Les Cahiers d'Orphanet
série Médicaments Orphelins

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# Listes des médicaments pour les maladies rares en Europe*

**Autorisation de mise sur le marché de la Communauté Européenne par procédure centralisée*

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# Sommaire général

# PARTIE 1:

# Liste des médicaments orphelins en Europe avec désignation orpheline et autorisation de mise sur le marché européennes*

## Sommaire



## Méthodologie

Ce document contient la liste de tous les médicaments orphelins ayant reçu une autorisation de mise sur le marché (AMM) européenne à la date indiquée dans le document. Ces produits de santé peuvent n'être accessibles actuellement que dans certains pays européens. En effet, l'accessibilité dans les pays dépend de la stratégie du laboratoire et de la décision de remboursement prise par les autorités de santé nationales.

La définition de médicament orphelin en Europe concerne des produits de santé ayant obtenu une désignation orpheline européenne (établie selon la loi (EC) No 141/2000), suivie d'une autorisation de mise sur le marché européenne et, le cas échéant, d'une appréciation positive du service médical rendu.

La liste des médicaments orphelins en Europe (avec désignation orpheline et autorisation de mise sur le marché européennes) est donc établie par croisement de la liste des produits de santé ayant obtenu une désignation orpheline (http://ec.europa.eu/health/documents/community-register/html/alforphreg.htm) avec la liste des produits ayant obtenu une autorisation de mise sur le marché (http://ec.europa.eu/health/documents/community-register/html/alfregister.htm).

Ces deux listes sont disponibles sur le site Internet de la Direction Générale de la santé et des consommateurs (DG Sanco) de la Commission Européenne.

Un premier classement par spécialité donne le nom de la substance active, l'indication de l'AMM, la date d'AMM et le titulaire de l'AMM.

Ce premier classement est complété par deux tableaux annexes précisant :

- la liste des médicaments orphelins retirés/supprimés du Registre Communautaire des médicaments orphelins à usage humain mais toujours indiqués dans des maladies rares (voir Annexe 1 ; leurs indications sont détaillées en Partie II, « Liste des médicaments avec une ou plusieurs indications de maladie rare en Europe ») ;
- la liste des médicaments orphelins dont l'AMM Européenne est abrogée (voir Annexe 2). Plus d'information sur le site de l'EMA : www.ema.europa.eu.

** Autorisation de mise sur le marché de la Communauté Européenne par procédure centralisée*

Trois listes annexes donnent le classement des mêmes spécialités par :

- date décroissante d'AMM ;
- classe ATC ;
- titulaire d'AMM.

Toutes les spécialités sont présentées par ordre alphabétique.

Vous pouvez trouver des informations complémentaires sur chaque médicament dans l'onglet « Médicaments orphelins » du site www.orphanet.fr ou sur le site de l'EMA (Agence Européenne du Médicament) http://www.ema.europa.eu. Le registre de l'EMA liste tous les médicaments avec AMM, pas seulement les médicaments orphelins. Les médicaments orphelins ayant obtenu une désignation orpheline européenne sont identifiables grâce au logo O.

L'information officielle et actualisée sur les médicaments orphelins est disponible sur le site du Registre Communautaire des médicaments orphelins à usage humain :
http://ec.europa.eu/health/documents/community-register/html/alforphreg.htm

