercise ability		
274	Tafamidis meglumine (VYMDAQEL) cap	Pfizer Australia Pty Ltd	22/07/11
	For Transthyretin Amyloidosis in adult patients with Symptomatic Polyneuropathy		
275	Taliglucerase Powder for injection (ELELYSO)	Pfizer Australia Pty Ltd	11/03/11
	For the treatment of Gaucher's Disease		
276	Temozolomide (TEMODAL)	Schering-Plough Pty Ltd	24/07/03
	For anaplastic astrocytoma and glioblastoma multiforme in children		
277	Temozolomide (TEMODAL)	Schering-Plough Pty Ltd	21/09/04
	For the treatment of newly diagnosed anaplastic astrocytoma and glioblastoma multiforme		
278	Temsirolimus Concentrate for injection (TORISEL)	Wyeth Australia Pty Ltd	17/03/08
	For the treatment of patients with mantle cell lymphoma		
279	Tenofovir disoproxil fumarate Oral powder	Gilead Sciences Pty Ltd	13/10/09
	In combination with other antiretroviral agents for HIV-infected patients 2-17 years of age		
280	Terlipressin (GLYPRESSIN)	Ferring Pharmaceuticals Pty Ltd	21/01/04
	For the treatment of bleeding oesophageal varices and for hepatorenal syndrome		
281	Terlipressin acetate Powder for injection (LUCASSIN)	Ikaria Australia Pty Ltd	25/06/10
	For treatment of hepatorenal syndrome type 1 (HRS-1) and oesophageal variceal haemorrhage		
282	Thalidomide (THALIDOMIDE PHARMION) 50mg hard capsules	Celgene Ltd	10/10/08
	For multiple myeloma and erythema nodosum leprosum or Type II lepra reactions		
283	Thalidomide (THALOMID)	Pharmion Pty Ltd	13/03/02
	For erythema nodosum leprosum/Type II lepra reaction, relapsing/ refractory myeloma		
284	Thymoglobuline (rabbit anti-human thymocyte Ig)	Genzyme Australasia Pty Ltd	22/02/07
	For graft rejection in renal, heart transplantation and aplastic anaemia		
285	Thyrotropin alfa-rch powder for injection	Genzyme Australasia Pty Ltd	24/01/05
	used in post-thyroidectomy in thyroid remnant tissue in combination with radioactive iodine		
286	Thyrotropin alfa (THYROGEN)	Genzyme Australasia Pty Ltd	07/10/99
	For use with radioactive iodine imaging and serum thyroglobulin (Tg) testing		
287	Tipifarnib (ZARNESTRA)	Janssen-Cilag Pty Ltd	17/11/04
	For the treatment of acute myeloid leukaemia		
288	Tobramycin Powder for inhalation	Novartis P'ceuticals Australia Pty Limited	08/11/10
	For the treatment of cystic fibrosis patients infected with Pseudomonas aeruginosa		
289	Tobramycin (TOBI)solution for inhalation	Pathogenesis Corporation	29/09/98
	For the treatment of cystic fibrosis patients infected with Pseudomonas aeruginosa		
290	Tobramycin sulfate	Ophthalmic Laboratories Pty Ltd (T/A Pharnalab)	28/04/06
	For treatment of patients with cystic fibrosis infected with Pseudomonas species		
291	Tobramycin sulfate solution for inhalation	Ophthalmic Laboratories Pty Limited	18/06/04
	For the treatment of patients with cystic fibrosis infected with Pseudomonas species		
292	Tracleer (BOSENTAN)	Actelion Pharmaceuticals Australia Pty Ltd	04/10/05
	For WHO Class PH I in patients with WHO Functional Class III or IV symptoms		
293	Trametinib Tablets	GlaxoSmithKline Australia Pty Ltd	01/06/12

