Orphan medicinal products with marketing authorisation

(http://ec.europa.eu/health/documents/community-register/html/orphreg.htm)

List of Orphan Medicinal Products with Marketing Authorisation (as of 20 January 2019)

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
2001					
1	1	**Fabrazyme** (agalsidase beta) **EXPIRED**	Genzyme BV	Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency).	
2	2	**Replagal** (agalsidase alpha) **EXPIRED**	Shire Human Genetic Therapies AB	Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency).	
3	3	**Glivec** (imatinib) **EXPIRED**	Novartis Europharm Limited	Treatment of adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcrabl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment. Glivec is also indicated for the treatment of adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis. The effect of Glivec on the outcome of bone marrow transplantation has not been determined.	
4		**Glivec** (imatinib) **WITHDRAWN**	Novartis Europharm Limited	Glivec is also indicated for the treatment of adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST).	2002
5		**Glivec** (imatinib) **WITHDRAWN**	Novartis Europharm Limited	Treatment of adult patients with unresectable recurrent and/or metastatic dermafibrosarcoma protuberans	2006
6		**Glivec** (imatinib) **WITHDRAWN**	Novartis Europharm Limited	Treatment of adult patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) as monotherapy	2006
7		**Glivec** (imatinib) **WITHDRAWN**	Novartis Europharm Limited	Treatment of adult patients with myelodysplastic/ myeloproliferative diseases (MDS/MPD) associated with PDGFR gene re-arrangement	2006
8		**Glivec** (imatinib) **WITHDRAWN**	Novartis Europharm Limited	Treatment of adult patients with hypereosinophilic syndrome (HES) and chronic eosinophilic leukaemia (CEL)	2006
2002					
9	4	**Trisenox** (arsenic trioxide) **EXPIRED**	Cephalon Europe	"For induction of remission and consolidation in adult patients with relapsed/refractory acute promyelocytic leukaemia (APL), characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene. Previous treatment	

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				should have included a retinoid and chemotherapy. The response rate of other acute myelogenous leukaemia subtypes to TRISENOX has not been examined."	
10	5	**Tracleer** (bosentan) **EXPIRED**	Actelion Registration Limited	"Treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity and symptoms in patients with WHO functional class III.Efficacy has been shown in: - Primary (idiopathic and familial) PAH. - PAH secondary to scleroderma without significant interstitial pulmonary disease. - PAH associated with congenital systemic-to-pulmonary shunts and Eisenmenger's physiology. - Some improvements have also been shown in patients with PAH WHO functional class II."	
11		**Tracleer** (bosentan) **WITHDRAWN**	Actelion Registration Limited	Indicated to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease.	2007
12	6	**Somavert** (pegvisomant) **EXPIRED**	Pfizer Limited	Treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalize IGF-I concentrations or was not tolerated.	
13	7	**Zavesca** (miglustat) **EXPIRED**	Actelion Registration Limited	Zavesca is indicated for the oral treatment of mild to moderate type 1 Gaucher disease. Zavesca may be used only in the treatment of patients for whom enzyme replacement therapy is unsuitable.	
14		**Zavesca** (miglustat)	Actelion Registration Limited	Extension of Indication – to include the treatment of progressive neurological manifestations in adult patients and paediatric patients with Niemann-Pick type C disease.	2009
2003					
15	8	**Carbaglu** (carglumic acid) **EXPIRED**	Orphan Europe Sarl	Treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency.	
16		**Carbaglu** (carglumic acid)	Orphan Europe SARL - France	This variation concerns an extension of indication of Carbaglu to add the treatment of hyperammoniemia due to isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia. 2021	2011
17	9	**Aldurazyme** (laronidase) **EXPIRED**	Genzyme Europe BV	Aldurazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis I (MPSI; a [alpha]-L-iduronidase deficiency) to treat the non-neurological manifestations of the disease	
18	10	**Busilvex** (busulfan) **EXPIRED**	Pierre Fabre Medicament	Busilvex followed by cyclophosphamide (BuCy2) is indicated as conditioning treatment prior to conventional haematopoietic progenitor cell transplantation (HPCT) in adult patients when the combination is considered the best available option. Busilvex followed by cyclophosphamide (BuCy4) or melphalan (BuMel) is indicated as conditioning treatment prior to conventional haematopoietic progenitor cell	