# Classification par spécialités

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| ADCETRIS | Brentuximab vedotin | *Treatment of adult patients with relapsed or refractory CD30+ **Hodgkin lymphoma** (HL):<br>1. following autologous stem cell transplant (ASCT) or<br>2. following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option.<br>*Treatment of adult patients with relapsed or refractory systemic **anaplastic large cell lymphoma** (sALCL). | 25/10/2012 | Takeda Global Research and Development Centre (Europe) Ltd |
| ARZERRA | Ofatumumab | Treatment of **chronic lymphocytic leukaemia** (CLL) in patients who are refractory to fludarabine and alemtuzumab. | 19/04/2010 | Glaxo Group Ltd |
| ATRIANCE | Nelarabine | 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.<br>Due to the small patient populations in these disease settings, the information to support these indications is based on limited data. | 22/08/2007 | Glaxo Group Ltd |
| BOSULIF | Bosutinib | Treatment of adult patients with chronic phase (CP), accelerated phase (AP), and blast phase (BP) **Philadelphia chromosome positive chronic myelogenous leukaemia** (Ph+ CML) previously treated with one or more tyrosine kinase inhibitor(s) and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. | 27/03/2013 | Pfizer Ltd |
| BRONCHITOL | Mannitol | For the treatment of **cystic fibrosis** (CF) in adults aged 18 years and above as an add-on therapy to best standard of care. | 13/04/2012 | Pharmaxis Pharmaceuti-cals Limited |
| CARBAGLU | Carglumic acid | Treatment of **hyperammonaemia** due to **N-acetylglutamate synthase primary deficiency**, hyperammonaemia due to **isovaleric acidaemia**, hyperammonaemia due to **methymalonic acidaemia**, hyperammonaemia due to **propionic acidaemia.**<br>*This orphan designated product has completed its 10 years of "market exclusivity" **for its indication in hyperammonaemia due to N-acetylglutamate synthetase (NAGS) deficiency.*** | 24/01/2003 | Orphan Europe S.a.r.l. |
| CAYSTON | Aztreonam | Suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with **cystic fibrosis** (CF) aged 6 years and older. | 21/09/2009 | Gilead Sciences International Limited |
| CEPLENE | Histamine dihydrochloride | Maintainance therapy 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. | 07/10/2008 | Meda AB |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| CYSTADANE | Betaine anhydrous | 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. | 15/02/2007 | Orphan Europe S.a.r.l. |
| DACOGEN | Decitabine | 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 Organization (WHO) classification, who are not candidates for standard induction chemotherapy. | 20/09/2012 | Janssen-Cilag International N V |
| DEFITELIO | Defibrotide | Defitelio is indicated for the treatment of **severe hepatic veno-occlusive disease (VOD)** also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy. It is indicated in adults and in adolescents, children and infants over 1 month of age. | 18/10/2013 | Gentium S.p.a. |
| DIACOMIT | Stiripentol | 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. | 04/01/2007 | Biocodex |
| ELAPRASE | Idursulfase | Long-term treatment of patients with **Hunter syndrome** (Mucopolysaccharidosis II, MPS II). | 08/01/2007 | Shire Human Genetic Therapies AB |
| ESBRIET | Pirfenidone | In adults for the treatment of mild to moderate **Idiopathic Pulmonary Fibrosis** (IPF). | 28/02/2011 | InterMune UK Ltd. |
| EVOLTRA | Clofarabine | 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. | 29/05/2006 | Genzyme Europe B.V. |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| EXJADE | Deferasirox | *Treatment of **chronic iron overload due to frequent blood transfusions** (≥ 7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older.<br>*Treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups:<br>- in patients with **beta thalassaemia major with iron overload** due to frequent blood transfusions in (≥ 7 ml/kg/month of packed red blood cells) patients aged 2 to 5 years<br>- in patients with **beta thalassaemia major with iron overload** due to infrequent blood transfusions (< 7 ml/kg/month of packed red blood cells) aged 2 years and older,<br>- in patients with other anaemias aged 2 years and older. | 28/08/2006 | Novartis Europharm Ltd |
| FIRAZYR | Icatibant acetate | Symptomatic treatment of acute attacks of **hereditary angioedema** (HAE) in adults (with C1-esterase-inhibitor deficiency). | 11/07/2008 | Shire Orphan Therapies GmbH |
| FIRDAPSE (ex-ZENAS) | Amifampridine | Symptomatic treatment of **Lambert-Eaton myasthenic syndrome** (LEMS) in adults. | 23/12/2009 | Biomarin Europe Ltd |
| GLIOLAN | 5-aminolevulinic acid hydrochloride | In adult patients for visualisation of malignant tissue during surgery for **malignant glioma** (World Health Organization grade III and IV). | 07/09/2007 | Medac GmbH |
| GLYBERA | Alipogene tiparvovec | 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. | 29/10/2012 | uniQure biopharma B.V. |
| ICLUSIG | Ponatinib | Iclusig is indicated in adult patients with :<br>- 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 ;<br>- **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. | 01/07/2013 | ARIAD Pharma Ltd |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| IMNOVID (ex POMALIDOMIDE CELGENE) | Pomalidomide | In combination with dexamethasone, 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. | 05/08/2013 | Celgene Europe Limited |
| INCRELEX | Mecasermin | Long-term treatment of **growth failure** in children and adolescents with severe **primary insulin-like growth factor 1 deficiency** (Primary IGFD). | 03/08/2007 | Ipsen Pharma |
| INOVELON | Rufinamide | Adjunctive therapy in the treatment of seizures associated with **Lennox Gastaut syndrome** in patients aged 4 years and older. | 16/01/2007 | Eisai Ltd |
| JAKAVI | Ruxolitinib | 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.** | 23/08/2012 | Novartis Europharm Ltd |
| KALYDECO | Ivacaftor | Kalydeco is indicated for the treatment of **cystic fibrosis** (CF) in patients age 6 years and older who have a *G551D* mutation in the *CFTR* gene. | 23/07/2012 | Vertex Pharmaceuticals (U.K.) Limited |
| KUVAN | Sapropterin dihydrochloride | *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<br>*Treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients with **tetrahydrobiopterin (BH4) deficiency** who have been shown to be responsive to such treatment. | 02/12/2008 | Merck Serono Europe Ltd |
| LITAK | Cladribine (subcutaneous use) | Treatment of **hairy cell leukaemia.** | 14/04/2004 | Lipomed GmbH |
| LYSODREN | Mitotane | Symptomatic treatment of advanced (unresectable, metastatic or relapsed) **adrenal cortical carcinoma.** | 28/04/2004 | Laboratoire HRA Pharma |
| MEPACT | Mifamurtide | 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. | 06/03/2009 | IDM Pharma SAS |
| MOZOBIL | Plerixafor | 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. | 31/07/2009 | Genzyme Europe B.V. |
| MYOZYME | Recombinant human acid alpha-glucosidase<br>INN = Alglucosidase alpha | Long-term enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of **Pompe disease** (acid $\alpha$-glucosidase deficiency). | 29/03/2006 | Genzyme Europe B.V. |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| NAGLAZYME | N-acetylgalac-tosamine-4-sulfatase INN = Galsulfase | Long-term enzyme replacement therapy in patients with a confirmed diagnosis of **Mucopolysaccharidosis VI** (MPS VI; N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux-Lamy syndrome). | 24/01/2006 | BioMarin Europe Ltd |
| NEXAVAR | Sorafenib tosylate | *Treatment of **hepatocellular carcinoma**<br>*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. | 19/07/2006 | Bayer Pharma AG |
| NEXOBRID | Concentrate of proteolytic en-zymes enriched in bromelain | Removal of eschar in adults with **deep partial- and full-thickness thermal burns.** | 18/12/2012 | Mediwound Germany Gmbh |
| NPLATE | Romiplostim | Adult chronic **immune (idiopathic) thrombocytopenic purpura** (ITP) in splenectomised patients who are 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. | 04/02/2009 | Amgen Europe B.V. |
| ORFADIN | Nitisinone | Treatment of patients with confirmed diagnosis of **hereditary tyrosinemia type 1** (HT-1) in combination with dietary restriction of tyrosine and phenylalanine. | 21/02/2005 | Swedish Orphan Biovi-trum Interna-tional AB |
| ORPHACOL | Cholic acid | Treatment of **inborn errors in primary bile acid synthesis due to 3bêta-Hydroxy-delta5-C27-steroid oxidoreductase deficiency or delta4-3-Oxosteroid-5bêta-reductase deficiency** in infants, children and adolescents aged 1 month to 18 years and adults. | 12/09/2013 | Laboratoires CTRS |
| PEDEA | Ibuprofen | Treatment of a haemodynamically significant **patent *ductus arteriosus*** in preterm newborn infants less than 34 weeks of gestational age. | 29/07/2004 | Orphan Europe S.a.r.l. |
| PEYONA (ex-NYMUSA) | Caffeine citrate | Treatment of **primary apnea** of premature newborns. | 02/07/2009 | Chiesi Farma-ceutici SpA |
| PLENADREN | Hydrocortisone | Treatment of **adrenal insufficiency** in adults. | 03/11/2011 | ViroPharma SPRL |
| PRIALT | Ziconotide (intraspinal use) | Treatment of severe, **chronic pain** in patients who require **intrathecal (IT) analgesia.** | 21/02/2005 | Eisai Ltd |
| PROCYSBI | Mercaptamine bitartrate | 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. | 06/09/13 | Raptor Phar-maceuticals Europe B.V. |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| REVATIO | Sildenafil citrate | *Treatment of adult patients with **pulmonary arterial hypertension** classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in primary pulmonary hypertension and pulmonary hypertension associated with connective tissue disease.<br>*Treatment of paediatric patients aged 1 year to 17 years old with **pulmonary arterial hypertension**. Efficacy in terms of improvement of exercise capacity or pulmonary haemodynamics has been shown in primary pulmonary hypertension and pulmonary hypertension associated with congenital heart disease.<br>Revatio solution for injection is for the treatment of adult patients with pulmonary arterial hypertension who are currently prescribed oral Revatio and who are temporarily unable to take oral therapy, but are otherwise clinically and haemodynamically stable. | 28/10/2005 | Pfizer Ltd |
| REVESTIVE | Teduglutide | Treatment of adult patients with **Short Bowel Syndrome**. Patients should be stable following a period of intestinal adaptation after surgery. | 30/08/2012 | Nycomed Danmark ApS |
| REVLIMID | Lenalidomide | * Revlimid in combination with dexamethasone is indicated for the treatment of **multiple myeloma** in adult patients who have received at least one prior therapy.<br>* 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. | 14/06/2007 | Celgene Europe Ltd |
| SAVENE | Dexrazoxane | In adults for the treatment of **anthracycline extravasation.** | 28/07/2006 | SpePharm Holding B.V. |
| SIGNIFOR | Pasireotide | Treatment of adult patients with **Cushing's disease** for whom surgery is not an option or for whom surgery has failed. | 24/04/2012 | Novartis Europharm Ltd |
| SIKLOS | Hydroxycarbamide | 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.** | 29/06/2007 | Addmedica |
| SOLIRIS | Eculizumab | For the treatment of adults and children with :<br>- **paroxysmal nocturnal haemoglobinuria** (PNH). Evidence of clinical benefit of Soliris in the treatment of patients with PNH is limited to patients with history of transfusions;<br>- **atypical haemolytic uraemic syndrome** (aHUS). | 20/06/2007 | Alexion Europe SAS |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| SPRYCEL | Dasatinib | Treatment of adult patients with:<br>- newly diagnosed Philadelphia chromosome positive (Ph+) **chronic myelogenous leukaemia** (CML) in the chronic phase.<br>- chronic, accelerated or blast phase CML with resistance or intolerance to prior therapy including imatinib mesilate.<br>- Ph+ **acute lymphoblastic leukaemia** (ALL) and lymphoid blast CML with resistance or intolerance to prior therapy. | 20/11/2006 | Bristol-Myers Squibb Pharma EEIG |
| TASIGNA | Nilotinib | * Tasigna 150 mg<br>Treatment of adult patients with newly diagnosed Philadelphia-chromosome-positive **chronic myelogenous leukaemia (CML)** in the chronic phase.<br>* Tasigna 200 mg<br>Treatment of adult patients with :<br>- newly diagnosed Philadelphia-chromosome-positive **CML** in the chronic phase;<br>- chronic phase and accelerated phase Philadelphia-chromosome-positive **CML** with resistance or intolerance to prior therapy including imatinib.<br>Efficacy data in patients with CML in blast crisis are not available. | 19/11/2007 | Novartis Europharm Ltd |
| TEPADINA | Thiotepa | In combination with other chemotherapy medicinal products:<br>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;<br>2) when high dose chemotherapy with **HPCT** support is appropriate for the treatment of solid tumours in adult and paediatric patients. It is proposed that Tepadina must be prescribed by physicians experienced in conditioning treatment prior to haematopoietic progenitor cell transplantation. | 15/03/2010 | Adienne S.r.l. |
| THALIDOMIDE CELGENE | Thalidomide | 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. | 16/04/2008 | Celgene Europe Ltd |
| TOBI PODHALER | Tobramycin | Suppressive therapy of **chronic pulmonary infection due to *Pseudomonas aeruginosa*** in adults and children aged 6 years and older with **cystic fibrosis.** | 20/07/2011 | Novartis Europharm Limited |
| TORISEL | Temsirolimus | *First-line treatment of adult patients with advanced **renal cell carcinoma** (RCC) who have at least three of six prognostic risk factors.<br>*Treatment of adult patients with relapsed and / or refractory **mantle cell lymphoma** (MCL). | 19/11/2007 | Pfizer Limited |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| TRACLEER | Bosentan monohydrate | * Treatment of **pulmonary arterial hypertension** (PAH) to improve exercise capacity and symptoms in patients with WHO functional class III. Efficacy has been shown in :<br>- primary (idiopathic and heritable) PAH,<br>- PAH secondary to scleroderma without significant interstitial pulmonary disease,<br>- 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.<br>* To reduce the number of new digital ulcers in patients with **systemic sclerosis** and ongoing digital ulcer disease.<br>*This orphan designated product has completed its 10 years of "market exclusivity"* ***for its indication in pulmonary arterial hypertension.*** | 15/05/2002 | Actelion Registration Ltd |
| VIDAZA | Azacitidine | Treatment of adult patients who are not eligible for haematopoietic stem cell transplantation with:<br>- intermediate-2 and high-risk **myelodysplastic syndromes** (MDS) according to the International Prognostic Scoring System (IPSS),<br>- **chronic myelomonocytic leukaemia** (CMML) with 10-29% marrow blasts without myeloproliferative disorder,<br>- **acute myeloid leukaemia** (AML) with 20-30 % blasts and multi-lineage dysplasia, according to World Health Organisation (WHO) classification. | 17/12/2008 | Celgene Europe Ltd |
| VOLIBRIS | Ambrisentan | Treatment of patients with **pulmonary arterial hypertension** (PAH) classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in idiopathic PAH (IPAH) and in PAH associated with connective tissue disease. | 21/04/2008 | Glaxo Group Ltd |
| VOTUBIA | Everolimus | * Treatment of adult patients with **renal angiomyolipoma** associated with **tuberous sclerosis complex** (TSC) who are at risk of complications (based on factors such as tumour size or presence of aneurysm, or presence of multiple or bilateral tumours) but who do not require immediate surgery.<br>The evidence is based on analysis of change in sum of angiomyolipoma volume.<br>* Treatment of patients with **subependymal giant cell astrocytoma** (SEGA) associated with **tuberous sclerosis complex** (TSC) who require therapeutic intervention but are not amenable to surgery.<br>The evidence is based on analysis of change in SEGA volume. Further clinical benefit, such as improvement in disease-related symptoms, has not been demonstrated. | 02/09/2011 | Novartis Europharm Ltd |
| VPRIV | Velaglucerase alfa | Long-term enzyme replacement therapy (ERT) in patients with **type 1 Gaucher disease.** | 26/08/2010 | Shire Pharmaceuticals Ireland Ltd |
| VYNDAQEL | Tafamidis | Treatment of **transthyretin amyloidosis** in adult patients with stage 1 symptomatic polyneuropathy to delay peripheral neurologic impairment. | 16/11/2011 | Pfizer Ltd |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| WILZIN | Zinc acetate dihydrate | Treatment of **Wilson's disease.** | 13/10/2004 | Orphan Europe S.a.r.l. |
| XAGRID | Anagrelide hydrochloride | Reduction of elevated platelet counts in at-risk **essential-thrombocythaemia** (ET) patients who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.<br>**An at-risk patient**<br>An at risk ET is defined by one or more of the following features:<br>- > 60 years of age or<br>- a platelet count > 1000 x $10^9$/l or<br>- a history of thrombo-haemorrhagic events. | 16/11/2004 | Shire Pharmaceutical Contracts Ltd |
| XALUPRINE (ex-MERCAPTOPURINE NOVA) | Mercaptopurine | Treatment of **acute lymphoblastic leukaemia** (ALL) in adults, adolescents and children. | 09/03/2012 | Nova Laboratories Ltd |
| YONDELIS | Trabectedin | *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.<br>*In combination with pegylated liposomal doxorubicin (PLD), treatment of patients with relapsed platinum-sensitive **ovarian cancer.** | 17/09/2007 | Pharma Mar S.A. |
| ZAVESCA | Miglustat | *Oral treatment of adult patients with mild to moderate **type 1 Gaucher disease**. Zavesca may be used only in the treatment of patients for whom enzyme replacement therapy is unsuitable<br>*Treatment of progressive neurological manifestations in adult patients and paediatric patients with **Niemann-Pick type C disease.**<br>*This orphan designated product has completed its 10 years of "market exclusivity" **for its indication in Gaucher Disease.*** | 20/11/2002 | Actelion Registration Ltd |