	For patients of BRAF V600 mutation positive unresectable or metastatic (Stage IV) melanoma		
294	Trastuzumab emtansine (RCH) Powder	Roche Products Pty Ltd	02/05/12
	For HER-2 positive breast cancer of locally recurrent, locally advanced/ metastatic (Stage IV)		
295	Tremelimumab Solution for infusion	AstraZeneca	26/11/15
	For the treatment of malignant mesothelioma		
296	Treprostinil (REMODULIN)	Orphan Australia Pty Ltd	29/05/01
	For the treatment of pulmonary arterial hypertension.		
297	Tumour necrosis factor alpha 1-a	Boehringer Ingleheim (Australia) Pty Ltd	21/10/98
	In soft tissue sarcoma in conjunction with melphalan in hyperthermic isolated limb perfusion		
298	Turoctocog alpha (RCH) Powder injection soln	Novo Nordisk P'ceuticals Pty Ltd	04/09/12
	For the treatment and prophylaxis of bleeding episodes in patients with haemophilia A.		
299	Vandetanib Tablets (brand name yet to be advised)	AstraZeneca Pty Ltd	15/09/10
	For the treatment of unresectable locally advanced or metastatic medullary thyroid cancer		
300	Velaglucerase alfa Powder for solution for injection	Shire Australia Pty Ltd	08/12/09
	For the treatment of Gaucher disease		
301	Vemurafenib Tablets	Roche Products Pty Ltd	14/04/11
	For unresectable Stage IIIC/ IV metastatic melanoma tumours harbour the BRAF mutation		
302	Vinflunine ditartrate Injection (JAVLOR)	Pierre Fabre Australia	21/01/15
	For the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen		
303	Vorinostat Capsules (ZOLINZA)	Merck Sharp & Dohme (Australia) Pty Ltd	21/10/08
	For T-cell lymphoma of progressive, persistent disease subsequent to prior systemic therapy		
304	VX-770 100 mg and 150 mg film coated tab	Voisin Consulting Australia Pty Ltd	15/06/10
	For G551D-CF transmembrane CFTR mutation or homozygous for F508del-CFTR mutation		
305	Zanolimumab Solution for infusion at 20 mg/mL	Merck Serono Australia Pty Ltd	10/07/07
	For the treatment of patients with cutaneous T cell lymphoma		
306	Zemaira Brand of alpha proteinase inhibitor (Human) injection Powder	CSL Ltd	08/08/07
	For the treatment of chronic IV augmentation, and alpha1-proteinase inhibitor deficiency		
307	Zoledronic acid (ZOMETA)	Novartis Pharmaceuticals Australia Pty Limited	08/05/09
	For the treatment of paediatric patients with severe osteogenesis imperfecta (OI)		

Innovation and the Orphan Drug Act, 1983-2009

The Orphan Drug Act provided manufacturers with three primary incentives: federal funding of grants and contracts to perform clinical trials of orphan products; a tax credit of 50 percent of clinical testing costs; and an exclusive right to market the orphan drug for 7 years from the date of marketing approval. The market exclusivity incentive protects orphan drug manufacturers from competition for 7 years, which allows greater discretion in pricing.^[2] Additional benefits available to sponsors of orphan-designated products include close coordination with the Food and Drug Administration throughout the drug's development, priority FDA review, and a waiver of drug application fees. The legislation initially targeted drugs for which there was "no reasonable expectation" that sale in the United States could support development of the drug. Because that criterion was difficult to assess and manufacturers were wary of showing the government their internal financial projections,^[3] An amendment in 1984 defined a rare disease as a condition affecting fewer than 200,000 people in the United States. The act empowered the FDA to review and approve requests for orphan drug status, coordinate drug development and award research grants. The FDA created the Office of Orphan Product Development (OOPD) to help manage this regulatory function. Although the initial legislation permitted manufacturers to apply for orphan product designation at

any time, a 1988 amendment required sponsors to apply for orphan designation before submitting applications for marketing approval. From 1983-2009, a total of 2,112 orphan designations were assigned by the OOPD. Of those designations, 347 had been approved by the FDA as of the end of 2009. In which, 34 drugs were approved from 1967-1983 would have qualified under the Orphan Drug Act based on their approval for a rare condition. Some authors have regarded the act as crucial in the development of an effective treatment for infant botulism, affecting about 100 U.S. children per year, was described as being developed due to concerted efforts of the California Department of Health Services, supported by OOPD grants and close coordination with the FDA.^[4] As pharmaceutical manufacturers are cited as focusing more attention on developing orphan products,^[5] policy makers are considering whether to offer orphan-like incentives to basic and translational research aimed at other conditions.^[6] Congress recently passed a law that directs the Commissioner of the FDA to "convene a public meeting regarding which serious and life threatening infectious diseases potentially qualify for available grants and contracts under the Orphan Drug Act or other incentives for development," thereby opening the door to providing orphan drug-like incentives for new antibiotics to treat multidrug-resistant infections in the United States.^[7] This appendix was developed to provide some background data on the

implementation of the Orphan Drug Act. Data from publicly available FDA files were collected to provide a comprehensive overview of drugs approved with orphan designations, with attention paid to the drugs' innovativeness as well as their scientific and regulatory characteristics. Prior research has been done on various aspects of the Orphan Drug Act. A few studies provided perspectives on the early implementation of the incentive. One analysis by Asbury of the first 42 orphan-designated products approved from 1983 to 1989 found that among the 33 nonbiologic drugs, 21 (64 %) were New Molecular Entities. The FDA ranked 38 percent of these NMEs as "important" therapeutic gains and 48 percent as "moderate" therapeutic gains.^[8] Asbury reported that annual sales of 25 of 40 orphan drugs were less than \$1 million, while annual sales of 3 were for greater than \$100 million. A study by Shulman and Manocchia analyzed 121 orphan drug approvals from 1983 to 1995 (involving 102 different drugs).^[9] Fifteen drugs were approved for more than one orphan indication. They found that the drugs averaged about 8 years in clinical development (from IND to NDA) and approximately 1.8 years in FDA review.

CONCLUSION

The growing number of rare diseases awaiting treatment is a public health issue. The scarcity of incentives for medicines manufacturers and the lack of documentation supporting the applications limit the number of new orphan medicines products. The first step in the development of any orphan medicinal product is to obtain designation as an Orphan Medicinal Product. Treatments of such diseases are challenges and number is increases day by day under various regulatory authorities.

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