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				transplantation in paediatric patients.	
19	11	**Ventavis** (iloprost) **EXPIRED**	Schering AG	Treatment of patients with primary pulmonary hypertension, classified as NYHA functional class III, to improve exercise capacity and symptoms.	
20	12	**Onsenal** (celecoxib) **WITHDRAWN FROM THE MARKET - SAFETY**	Pharmacia-Pfizer EEIG	For the reduction of the number of adenomatous intestinal polyps in familial adenomatous polyposis (FAP), as an adjunct to surgery and further endoscopic surveillance.	
2004					
21	13	**Photobarr** (porfimer sodium) **WITHDRAWN FROM THE MARKET - SAFETY**	Axcan Pharma International BV	Photodynamic therapy (PDT) with porfimer sodium is indicated for ablation of high grade dysplasia (HGD) in patients with Barrett's Esophagus (BE)	
22	14	**Litak** (cladribine,B) **EXPIRED**	Lipomed GmbH	Treatment of hairy cell leukaemia	
23	15	**Lysodren** (mitotane) **EXPIRED**	Laboratoire HRA Pharma	Symptomatic treatment of advanced (unresectable, metastatic or relapsed) adrenal cortical carcinoma. The effect of Lysodren on non-functional adrenal cortical carcinoma is not established.	
24	16	**Pedea** (ibuprofen) **EXPIRED**	Orphan Europe SARL	Indicated to close a patent ductus arteriosus in preterm newborn infants	
25	17	**Wilzin** (zinc-acetate dihydrate) **EXPIRED**	Orphan Europe SARL	Treatment of Wilson's disease	
26	18	**Xagrid** (anegrelide hydrochloride) **EXPIRED**	Shire Pharmaceutic als Ltd	Reduction of elevated platelet counts in at risk essential thrombocythaemia patients who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.	
2005					
27	19	**Prialt** (ziconotide) **EXPIRED**	Elan Pharma Int.	Treatment of chronic pain requiring intrathecal (IT) analgesia in patients who fail to obtain adequate analgesia and/or suffer intolerable adverse events with systemic opioids	
28	20	**Orfadin** (nitisinone) **EXPIRED**	Swedish Orphan Int.	Treatment of patients with confirmed diagnosis of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.	
29	21	**Xyrem** (sodium oxybate) **WITHDRAWN**	UCB Pharma Ltd	Treatment of narcolepsy with cataplexy in adult patients.	

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30	22	**Revatio** (sidenafil citrate) **EXPIRED**	Pfizer limited	Treatment of pulmonary arterial hypertension. Revatio has been shown to improve exercise ability and to reduce mean pulmonary arterial pressure	
2006					
31	23	**Naglazyme** (N-acetylgalactosamine 4-sulfatase,A) **EXPIRED**	BioMarin Europe	Long term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis VI (MPS VI; (N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux Lamy syndrome) .	
32	24	**Myozyme** (recombinant human acid alpha-glucosidase **EXPIRED**	Genzyme Europe	Myozyme is indicated for long-term enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of Pompe disease (acid alpha-glucosidase deficiency). Myozyme is indicated in adults and paediatric patients of all ages. In patients with late-onset Pompe disease the evidence of efficacy is limited.	
33	25	**Evoltra** (clofarabine) **EXPIRED**	Genzyme Europe BV	Treatment of acute lymphoblastic leukaemia (ALL) in paediatric patients who have relapsed or are refractory after receiving at least two prior regimens and where there is no other treatment option anticipated to result in a durable response. Safety and efficacy have been assessed in studies of patients ≤ 21 years old at initial diagnosis.	
34	26	**Nexavar** (sorafenib tosylate) **EXPIRED**	Bayer Healthcare AG	For the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.	
35		**Nexavar** (sorafenib tosylate)	Bayer Healthcare AG	Extension of Indication to include treatment of hepatocellular carcinoma. 2024	2007
36		**Nexavar** (sorafenib tosylate)	Bayer Healthcare AG	Extension of indication for the treatment of patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine.	2014
37	27	**Savene** (dexrazoxane) **EXPIRED**	SpePharm Holding BV	Treatment of anthracycline extravasation	
38	28	**Exjade** (4-(3,5-Bis (hydroxiphenyl) -1,2,4) triazol-1-yl)benzoic acid, B) **EXPIRED**	Novartis Europharm Limited	Treatment of chronic iron overload due to blood transfusions (transfusion haemosiderosis) in adult and paediatric patients (aged 2 years and over)	