## Annexe 1

*Liste des médicaments orphelins retirés/supprimés du Registre Communautaire des médicaments orphelins à usage humain mais toujours indiqués dans des maladies rares*

*Cf. Partie II "Liste des médicaments avec une ou plusieurs indications de maladie rare en Europe avec autorisation de mise sur le marché européenne sans désignation orpheline".*

| TRADENAME | ACTIVE SUBSTANCE | REGULAR STATUS |
|---|---|---|
| AFINITOR | Everolimus | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 5 June 2007. Upon request of the marketing authorisation holder, Afinitor has now been removed from the Community Register of orphan medicinal products. |
| ALDURAZYME | Laronidase | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 14 February 2001. Aldurazyme was withdrawn from the Community register of orphan medicinal products in June 2013 at the end of the period of market exclusivity. |
| BUSILVEX | Busulfan | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 29 December 2001. Busilvex was withdrawn from the Community register of orphan medicinal products in October 2013 at the end of the period of market exclusivity. |
| FABRAZYME | Recombinant human alphagalactosidase A INN = Agalsidase beta | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 8 August 2000. Fabrazyme was withdrawn from the Community register of orphan medicinal products in August 2011 at the end of the period of market exclusivity. |
| GLIVEC | Imatinib mesilate | This product is no longer an orphan medicine. It was originally designated an orphan medicine for the following conditions:<br>- treatment of chronic myeloid leukaemia (14/02/2001);<br>- treatment of malignant gastrointestinal stromal tumours (20/11/2001);<br>- treatment of dermatofibrosarcoma protuberans (26/08/2005);<br>- treatment of acute lymphoblastic leukaemia (26/08/2005);<br>- treatment of chronic eosinophilic leukaemia and the hypereosinophilic syndrome (28/10/2005);<br>- treatment of myelodysplastic / myeloproliferative diseases (23/12/2005).<br>Upon request of the marketing-authorisation holder, Glivec has now been removed from the Community register of orphan medicinal products. |
| ILARIS | Canakinumab | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 20 March 2007. Upon request of the marketing authorisation holder, Ilaris has now been removed from the Community Register of orphan medicinal products. |
| NOVOTHIRTEEN | Catridecacog | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 12 December 2003. Upon request of the marketing-authorisation holder, NovoThirteen has now been removed from the Community Register of orphan medicinal products. |
| REPLAGAL | Agalsidase alfa | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 8 August 2000. Replagal was withdrawn from the Community register of orphan medicinal products in August 2011 at the end of the period of market exclusivity. |
| REVOLADE | Eltrombopag | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 3 August 2007. Upon request of the marketing authorisation holder, Revolade has now been removed from the Community Register of orphan medicinal products. |