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39	29	**Sprycel** (dasatinib) **EXPIRED**	Bristol-Myers Squibb Pharma	Treatment of adults with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) and lymphoid blast CML with resistance or intolerance to prior therapy. Treatment of adults with chronic, accelerated or blast phase chronic myeloid leukaemia (CML) with resistance or intolerance to prior therapy including imatinib mesilate.	
40	30	**Sutent** (sunitinib) **WITHDRAWN**	Pfizer Ltd.	Sutent is indicated for the treatment of advanced and/or metastatic renal cell carcinoma. Sutent is indicated for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST) after failure of imatinib mesylate treatment due to resistance or intolerance.	
41	31	**Thelin** (sitaxentan sodium) **WITHDRAWN FROM THE MARKET - SAFETY**	Pfizer Limited.	Treatment of patients with pulmonary arterial hypertension classified as WHO functional class III, to improve exercise capacity. Efficacy has been shown in primarily pulmonary hypertension and in pulmonary hypertension associated with connective tissue disease.	
2007					
42	32	**Diacomit** (stiripentol) **EXPIRED**	BIOCODEX	Indicated for use in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet's syndrome) whose seizures are not adequately controlled with clobazam and valproate.	
43	33	**Elaprase** (iduronate-2-sulfatase) **EXPIRED**	Shire Human Genetic Therapies AB - Sweden	"Elaprase is indicated for the long-term treatment of patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). Heterozygous females were not studied in the clinical trials."	
44	34	**Inovelon** (rufinamide)	Esai Limited	Adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients 4 years and older. 18/01/2019	
45	35	**Cystadane** (betaine anhydrous A) **EXPIRED**	Orphan Europe	Adjunctive treatment of homocystinuria, involving deficiencies or defects in: - cystathionine beta-synthase (CBS), - 5,10-methylene-tetrahydrofolate reductase (MTHFR), - cobalamin cofactor metabolism (cbl). Cystadane should be used as supplement to other therapies such as vitamin B6 (pyridoxine), vitamin B12 (cobalamin), folate and a specific diet.	
46	36	**Revlimid** (lenalidomide) **EXPIRED**	Celgene Europe Ltd	Revlimid is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant. Revlimid in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.	

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47		**Revlimid** (lenalidomide)	Celgene Europe Limited	Revlimid is indicated for the treatment of patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate. 2026	2013
48	37	**Soliris** (eculizumab)	Alexion Europe	Indicated in adults and **children** for the treatment of patients with paroxysmal nocturnal haemoglobinuria (PNH). Evidence of clinical benefit demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history.2027	2017
49		**Soliris** (eculizumab)	Alexion Europe SAS - France	Extension Of Indication for atypical haemolytic uremic syndrome (aHUS)	
50	38	**Siklos** (hydroxycarbamide)	Addmedica SAS - France	"Indicated for the prevention of recurrent painful vaso-occlusive crises including acute chest syndrome in adults, adolescents and **children** older than 2 years suffering from symptomatic Sickle Cell Syndrome."	
51	39	**Increlex** (mecasermin) **EXPIRED**	Ipsen Pharma	Long-term treatment of growth failure in **children** and adolescents with severe primary insulin like growth factor-1 deficiency (Primary IGFD). Severe Primary IGFD is defined by: • height standard deviation score ≤ –3.0 and • basal IGF-1 levels below the 2.5th percentile for age and gender and • GH sufficiency. • Exclusion of secondary forms of IGF-1 deficiency, such as malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Severe Primary IGFD includes patients with mutations in the GH receptor (GHR), post-GHR signalling pathway, and IGF-1 gene defects; they are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. It is recommended to confirm the diagnosis by conducting an IGF-1 generation test.	
52	40	**Atriance** (nelarabine) **EXPIRED**	Glaxo Group Ltd	Treatment of patients with T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens. Due to the small patient populations in these disease settings, the information to support these indications is based on limited data.	
53	41	**Gliolan** (5 aminolevulinic acid hydrochloride L) **EXPIRED**	Medac GmbH	Visualisation of malignant tissue during surgery for malignant glioma	
54	42	**Yondelis** (trabectedin) **EXPIRED**	PharmaMar SA	Treatment of patients with advanced soft tissue sarcoma, after failure of anthracyclines and ifosfamide, or who are unsuited to receive these agents. Efficacy	

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				data are based mainly on liposarcoma and leiomyosarcoma patients	
55		**Yondelis** (trabectedin)	PharmaMar SA	EXTENSION OF INDICATION Indicated for the treatment of patients with advanced soft tissue sarcoma, after failure of anthracyclines and ifosfamide, or who are unsuited to receive these agents. Efficacy data are based mainly on liposarcoma and leiomyosarcoma patients. In combination with pegylated liposomal doxorubicin (PLD) is indicated for the treatment of patients with relapsed platinum-sensitive ovarian cancer. 30/10/2019	2009
56	43	**Torisel** (temsirolimus) **EXPIRED**	Pfizer Limited	First-line treatment of patients with advanced renal cell carcinoma who have at least three of six prognostic risk factors.	
57		**Torisel** (temsiroliums)	Pfizer Limited	EXTENSION OF INDICATION to include treatment of adult patients with relapsed and/or refractory mantle cell lymphoma. 25/08/2019	2009
58	44	**Tasigna** (nilotinib)	Novartis Europharm Ltd	Treatment of Philadelphia chromosome positive chronic myelogenous leukaemia (CML) – *2 additional years of market exclusivity as paediatric reward granted on 17 Nov 2017 – will expire in 21/11/2019*	
2008					
59	45	**Thalidomide Celgene** (thalidomide) **EXPIRED**	Celgene Europe Limited	Thalidomide Celgene in combination with melphalan and prednisone as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy.	
60	46	**Volibris** (ambrisentan) **EXPIRED**	Glaxo Group Ltd	Treatment of patients with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity.	
61	47	**Firazyr** (icatibant acetate L)	Shire Orphan Therapies GmbH	Indicated for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults (with C1-esterase-inhibitor deficiency). - *2 additional years of market exclusivity as paediatric reward granted on 15/07/2020*	
62	48	**Ceplene** (histamine dihydrochloride) **EXPIRED**	Meda AB	Ceplene maintenance therapy is indicated for adult patients with acute myeloid leukaemia in first remission concomitantly treated with interleukin-2 (IL-2). The efficacy of Ceplene has not been fully demonstrated in patients older than age 60.	
63	49	**Kuvan** (sapropterin dihydrochloride)	Merck Serono Europe Limited	Treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients of 4 years of age and over with phenylketonuria (PKU) who have been shown to be responsive to such treatment. Kuvan is also indicated for the treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients with tetrahydrobiopterin (BH4) deficiency who have been shown to be responsive to such treatment. *2 additional years of market exclusivity as paediatric reward granted on 24/06/2015-expires 4/12/2020*	
64	50	**Vidaza** (azacitidine)	Celgene Europe Ltd-United	Treatment of adult patients who are not eligible for haematopoietic stem cell transplantation with: • intermediate-2 and high-risk	

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		EXPIRED	Kingdom	myelodysplastic syndromes (MDS) according to the International Prognostic Scoring System (IPSS), • chronic myelomonocytic leukaemia (CMML) with 10-29% marrow blasts without myeloproliferative disorder, • acute myeloid leukaemia (AML) with 20-30% blasts and multi-lineage dysplasia, according to World Health Organisation (WHO) classification.	
2009					
65	51	**Nplate** (romiplostim)	Amgen Europe BV	Indicated for adult chronic immune (idiopathic) thrombocytopenic purpura (ITP) splenectomised patients refractory to other treatments (e.g. corticosteroids, immunoglobulins). Nplate may be considered as second line treatment for adult non-splenectomised patients where surgery is contra-indicated. 6/02/2019	
66	52	**Mepact** (mifamurtide)	Takeda France SAS	Indicated in **children**, adolescents and young adults for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection. It is used in combination with post-operative multi-agent chemotherapy. 23/03/2019	
67	53	**Peyona** (previously Nymusa, caffeine citrate	Chiesi Farmaceutici S.P.A. - Italy	Treatment of primary apnoea of premature newborns. 6/07/2019	
68	54	**Mozobil** (plerixafor)	Genzyme BV The Netherlands	Indicated in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma whose cells mobilise poorly. 4/08/2019	
69	55	**Cayston** (aztreonam lysinate inhalation use)	Gilead Sciences International Ltd – UK	Suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis (CF) aged 18 years and older. 23/09/2019	
70	56	**Rilonacept Regeneron** (formerly Arcalyst; rilonacept) **WITHDRAWN FROM THE MARKET – SAFETY**	Regeneron UK	Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and **children** aged 12 years and older.	
71	57	**Firdapse** (amifampridine)	BioMarin Europe Ltd	Symptomatic treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults. 28/12/2019	
72	58	**Revolade** (eltrombopag) **WITHDRAWN**	GlaxoSmithKline Trading Services Limited – Ireland	Indicated for adult chronic immune (idiopathic) thrombocytopenic purpura (ITP) splenectomised patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). Revolade may be considered as second line treatment for adult non-splenectomised patients where surgery is contraindicated.	

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73	59	**Afinitor** (everolimus) **WITHDRAWN**	Novartis Europharm Ltd	Treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy.	
74	60	**Ilaris** (canakinumab) **WITHDRAWN**	Novartis Europharm Ltd.	Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults, adolescents and **children** aged 4 years and older with body weight above 15 kg, including Muckle-Wells Syndrome (MWS), Neonatal-Onset Multisystem Inflammatory Disease (NOMID) / Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA), Severe forms of Familial Cold Autoinflammatory Syndrome (FCAS) / Familial Cold Urticaria (FCU) presenting with signs and symptoms beyond cold-induced urticarial skin rash.	
2010					
75	61	**Tepadina** (thiotepa)	Adienne S.r.l - Italy	Indicated, in combination with other chemotherapy medicinal products: 1) with or without total body irradiation (TBI), as conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases in adult and paediatric patients; 2) when high dose chemotherapy with HPCT support is appropriate for the treatment of solid tumours in adult and paediatric patients."	
76	62	**Arzerra** (ofatumumab)	Glaxo Group Limited - UK	Refractory chronic lymphocytic leukaemia (CLL): Arzerra is indicated for the treatment of CLL in patients who are refractory to fludarabine and alemtuzumab.	
77		**Arzerra** (ofatumumab)	Glaxo Group Limited - UK	Previously untreated chronic lymphocytic leukaemia (CLL): Arzerra in combination with chlorambucil or bendamustine is indicated for the treatment of patients with CLL who have not received prior therapy and who are not eligible for fludarabine-based therapy.	2014
78	63	**VPRIV** (velaglucerase alfa)	Shire Pharmaceuticals Ireland Limited – Ireland	Treatment of type 1 Gaucher disease	
2011					
79	64	**Esbriet** (perfenidone)	InterMune UK Ltd.	Treatment of idiopathic pulmonary fibrosis	
80	65	**TOBI podhaler** (tobramycin)	Novartis Europharm Limited	Suppressive therapy of chronic pulmonary infection due to *Pseudomonas aeruginosa* in adults and **children** aged 6 years and older with cystic fibrosis	
81	66	**Votubia** (everolimus)	Novartis Europharm Limited	Treatment of patients aged 3 years and older with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) who require therapeutic intervention but are not amenable to surgery	