| TRADENAME | ACTIVE SUBSTANCE | REGULAR STATUS |
|---|---|---|
| SOMAVERT | Pegvisomant | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 14 February 2001. Somavert was withdrawn from the Community register of orphan medicinal products in November 2012 at the end of the period of market exclusivity. |
| SUTENT | Sunitinib malate | This product is no longer an orphan medicine. This product was originally an orphan designated on 10 March 2005. Upon request of the marketing authorisation holder, Sutent has now been removed from the Community register of orphan medicinal products. |
| TRISENOX | Arsenic trioxide | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 18 October 2000. Trisenox was withdrawn from the Community register of orphan medicinal products in March 2012 at the end of the 10-year period of market exclusivity. |
| VENTAVIS | Iloprost | This product is no longer an orphan medicine. It was originally designated an orphan medicine on 29 December 2000. VENTAVIS was withdrawn from the Community register of orphan medicinal products in September 2013 at the end of the 10-year period of market exclusivity. |
| XYREM | Sodium oxybate | This product is no longer an orphan medicine. This product was originally an orphan designated on 3 February 2003. Upon request of the marketing authorisation holder, Xyrem has now been removed from the Community register of orphan medicinal products. |

## Annexe 2

*Liste des médicaments orphelins dont l'AMM Européenne est abrogée*

*Plus d'informations sur [www.ema.europa.eu](http://www.ema.europa.eu)*

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION (MA) INDICATION | MA DATE / MA HOLDER | MA WITHDRAWN DATE |
|---|---|---|---|---|
| ONSENAL | Celecoxib | Reduction of the number of adenomatous intestinal polyps in **familial adenomatous polyposis** (FAP), as an adjunct to surgery and further endoscopic surveillance. | 17/10/2003 Pfizer Ltd | 24/03/2011 |
| PHOTOBARR | Porfimer sodium (for use with photodynamic therapy) | Ablation of high-grade dysplasia (HGD) in patients with **Barrett's Oesophagus.** | 25/03/2004 Pinnacle Biologics B.V. | 20/04/2012 |
| RILONACEPT REGENERON (ex-ARCALYST) | Rilonacept | Treatment of **Cryopyrin-Associated Periodic Syndromes** (CAPS) with severe symptoms, including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS), in adults and children aged 12 years and older. | 23/10/2009 Regeneron UK Limited | 24/10/2012 |
| THELIN | Sitaxentan sodium | Treatment of patients with **pulmonary arterial hypertension** classified as WHO functional class III, to improve exercise capacity. Efficacy has been shown in primary pulmonary hypertension and in pulmonary hypertension associated with connective tissue disease. | 10/08/2006 Pfizer Ltd | 06/01/2011 |

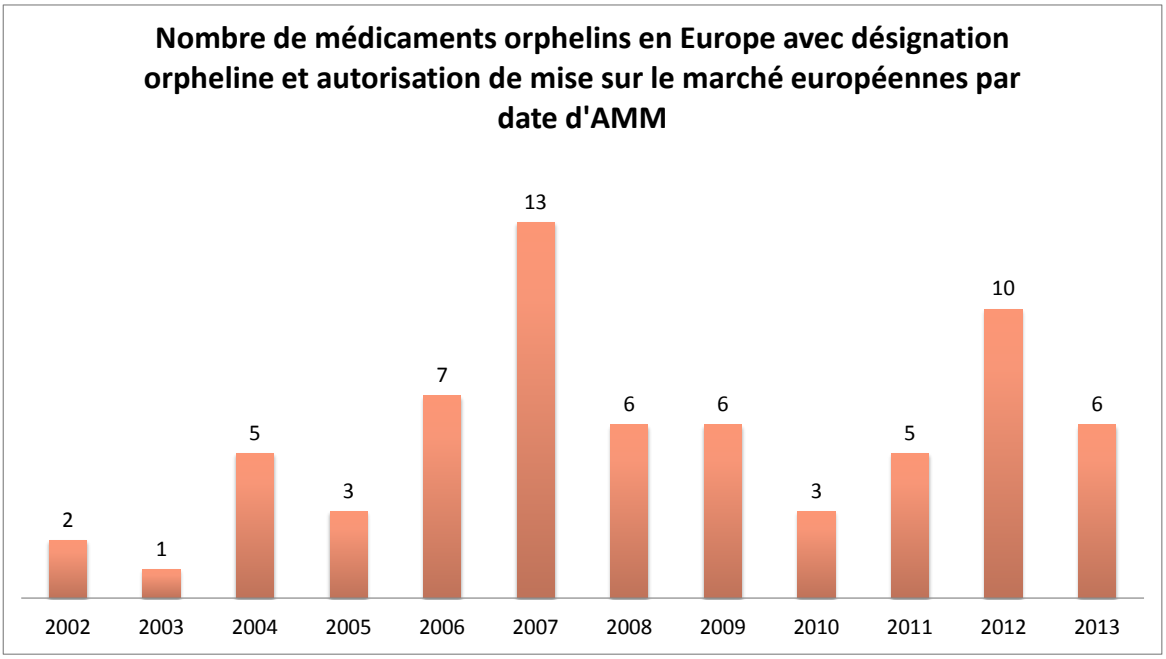
# Classification par date décroissante d'AMM

| 2013 |
|---|
| BOSULIF |
| DEFITELIO |
| ICLUSIG |
| IMNOVID |
| ORPHACOL |
| PROCYSBI |
| **2012** |
| ADCETRIS |
| BRONCHITOL |
| DACOGEN |
| GLYBERA |
| JAKAVI |
| KALYDECO |
| NEXOBRID |
| REVESTIVE |
| SIGNIFOR |
| XALUPRINE |
| **2011** |
| ESBRIET |
| PLENADREN |
| TOBI PODHALER |
| VOTUBIA |

| VYNDAQEL |
|---|
| **2010** |
| ARZERRA |
| TEPADINA |
| VPRIV |
| **2009** |
| CAYSTON |
| FIRDAPSE |
| MEPACT |
| MOZOBIL |
| NPLATE |
| PEYONA |
| **2008** |
| CEPLENE |
| FIRAZYR |
| KUVAN |
| THALIDOMIDE CELGENE |
| VIDAZA |
| VOLIBRIS |
| **2007** |
| ATRIANCE |
| CYSTADANE |
| DIACOMIT |

| ELAPRASE |
|---|
| GLIOLAN |
| INCRELEX |
| INOVELON |
| REVLIMID |
| SIKLOS |
| SOLIRIS |
| TASIGNA |
| TORISEL |
| YONDELIS |
| **2006** |
| EVOLTRA |
| EXJADE |
| MYOZYME |
| NAGLAZYME |
| NEXAVAR |
| SAVENE |
| SPRYCEL |
| **2005** |
| ORFADIN |
| PRIALT |
| REVATIO |