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82	67	**Plenadren** (hydrocortisone (modified release tablet)	ViroPharma SPRL	Treatment of adrenal insufficiency	
83	68	**Vyndaqel** (tafamidis)	Pfizer Limited - UK	Treatment of transthyretin amyloidosis in patients with symptomatic polyneuropathy	
2012					
84	69	**Xaluprine** (previously known as Mercaptopurine Nova Laboratories and Novapurine)	Nova Laboratories Limited - UK	Treatment of acute lymphoblastic leukaemia	
85	70	**Bronchitol** (manitolum)	Pharmaxis Pharmaceuticals	Treatment of cystic fibrosis	
86	71	**Signifor** (pasireotide)	Novartis Europharm Limited UK	Treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed	
87		**Signifor** (pasireotide)	Novartis Europharm Limited UK	Treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative and who are inadequately controlled on treatment with another somatostatin analogue.	2014
88	72	**Kalydeco** ivacaftor	Vertex Pharmaceuticals (U.K.) Limited	Treatment of cystic fibrosis (CF) in patients age 6 years and older who have a G551D mutation in the CFTR gene	
89	73	**Jakavi** (ruxolitinib) **WITHDRAWN**	Novartis Europharm Limited - UK	Treatment of disease related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.	
90	74	**Revestive** (teduglutide)	NPS Pharma Holdings Limited	Treatment of adult patients with Short Bowel Syndrome. Patients should be stable following a period of intestinal adaptation after surgery.	
91	75	**NovoThirteen** (catridecacog) **WITHDRAWN**	Novo Nordisk A/S	Long-term prophylactic treatment of bleeding in adult and paediatric patients 6 years and above with congenital factor-XIII-A-subunit deficiency.	
92	76	**Dacogen** (decitabine)	Janssen-Cilag International NV - Belgium	Treatment of adult patients aged 65 years and above with newly diagnosed de novo or secondary acute myeloid leukaemia (AML), according to the World Health Organisation (WHO) classification, who are not candidates for standard induction chemotherapy".	
93	77	**Glybera** (adeno-associated viral vector expressing lipoprotein lipase	uniQure biopharma B.V. - The Netherlands	Glybera is indicated for adult patients diagnosed with familial lipoprotein lipase deficiency (LPLD) and suffering from severe or multiple pancreatitis attacks despite dietary fat restrictions. The diagnosis of LPLD has to be confirmed by genetic testing. The indication is restricted to patients with detectable levels of LPL protein	

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94	78	**Adcetris** (brentuximab vedotin)	Takeda Global Research and Development Centre (Europe) Ltd - UK	Adcetris is indicated for the treatment of adult patients with relapsed or refractory CD30+ H83 (Hodgkin's lymphoma): 1.following autologous stem-cell transplant (ASCT) or; 2.following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. Adcetris is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL).	
95	79	**NexoBrid** (concentrate of proteolytic enzymes enriched in bromelain)	MediWound Germany GmbH	NexoBrid is indicated for removal of eschar in adults with deep partial- and full-thickness thermal burns.	
2013					
96	80	**Bosulif** (bosutinib)	Pfizer Limited United Kingdom	Treatment of chronic myeloid leukaemia	
97	81	**Iclusig** (ponatinib)	ARIAD Pharma Ltd - UK	Iclusig is indicated in adult patients with: 1) chronic-phase, accelerated-phase or blast-phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib, who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate, or who have the T315I mutation; 2) Philadelphia-chromosome-positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib, who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate, or who have the T315I mutation.	
98	82	**Imnovid** (previously Pomalidomide Celgene; pomalidomide)	Celgene Europe Limited - UK	Pomalidomide Celgene in combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.	
99	83	**Procysbi** (cysteamine bitartrate)	Raptor Pharmaceuticals Europe BV - The Netherlands	Probysbi is indicated for the treatment of proven nephropathic cystinosis. Cysteamine reduces cystine accumulation in some cells (e.g. leukocytes, muscle and liver cells) of nephropathic cystinosis patients and, when treatment is started early, it delays the development of renal failure.	
100	84	**Orphacol** (cholic acid)	Laboratoires CTRS	Orphacol is indicated for the treatment of inborn errors in primary bile-acid synthesis due to 3β-hydroxy-Δ5-C27-steroid oxidoreductase deficiency or Δ4-3-oxosteroid-5β-reductase deficiency in infants, **children** and adolescents aged one month to 18 years and adults	
101	85	**Defitelio** (defibrotide)	Gentium S.p.A. - Italy	Defitelio is indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell	

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
				transplantation (HSCT) therapy.	
102	86	**Opsumit** (macitentan)	Actelion Registration	Opsumit, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.	
103	87	**Jinarc** (tolvaptan) **WITHDRAWN**	Otsuka Pharmaceutical Europe Ltd	Autosomal dominant polycystic kidney disease	
2014					
104	88	**Sirturo** (bedaquiline fumarate)	Janssen-Cilag International N.V. Belgium	Indicated for use as part of an appropriate combination regimen for pulmonary multidrug resistant tuberculosis (MDR TB) in adult patients when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability	
105	89	**Cometriq** (cabozantinib)	TMC Pharma	Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma	
106	90	**Adempas** (riociguat)	Bayer Pharma AG	Treatment of Chronic thromboembolic pulmonary hypertension (CTEPH) and Pulmonary arterial hypertension (PAH)	
107	91	**Kolbam** (cholic acid) **WITHDRAWN**	FGK Representative Service GmbH, Germany	Inborn errors in primary bile-acid synthesis	
		Kolbam (cholic acid)	Retrophin Europe Ltd	Inborn errors in primary bile-acid synthesis	2015
108	92	**Granupas** (previously para-aminosalicylic acid Lucane or PAS-GR)	Lucane Pharma SA - France	Treatment of tuberculosis	
109	93	**Deltyba** (delamanid)	Otsuka Novel Products GmbH - Germany	Treatment of multidrug-resistant tuberculosis (MDR-TB)	
110	94	**Vimizim** (elosulfase alfa)	BioMarin Europe Ltd	Treatment of mucopolysaccharidosis, type IVA (Morquio A Syndrome, MPS IVA) in patients of all ages.	
111	95	**Sylvant** (siltuximab)	Janssen-Cilag International NV	Treatment of adult patients with multicentric Castleman's disease (MCD who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.	
112	96	**Gazyvaro** (obinutuzumab)	Roche Registration Ltd	Gazyvaro in combination with chlorambucil is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL) and with comorbidities making them unsuitable for full-dose fludarabine based therapy	
113	97	**Translarna** (ataluren)	PTC Therapeutics Limited	Translarna is indicated for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 5 years and older. Efficacy has not been demonstrated in non-ambulatory patients. The presence of a nonsense mutation in the	

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
				dystrophin gene should be determined by genetic testing.	
114	98	**Imbruvica** (ibrutinib)	Janssen-Cilag International NV	Imbruvica is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).	
115		**Imbruvica** (ibrutinib)	Janssen-Cilag International NV	Imbruvica is indicated for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo immunotherapy.	
116	99	**Ketoconazole HRA** (ketoconazole)	Laboratoire HRA Pharma	Ketoconazole HRA is indicated for the treatment of endogenous Cushing's syndrome in adults and adolescents above the age of 12 years.	
117	100	**Lynparza** (olaparib)	AstraZeneca AB	Lynparza is indicated as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy.	
118	101	**Cyramza** (ramucirumab) **WITHDRAWN**	Eli Lilly Nederland B.V.	In combination with paclitaxel is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy. Monotherapy is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum or fluoropyrimidine chemotherapy, for whom treatment in combination with paclitaxel is not appropriate.	
119	102	**Scenesse** (afamelanotide)	Clinuvel UK Limited	Prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP).	
2015					
120	103	**Ofev** (nibtedanib)	Boehringer Ingelheim Pharma GmbH & Co. KG	Ofev is indicated in adults for the treatment of Idiopathic Pulmonary Fibrosis (IPF).	
121	104	**Cerdelga** (eliglustat)	Genzyme Europe BV	Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1), who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs).	
122	105	**Holoclar** (*ex vivo* expanded autologous human corneal epithelial cells containing stem cells)	Chiesi Farmaceutici S.p.A.	Treatment of adult patients with moderate to severe limbal stem cell deficiency (defined by the presence of superficial corneal neovascularisation in at least two corneal quadrants, with central corneal involvement, and severely impaired visual acuity), unilateral or bilateral, due to physical or chemical ocular burns. A minimum of 1-2 mm2 of undamaged limbus is required for biopsy.	