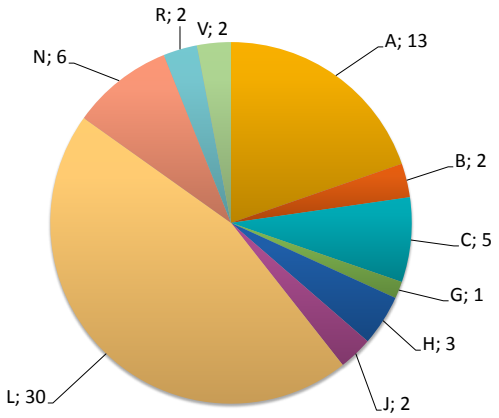
| 2004 |
|---|
| LITAK |
| LYSODREN |
| PEDEA |
| WILZIN |
| XAGRID |
| **2003** |
| CARBAGLU |
| **2002** |
| TRACLEER |
| ZAVESCA |



# Classification par classe ATC

| A- ALIMENTARY TRACT AND METABOLISM |
|---|
| CARBAGLU |
| CYSTADANE |
| ELAPRASE |
| KUVAN |
| MYOZYME |
| NAGLAZYME |
| ORFADIN |
| ORPHACOl |
| PROCYSBI |
| REVESTIVE |
| VPRIV |
| WILZIN |
| ZAVESCA |
| **B- BLOOD AND BLOOD FORMING ORGANS** |
| DEFITELIO |
| NPLATE |
| **C- CARDIOVASCULAR SYSTEM** |
| FIRAZYR |
| GLYBERA |
| PEDEA |
| TRACLEER |
| VOLIBRIS |
| **G- GENITO URINARY SYSTEM AND SEX HORMONES** |
| REVATIO |
| **H- SYSTEMIC HORMONAL PREPARATIONS, EXCL, SEX HORMONES AND INSULINS** |
| INCRELEX |
| PLENADREN |
| SIGNIFOR |
| **J- GENERAL ANTIINFECTIVES FOR SYSTEMIC USE** |
| CAYSTON |
| TOBI PODHALER |
| **L- ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS** |
| ADCETRIS |
| ARZERRA |
| ATRIANCE |
| BOSULIF |
| CEPLENE |
| DACOGEN |
| ESBRIET |
| EVOLTRA |
| GLIOLAN |
| ICLUSIG |
| IMNOVID |
| JAKAVI |
| LITAK |
| LYSODREN |
| MEPACT |
| MOZOBIL |
| NEXAVAR |
| REVLIMID |
| SIKLOS |
| SOLIRIS |
| SPRYCEL |
| TASIGNA |
| TEPADINA |
| THALIDOMIDE CELGENE |
| TORISEL |
| VIDAZA |
| VOTUBIA |
| XAGRID |
| XALUPRINE |
| YONDELIS |
| **N- NERVOUS SYSTEM** |
| DIACOMIT |
| FIRDAPSE |
| INOVELON |
| PEYONA |
| PRIALT |
| VYNDAQEL |
| **R- RESPIRATORY SYSTEM** |
| BRONCHITOL |
| KALYDECO |
| **V- VARIOUS** |
| EXJADE |
| SAVENE |
| **ATC CODE NOT YET ASSIGNED** |
| NEXOBRID |

**Nombre de médicaments orphelins en Europe avec désignation orpheline et autorisation de mise sur le marché européennes par catégorie ATC**



# Classification par titulaire d'AMM

| |
|---|
| **ACTELION REGISTRATION LTD** |
| TRACLEER |
| ZAVESCA |
| **ADDMEDICA** |
| SIKLOS |
| **ADIENNE SRL** |
| TEPADINA |
| **ALEXION EUROPE SAS** |
| SOLIRIS |
| **AMGEN EUROPE B.V.** |
| NPLATE |
| **ARIAD PHARMA LTD** |
| ICLUSIG |
| **BAYER PHARMA AG** |
| NEXAVAR |
| **BIOCODEX** |
| DIACOMIT |
| **BIOMARIN EUROPE LTD** |
| FIRDAPSE |
| NAGLAZYME |
| **BRISTOL MYERS SQUIBB EEIG** |
| SPRYCEL |
| **CELGENE EUROPE LTD** |
| IMNOVID |
| REVLIMID |
| THALIDOMIDE CELGENE |
| VIDAZA |
| **CHIESI FARMACEUTICI SPA** |
| PEYONA |
| **ESAI LTD** |
| INOVELON |
| PRIALT |
| **GENTIUM SPA** |
| DEFITELIO |

| |
|---|
| **GENZYME EUROPE B.V.** |
| EVOLTRA |
| MOZOBIL |
| MYOZYME |
| **GILEAD SCIENCES INTERNATIONAL LTD** |
| CAYSTON |
| **GLAXO GROUP LTD** |
| ARZERRA |
| ATRIANCE |
| VOLIBRIS |
| **IDM PHARMA SAS** |
| MEPACT |
| **INTERMUNE UK LTD** |
| ESBRIET |
| **IPSEN PHARMA** |
| INCRELEX |
| **JANSSEN-CILAG INTERNATIONAL NV** |
| DACOGEN |
| **LABORATOIRES CTRS** |
| ORPHACOL |
| **LABORATOIRE HRA PHARMA** |
| LYSODREN |
| **LIPOMED GMBH** |
| LITAK |
| **MEDA AB** |
| CEPLENE |
| **MEDAC GMBH** |
| GLIOLAN |
| **MEDIWOUND GERMANY GMBH** |
| NEXOBRID |
| **MERCK SERONO EUROPE LTD** |
| KUVAN |
| **NOVA LABORATORIES LTD** |
| XALUPRINE |

| |
|---|
| **NOVARTIS EUROPHARM LTD** |
| EXJADE |
| JAKAVI |
| SIGNIFOR |
| TASIGNA |
| TOBI PODHALER |
| VOTUBIA |
| **NYCOMED DANMARK APS** |
| REVESTIVE |
| **ORPHAN EUROPE S.A.R.L** |
| CARBAGLU |
| CYSTADANE |
| PEDEA |
| WILZIN |
| **PFIZER LTD** |
| BOSULIF |
| REVATIO |
| TORISEL |
| VYNDAQEL |
| **PHARMA MAR S.A.** |
| YONDELIS |
| **PHARMAXIS PHARMACEUTICALS LTD** |
| BRONCHITOL |
| **RAPTOR PHARMACEUTICALS EUROPE B.V.** |
| PROCYSBI |
| ELAPRASE |
| **SHIRE ORPHAN THERAPIES GMBH** |
| FIRAZYR |
| XAGRID |
| **SHIRE PHARMACEUTICALS IRELAND LTD** |
| VPRIV |
| **SPEPHARM HOLDING BV** |
| SAVENE |

| |
|---|
| **SWEDISH ORPHAN BIOVITRUM INTERNATIONAL AB** |
| ORFADIN |
| **TAKEDA GLOBAL RESEARCH AND DEVELOPMENT CENTRE (EUROPE) LTD** |
| ADCETRIS |
| **UNIQURE BIOPHARMA B.V.** |
| GLYBERA |
| **VERTEX PHARMACEUTICALS (U.K.) LTD** |
| KALYDECO |
| **VIROPHARMA SPRL** |
| PLENADREN |

PARTIE 2:

# Liste des médicaments avec une ou plusieurs indications de maladie rare en Europe avec autorisation de mise sur le marché européenne* sans désignation orpheline

## Sommaire



## Méthodologie

Cette liste présente l'ensemble des médicaments ayant obtenu une autorisation de mise sur le marché européenne pour une ou plusieurs indication(s) rare(s) mais n'ayant pas eu de désignation orpheline européenne ou pour lesquels la désignation orpheline est retirée/supprimée.