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
123	106	**Lenvima** (lenvatinib mesylate)	Eisai Europe Ltd	Lenvima is indicated for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI).	
124	107	**Hetlioz** (tasimelteon)	Vanda Pharmaceuticals Ltd	Hetlioz is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in totally blind adults.	
125	108	**Unituxin** (dinutuximab)	United Therapeutics Europe Ltd	Unituxin is indicated for the treatment of high-risk neuroblastoma in **children** aged 12 months to 17 years. who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and autologous stem cell transplantation. It is administered in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and isotretinoin.	
126	109	**Kanuma** (sebelipase alfa)	Synageva BioPharma Ltd	Kanuma is used to treat patients of all ages with lysosomal acid lipase deficiency.	
127	110	**Farydak** (panobinostat)	Novartis Europharm Ltd	Farydak is indicated in combination with bortezomib and dexamethasone, for the treatment of relapsed and/or refractory multiple myeloma in adults patients. who have received at least two prior regimens including bortezomib and an immunomodulatory agent.	
128	111	**Strensiq** (asfotase alfa)	Alexion Europe SAS	Strensiq is indicated for long-term enzyme replacement therapy in patients with paediatric-onset hypophosphatasia to treat the bone manifestations of the disease.	
129	112	**Raxone** (ibedenone)	Santera Pharmaceuticals Gmbh	Raxone is indicated for the treatment of visual impairment in adolescent and adult patients with Leber's Hereditary Optic Neuropathy.	
130	113	**Cresemba** (isavuconazole)	Basilea Medical Ltd	Cresemba is indicated for the treatment of adults with invasive aspergillosis and mucormycosis in patients for whom amphotericin B is inappropriate.	
131	114	**Kyprolis** (carfilzomib)	Amgen Europe BV	Kyprolis is indicated for the treatment of multiple myeloma	
132	115	**Orkambi** (lumacaftor/ ivacaftor) **WITHDRAWN**	Vertex Pharmaceuticals	Orkambi is indicated for the treatment of cystic fibrosis	
133	116	**Obizur** (susoctog alfa) **WITHDRAWN**	Baxalta Innovations GmbH	Obizur is indicated for the treatment of haemophilia A	
134	117	**Elocta** (efmoroctocog alfa) **WITHDRAWN**	Biogen Idec Ltd	Elocta is indicated for the treatment of haemophilia A	
135	118	**Blincyto** (blinatumomab)	Amgen Europe B.V.	Blincyto is indicated for the treatment of precursor cell lymphoblastic leukemia-lymphoma	
136	119	**Ravicti** (glycerol phenylbutyrate)	Horizon Therapeutics Limited	Ravicti is indicated for the treatment of inborn urea cycle disorders	

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
137	120	**Quinsair** (levofloxacin) **WITHDRAWN**	Regintel	Cystic fibrosis	
2016					
138	121	**Coagadex** (human coagulation factor X)	Bio Products Laboratory limited	Factor X deficiency	
139	122	**Wakix** (pitolisant)	Bioprojet Pharma	Narcolepsy	
140	123	**Idelvion** (albutrepenona cog alfa)	CSL Behring GmbH	Haemophilia B	
141	124	**Uptravi** (selexipag) **WITHDRAWN**	Actelion Registration Ltd	Pulmonary arterial hypertension	
142	125	**Alprolix** (eftrenacog alfa)	Biogen Idec Ltd	Haemophilia B	
143	126	**Darzalex** (daratumumab)	Janssen-Cilag International N.V.	Multiple myeloma	
144	127	**Galafold** (migalastat hydrochloride)	Amicus Therapeutics UK Ltd	Fabry disease	
145	128	**Strimvelis** (autologous CD34+ + cells transduced with retroviral vector encoding for the human adenosine deaminase (ADA))	GlaxoSmithKline Trading Services Limited	Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)	
146	129	**Zalmoxis** (allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor and the herpes simplex I virus thymidine kinase)	MolMed SpA	Adjunctive treatment in haematopoietic stem cell transplantation (HSCT) of adult patients with high-risk haematological malignancies	
147	130	**Onivivyde** (irinotecan hydrochloride trihydrate)	Baxalta Innovations GmbH	Metastatic adenocarcinoma of the pancreas	
148	131	**Lartruvo** (olaratumab)	Eli Lilly Nederland B.V.	Advanced soft tissue sarcoma	
149	132	**Ninlaro** (ixazomib)	Takeda Pharma A/S	Multiple myeloma	
150	133	**Venclyxto** (venetoclax)	AbbVie Ltd	Chronic lymphocytic leukemia	