Ces médicaments peuvent avoir fait ou non, l'objet d'une désignation orpheline dans une autre région du monde. Ils sont présents dans la liste des produits ayant obtenu une autorisation de mise sur le marché de la DG Sanco : http://ec.europa.eu/health/documents/community-register/html/alfregister.htm

Un premier classement des spécialités donne le nom de la substance active, l'indication « rare » de l'AMM, la date d'AMM et le titulaire de l'AMM.

Trois listes annexes donnent le classement des mêmes spécialités par :

- date décroissante d'AMM ;
- classe ATC ;
- titulaire d'AMM.

Toutes les spécialités sont présentées par ordre alphabétique.

Vous pouvez trouver des informations complémentaires sur chaque médicament dans l'onglet « Médicaments orphelins » du site www.orphanet.fr ou sur le site de l'EMA (Agence Européenne du Médicament) http://www.ema.europa.eu.

**Autorisation de mise sur le marché de la Communauté Européenne par procédure centralisée*

# Classification par spécialités

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| ADCIRCA | Tadalafil | In adults for the treatment of **pulmonary arterial hypertension** (PAH) classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in idiopathic PAH (IPAH) and in PAH related to collagen vascular disease. | 01/10/2008 | Eli Lilly Nederland B.V. |
| ADVATE | Octocog alpha | Treatment and prophylaxis of bleeding in patients with **haemophilia A** (congenital factor VIII deficiency).<br>Advate does not contain von Willebrand Factor in pharmacologically effective quantities and is therefore not indicated in von Willebrand disease. | 02/03/2004 | Baxter AG |
| AFINITOR | Everolimus | *Treatment of unresectable or metastatic, well- or moderately-differentiated **neuroendocrine tumours of pancreatic origin** in adults with progressive disease.<br>*Treatment of patients with advanced **renal cell carcinoma**, whose disease has progressed on or after treatment with VEGF-targeted therapy. | 03/08/2009 | Novartis Europharm Ltd |
| ALDURAZYME | Laronidase | Long-term enzyme replacement therapy in patients with a confirmed diagnosis of **Mucopolysaccharidosis I** (MPS I; a [alpha]-L-iduronidase deficiency) to treat the non-neurological manifestations of the disease. | 10/06/2003 | Genzyme Europe B.V. |
| ALIMTA | Pemetrexed | In combination with cisplatin for the treatment of chemotherapy naïve patients with unresectable malignant pleural **mesothelioma.** | 20/09/2004 | Eli Lilly Nederland B.V. |
| AMMONAPS | Sodium phenylbutyrate | Adjunctive therapy in the chronic management of **urea cycle disorders**, involving deficiencies of carbamyl phosphate synthetase, ornithine transcarbamylase, or argininosuccinate synthetase. It is indicated in all patients with *neonatal-onset* presentation (complete enzyme deficiencies, presenting within the first 28 days of life). It is also indicated in patients with *late-onset* disease (partial enzyme deficiencies, presenting after the first month of life) who have a history of hyperammonaemic encephalopathy. | 08/12/1999 | Swedish Orphan Biovitrum International AB |
| ATRYN | Antithrombin alpha | Prophylaxis of venous thromboembolism in surgery of adult patients with **congenital antithrombin deficiency**. Atryn is normally given in association with heparin or low molecular weight heparin. | 28/07/2006 | GTC Biotherapeutics UK Limited |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| AVASTIN | Bevacizumab | * In combination with interferon alfa-2a for first line treatment of adult patients with advanced and/or metastatic **renal cell cancer**.<br>* In combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) **epithelial ovarian, fallopian tube, or primary peritoneal cancer**.<br>* In combination with carboplatin and gemcitabine for treatment of adult patients with first recurrence of platinum-sensitive **epithelial ovarian, fallopian tube or primary peritoneal cancer** who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents. | 12/01/2005 | Roche Registration Limited |
| BENEFIX | Recombinant coagulation Factor IX INN = Nonacog alpha | Treatment and prophylaxis of bleeding in patients with **haemophilia B** (congenital factor IX deficiency). | 27/08/1997 | Pfizer Ltd |
| BIOGRASTIM | Filgrastim | In patients, children or adults, with **severe congenital, cyclic, or idiopathic neutropenia** with an absolute neutrophil count (ANC) of $\leq 0.5 \times 10^9$/l, and a history of severe or recurrent infections, long term administration of Biograstim is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events. | 15/09/2008 | CT Arzneimittel GmbH |
| BUCCOLAM | Midazolam | Treatment of prolonged, acute, convulsive **seizures** in infants, toddlers, children and adolescents (from 3 months to < 18 years).<br>Buccolam must only be used by parents/carers where the patient has been diagnosed to have epilepsy.<br>For infants between 3-6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available. | 05/09/2011 | ViroPharma SPRL |
| BUSILVEX | Busulfan (Intravenous use) | 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.<br>Followed by cyclophosphamide (BuCy4) or melphalan (BuMel) is indicated as conditioning treatment prior to conventional haematopoietic progenitor cell transplantation in paediatric patients. | 09/07/2003 | Pierre Fabre Médicament |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| CAELYX | Doxorubicin hydrochloride (pegylated liposomal) | *For treatment of advanced **ovarian cancer** in women who have failed a first-line platinum-based chemotherapy regimen.<br>*In combination with bortezomib for the treatment of progressive **multiple myeloma** in patients who have received at least one prior therapy and who have already undergone or are unsuitable for bone marrow transplant.<br>*Treatment of AIDS-related **Kaposi's sarcoma** (KS) in patients with low CD4 counts (< 200 CD4 lymphocytes/mm$^3$) and extensive mucocutaneous or visceral disease. | 21/06/1996 | Janssen-Cilag International N.V. |
| CANCIDAS | Caspofungin | Treatment of invasive **aspergillosis** in adult or paediatric patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B and/or itraconazole.<br>Empirical therapy for presumed fungal infections (such as Candida or Aspergillus) in febrile, neutropaenic adult or paediatric patients. | 24/10/2001 | Merck Sharp & Dohme Ltd |
| CAPRELSA | Vandetanib | Treatment of aggressive and symptomatic medullary **thyroid cancer** (MTC) in patients with unresectable locally advanced or metastatic disease.<br>For patients in whom Rearranged during Transfection (RET) mutation is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision. | 17/02/2012 | AstraZeneca AB |
| CEPROTIN | Human protein C | *In purpura fulminans and coumarin-induced skin necrosis in patients with severe **congenital protein C deficiency.**<br>*Short-term prophylaxis in patients with severe **congenital protein C deficiency** : if surgery or invasive therapy is imminent, while initiating coumarin therapy, when coumarin therapy alone is not sufficient, when coumarin therapy is not feasible. | 16/07/2001 | Baxter AG |
| CEREZYME | Imiglucerase | Long-term enzyme replacement therapy in patients with a confirmed diagnosis of non-neuronopathic (**Type 1**) or chronic neuronopathic (**Type 3**) **Gaucher disease** and who exhibit clinically significant non-neurological manifestations of the disease, including one or more of the following conditions: anaemia after exclusion of other causes, such as iron deficiency; thrombocytopenia; bone disease after exclusion of other causes such as Vitamin D deficiency; hepatomegaly or splenomegaly. | 17/11/1997 | Genzyme Europe B.V. |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| CINRYZE | C1 inhibitor (human) | *Treatment and pre-procedure prevention of angioedema attacks in adults and adolescents with **hereditary angioedema (HAE)**.<br>*Routine prevention of angioedema attacks in adults and adolescents with severe and recurrent attacks of **hereditary angioedema (HAE)**, who are intolerant to or insufficiently protected by oral prevention treatments, or patients who are inadequately managed with repeated acute treatment. | 15/06/2011 | ViroPharma SPRL |
| COLOBREATHE | Colistimethate sodium | Management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with **cystic fibrosis** (CF) aged 6 years and older. | 13/02/2012 | Forest Laboratories UK Ltd |
| CYSTAGON | Mercaptamine bitartrate | 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. | 23/06/1997 | Orphan Europe S.A.R.L. |
| DEPOCYTE | Cytarabine | Intrathecal treatment of **lymphomatous meningitis**. In the majority of patients such treatment will be part of symptomatic palliation of the disease. | 11/07/2001 | Pacira Limited |
| DUKORAL | Vibrio cholerae and recombinant cholera toxin B-subunit | Active immunisation against **disease caused by *Vibrio cholerae*** serogroup O1 in adults and children from 2 years of age who will be visiting endemic/epidemic areas. | 28/04/2004 | Crucell Sweden AB |
| ENBREL | Etanercept | *Treatment of **polyarthritis** (rheumatoid-factorpositive or -negative) and extended **oligoarthritis** in children and adolescents from the age of 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate.<br>*Treatment of **psoriatic arthritis** in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, methotrexate.<br>*Treatment of **enthesitis-related arthritis** in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, conventional therapy.<br>Enbrel has not been studied in children aged less than 2 years. | 03/02/2000 | Pfizer Ltd |
| ERBITUX | Cetuximab | Treatment of patients with **squamous cell cancer of the head and neck** :<br>- in combination with radiation therapy for locally advanced disease,<br>- in combination with platinum-based chemotherapy for recurrent and/or metastatic disease. | 29/06/2004 | Merck KGaA |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| EURARTESIM | Piperaquine tetraphosphate / dihydroartemisinin | Treatment of uncomplicated ***Plasmodium falciparum*** **malaria** in adults, children and infants 6 months and over and weighing 5 kg or more.<br>Consideration should be given to official guidance on the appropriate use of antimalarial agents. | 27/10/2011 | Sigma-Tau Industrie Farmaceutiche Riunite S.p.A |
| FABRAZYME | Recombinant human alphagalactosidase INN = Agalsidase beta | Long-term enzyme replacement therapy in patients with a confirmed diagnosis of **Fabry disease** (alphagalactosidase A deficiency). | 03/08/2001 | Genzyme Europe B.V. |
| FERRIPROX | Deferiprone | Treatment of iron overload in patients with **thalassaemia** major when deferoxamine therapy is contraindicated or inadequate. | 25/08/1999 | Apotex Europe B.V. |
| FILGRASTIM HEXAL | Filgrastim | In patients, children or adults, with **severe congenital, cyclic,** or **idiopathic neutropenia** with an absolute neutrophil count (ANC) of $\leq 0.5 \times 10^9$/l, and a history of severe or recurrent infections. | 06/02/2009 | Hexal AG |
| FLEBOGAMMA DIF | Human normal immunoglobulin | * Replacement therapy in adults, and children and adolescents (2-18 years) in:<br>- **Primary immunodeficiency** (PID) syndromes with impaired antibody production.<br>- **Hypogammaglobulinaemia** and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed.<br>- **Hypogammaglobulinaemia** and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation.<br>- **Hypogammaglobulinaemia** in patients after allogeneic haematopoietic stem cell transplantation (HSCT).<br>* Immunomodulation in adults, and children and adolescents (2-18 years) in:<br>- **Primary immune thrombocytopenia** (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count.<br>**- Guillain-Barré syndrome,**<br>**- Kawasaki disease.** | 23/07/2007 | Instituto Grifols S.A. |

| TRADENAME | ACTIVE SUBSTANCE | MARKETING AUTHORISATION INDICATION | MARKETING AUTHORISATION DATE (DD/MM/YYYY) | MARKETING AUTHORISATION HOLDER |
|---|---|---|---|---|
| GLIVEC | Imatinib mesilate | * Treatment of :<br>- adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+) **chronic myeloid leukaemia** (CML) for whom bone marrow transplantation is not considered as the first line of treatment;<br>- adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis;<br>- adult and paediatric patients with newly diagnosed Philadelphia chromosome positive **acute lymphoblastic leukaemia** (Ph+ ALL) integrated with chemotherapy;<br>- adult patients with relapsed or refractory Ph+ ALL as monotherapy;<br>- adult patients with **myelodysplastic/ myeloproliferative diseases** (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements;<br>- adult patients with advanced **hypereosinophilic syndrome** (HES) and/or **chronic eosinophilic leukaemia** (CEL) with FIP1L1-PDGFRα rearrangement;<br>- adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant **gastrointestinal stromal tumours** (GIST);<br>- adjuvant treatment of adult patients who are at significant risk of relapse following resection of Kit (CD117)-positive **GIST**. Patients who have a low or very low risk of recurrence should not receive adjuvant treatment;<br>- adult patients with unresectable **dermatofibrosarcoma protuberans** (DFSP) and adult patients with recurrent and/or metastatic DFSP who are not eligible for surgery. | 07/11/2001 | Novartis Europharm Ltd |
| GONAL-F | Recombinant human follicle stimulating hormone INN = Follitropin alpha | Stimulation of spermatogenesis in men who have **congenital** or **acquired hypogonadotrophic hypogonadism** with concomitant human Chorionic Gonadotrophin (hCG) therapy. | 20/10/1995 | Merck Serono Europe Ltd |
| GRASTOFIL | Filgrastim | In adult patients with **severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil** count (ANC) of < ou = 0.5 x $10^9$/L, and a history of severe or recurrent infections, long term administration of Grastofil is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events. | 18/10/2013 | Apotex Europe B.V. |
| HELIXATE NEXGEN | Octocog alpha | Treatment and prophylaxis of bleeding in patients with **haemophilia A** (congenital factor VIII deficiency). | 04/08/2000 | Bayer Pharma AG |

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| HERCEPTIN | Trastuzumab | *In combination with capecitabine or 5-fluorouracil and cisplatin, treatment of patients with HER2-positive metastatic **adenocarcinoma of the stomach or gastroesophageal junction** who have not received prior anticancer treatment for their metastatic disease.<br>*Herceptin should only be used in patients with metastatic **gastric cancer** whose tumours have HER2 overexpression as defined by IHC2+ and a confirmatory SISH or FISH result, or by an IHC3+ result. Accurate and validated assay methods should be used. | 28/08/2000 | Roche Registration Limited |
| HIZENTRA | Human normal immunoglobulin (SCIg) | * Replacement therapy in adults and children in **primary immunodeficiency syndromes** such as:<br>- congenital **agammaglobulinaemia** and **hypogammaglobulinaemia,**<br>- **common variable immunodeficiency,**<br>- **severe combined immunodeficiency,**<br>- **IgG subclass deficiencies** with recurrent infections.<br>* Replacement therapy in **myeloma** or **chronic lymphocytic leukaemia** with severe secondary hypogammaglobulinaemia and recurrent infections. | 14/04/2011 | CSL Behring GmbH |
| HUMIRA | Adalimumab | *In combination with methotrexate is indicated for the treatment of active polyarticular **juvenile idiopathic arthritis**, in children and adolescents aged 2 to 17 years who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs).<br>*As monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate<br>Humira has not been studied in children aged less than 2 years. | 08/09/2003 | Abbott Laboratories Ltd |
| HYCAMTIN | Topotecan | **HYCAMTIN powder for concentrate for solution for infusion:**<br>*Monotherapy for the treatment of:<br>- patients with metastatic **carcinoma of the ovary** after failure of first-line or subsequent therapy.<br>- patients with relapsed **small cell lung cancer** (SCLC) for whom re-treatment with the first-line regimen is not considered appropriate.<br>*In combination with cisplatin for patients with **carcinoma of the cervix** recurrent after radiotherapy and for patients with Stage IVB disease. Patients with prior exposure to cisplatin require a sustained treatment free interval to justify treatment with the combination.<br><br>**HYCAMTIN capsules:**<br>As monotherapy for the treatment of adult patients with relapsed **small cell lung cancer** (SCLC) for whom re-treatment with the first-line regimen is not considered appropriate. | 12/11/1996 | SmithKline Beecham Ltd |