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
151	134	**Ocaliva** (obeticholic acid)	Intercept Pharma Ltd	Primary biliary cholangitis	
152	135	**SomaKit TOC** (edotreotide)	Advanced Accelerator Applications	Gastroenteropancreatic neuroendocrine tumours	
2017					
153	136	**Cystadrops** (mercaptamine)	Orphan Europe S.A.R.L.	Cystinosis	
154	137	**Ledaga** (chlormethine)	Actelion Registration Ltd	Mycosis fungoides-type cutaneous T-cell lymphoma	
155	138	**Natpar** (parathyroid hormone)	Shire Pharmaceutic als Ireland Ltd	Hypoparathyroidism	
156	139	**Dinutuximab beta Apeiron** (dinutuximab beta)	Apeiron Biologics AG	Neuroblastoma (in patients over 1 year of age)	
157	140	**Spinraza** (nusinersen)	Biogen Idec Ltd	Spinal muscular atrophy	
158	141	**Brineura** (cerliponase alfa)	Biomarin International Limited	Neuronal ceroid lipofuscinosis type 2	
159	142	**Besponsa** (inotuzumab ozogamicin)	Pfizer Limited	Precursor Cell Lymphoblastic Leukemia-Lymphoma	
160	143	**Oxervate** (recombinant human nerve growth factor - cenegermin)	Dompe farmaceutici s.p.a.	Neurotrophic keratitis	
161	144	**Bavencio** (avelumab)	Merck Serono Europe Limited	Merkel cell carcinoma	
162	145	**Rydapt®** (midostaurin)	Novartis Europharm Ltd	Acute myeloid leukemia, systemic mastocytosis	
163	146	**Xermelo®** (telotristat etiprate)	Ipsen Pharma	Carcinoid syndrome	
164	147	**Zejula®** (niraparib)	Tesaro UK limited	Fallopian tube neoplasms, ovarian neoplasms, peritoneal neoplasms	
2018					
165	148	**Jorveza®** (budesonide)	Dr. Falk Pharma GmbH	Eosinophilic oesophagitis	
166	149	**Prevymis®** (letermovir)	Merck Sharp & Dohme Limited	Cytomegalovirus infection prevention following haematopoietic stem cell transplant	
167	150	**Crysvita®** (burosumab)	Kyowa Kirin Limited	X-linked hypophosphataemia (to be used in **children** over 1 year of age and adolescents)	
168	151	**Lamzede®** (velmanase alfa)	Chiesi Farmaceutici S.p.A.	Mild to moderate alpha-mannosidosis (to be used in **children** and adults)	
169	152	**Alofisel®**	Tigenix, S.A.U.	Complex anal fistulas in adults with	

N° CHMP + opinions*a*	N° products*b*	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication	New indic
		(darvadstrocel)		Crohn's disease	
170	153	**Mylotarg®** (gemtuzumab ozogamicin)	Pfizer Limited	Acute myeloid leukemia in patients aged **15 years** and above who are newly diagnosed	
171	154	**Amglidia®** (glibenclamide)	Ammtrek	Neonatal diabetes **(newborns and children)**	
172	155	**Rubraca®** (rucaparib)	Clovis Oncology UK Limited	High-grade cancers of the ovary, fallopian tubes and peritoneum	
173	156	**Verkazia®** (ciclosporin)	Santen Oy	Keratoconjunctivitis (VKC) in **children** and **adolescents** from 4 to 18 years of age.	
174	157	**Tegsedi®** (inotersen sodium)	Ionis USA Ltd	Hereditary transthyretin amyloidosis (hATTR)	
175	158	**Myalepta®** (metreleptin)	Aegerion Pharmaceutic als B.V.	Familial Partial Lipodystrophy; Barraquer-Simons syndrome; Lawrence syndrome; Berardinelli-Seip syndrome	
176	159	**Vyxeos®** (daunorubicin / cytarabine)	Jazz Pharmaceutic als Ireland Limited	Adults with newly diagnosed acute myeloid leukaemia	
177	160	**Mepsevii®** (vestronidase alfametreleptin)	Ultragenyx Germany GmbH	Mucopolysaccharidosis type VII (MPS VII, also known as Sly syndrome)	
178	161	**Kymriah®** (tisagenlecleucel)	Novartis Europharm Limited	B-cell acute lymphoblastic leukaemia (ALL), **in children** and young adults up to 25 years and diffuse large B-cell lymphoma (DLBCL) in adults	
179	162	**Yescarta®** (axicabtagene ciloleucel)	Kite Pharma EU B.V.	Diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL)	
180	163	**Onpattro®** (patisiran)	Alnylam Netherlands B.V.	Hereditary transthyretin-mediated amyloidosis (hATTR)	
181	164	**Cablivic®** (caplacizumab)	Ablynx NV	Acquired thrombotic thrombocytopenic purpura (aTTP)	
182	165	**Symkevi®** (patisiran)	Vertex Pharmaceutic als (Europe) Ltd	Cystic fibrosis in patients aged **12 years** and above	
183	166	**Luxturna®** (voretigene neparvovec)	Spark Therapeutics Ireland Ltd	Adults and **children** with loss of vision due to inherited retinal dystrophy	
184	167	**Namuscla®** (mexiletine hcl)	Lupin Europe GmbH	Non-dystrophic myotonic disorders	

a = Number of positive CHMP opinions; ***b*** =Number of *different* products ***c*** = International Non-proprietary Name (INN)

EXPIRED product reached the end of the period of market exclusivity

WITHDRAWN: withdrawn from the Community Register of orphan medicinal products upon request of the marketing authorisation holder

WITHDRAWN FROM THE MARKET – SAFETY withdrawn from the market in the European Union due to safety reasons

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