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| HYQVIA | Human normal immunoglobulin | * Replacement therapy in adults (> 18 years) in primary immunodeficiency syndromes such as:<br>- **congenital agammaglobulinaemia and hypogammaglobulinaemia**<br>- **common variable immunodeficiency**<br>- **severe combined immunodeficiency**<br>- **IgG subclass deficiencies** with recurrent infections.<br>* Replacement therapy in adults (> 18 years) in **myeloma or chronic lymphocytic leukaemia** with severe secondary hypogammaglobulinaemia and recurrent infections. | 16/05/2013 | Baxter Innovations GmbH |
| ILARIS | Canakinumab | *Treatment of **Cryopyrin-Associated Periodic Syndromes** (CAPS) in adults, adolescents and children aged **2** years and older with body weight of **7,5 kg** or above, including:<br>-Muckle-Wells Syndrome (MWS),<br>- Neonatal-Onset Multisystem Inflammatory Disease (NOMID) / Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA),<br>-Severe forms of Familial Cold Autoinflammatory Syndrome (FCAS) / Familial Cold Urticaria (FCU) presenting with signs and symptoms beyond cold-induced urticarial skin rash.<br>*Treatment of active **Systemic Juvenile Idiopathic Arthritis (SJIA)** in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. Ilaris can be given as monotherapy or in combination with methotrexate. | 23/10/2009 | Novartis Europharm Ltd |
| INLYTA | Axitinib | For the treatment of adult patients with advanced **renal cell carcinoma** (RCC) after failure of prior treatment with sunitinib or a cytokine. | 03/09/2012 | Pfizer Ltd. |
| INOMAX | Nitric oxide | In conjunction with ventilatory support and other appropriate active substances:<br>- for the treatment of newborn infants ≥ 34 weeks gestation with hypoxic respiratory failure associated with clinical or echocardiographic evidence of **pulmonary hypertension**, in order to improve oxygenation and to reduce the need for extracorporeal membrane oxygenation.<br>- as part of the treatment of peri- and post-operative pulmonary hypertension in adults and newborn infants, infants and toddlers, children and adolescents, ages 0-17 years in conjunction to heart surgery, in order to selectively decrease pulmonary arterial pressure and improve right ventricular function and oxygenation. | 01/08/2001 | INO Therapeutics AB |

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| INTRONA | Interferon alpha-2b | *Treatment of patients with **hairy cell leukaemia** Monotherapy treatment of adults with Philadelphia chromosome or bcr/abl translocation positive **chronic myelogenous leukaemia.** Combination therapy with cytarabine administered during the first 12 months of treatment has been demonstrated to significantly increase the rate of major cytogenetic responses and to significantly prolong the overall survival at three years when compared to interferon alfa-2b monotherapy *Treatment of patients with **multiple myeloma**, as maintenance therapy in patients who have achieved objective remission (more than 50 % reduction in myeloma protein) following initial induction chemotherapy. *Treatment of high tumour burden **follicular lymphoma** as adjunct to appropriate combination induction chemotherapy such as a CHOP-like regimen Treatment of carcinoid tumours with lymph node or liver metastases and with "carcinoid syndrome". | 09/03/2000 | Merck Sharp & Dohme Limited |
| IXIARO | Japanese Encephalitis Vaccine (inactivated, adsorbed) | For active immunization against **Japanese encephalitis** for adults, adolescents, children and infants aged 2 months and older. | 31/03/2009 | Intercell AG |
| KEPPRA | Levetiracetam | *As monotherapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 16 years of age with newly diagnosed **epilepsy**. *As adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults, children and infants from **1 month** of age with epilepsy ; in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with **Juvenile Myoclonic Epilepsy** ; in the treatment of primary generalised tonic-clonic seizures in adults and adolescents from 12 years of age with Idiopathic Generalised Epilepsy. | 29/09/2000 | UCB Pharma SA |
| KINERET | Anakinra | Kineret (100 mg/0.67 ml solution for injection) is indicated in adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above for the treatment of **Cryopyrin-Associated Periodic Syndromes (CAPS)**, including: - **Neonatal-Onset Multisystem Inflammatory Disease (NOMID) / Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA),** - **Muckle-Wells Syndrome (MWS),** - **Familial Cold Autoinflammatory Syndrome (FCAS).** | 08/03/2002 | Swedish Orphan Biovitrum AB |

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| KIOVIG | Human normal immunoglobulin | *Replacement therapy in adults, and children and adolescents (0-18 years) in:<br>- **Primary immunodeficiency syndromes** with impaired antibody production,<br>- **Hypogammaglobulinaemia** and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed,<br>- Hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation,<br>- Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT).<br>*Immunomodulation in adults, and children and adolescents (0-18 years) in:<br>- **Primary immune thrombocytopenia** (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count,<br>- **Guillain Barré syndrome,**<br>- **Kawasaki disease**,<br>- **Multifocal Motor Neuropathy** (MMN). | 19/01/2006 | Baxter AG |
| KOGENATE BAYER | Octocog alpha | Treatment and prophylaxis of bleeding in patients with **haemophilia A** (congenital factor VIII deficiency). | 04/08/2000 | Bayer Pharma AG |
| MABTHERA | Rituximab | * **Non-Hodgkin's lymphoma** (NHL)<br>- Treatment of previously untreated patients with stage III-IV **follicular lymphoma** in combination with chemotherapy.<br>- As maintenance therapy, the treatment of **follicular lymphoma** patients responding to induction therapy.<br>- In monotherapy, treatment of patients with stage III-IV **follicular lymphoma** who are chemoresistant or are in their second or subsequent relapse after chemotherapy.<br>- Treatment of patients with CD20 positive **diffuse large B cell non- Hodgkin's lymphoma** in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy.<br>* In combination with chemotherapy, treatment of patients with previously untreated and relapsed/ refractory **chronic lymphocytic leukaemia**. Only limited data are available on efficacy and safety for patients previously treated with monoclonal antibodies including MabThera or patients refractory to previous MabThera plus chemotherapy.<br>* **Granulomatosis with polyangiitis and Microscopic polyangiitis**<br>In combination with glucocorticoids, is indicated for the induction of remission in adult patients with severe, active **Granulomatosis with polyangiitis (Wegener's) (GPA)** and **Microscopic polyangiitis (MPA)**. | 02/06/1998 | Roche Registration Limited |

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| NIVESTIM | Filgrastim | In patients, children or adults, with **severe congenital, cyclic,** or **idiopathic neutropenia** with an absolute neutrophil count (ANC) of ≤ 0.5 x $10^9$/l, and a history of severe or recurrent infections. | 08/06/2010 | Hospira UK Ltd |
| NONAFACT | Human coagulation factor IX | Treatment and prophylaxis of bleeding in patients with **haemophilia B (congenital factor IX deficiency).** | 03/07/2001 | Sanquin |
| NOVOEIGHT | Turoctocog alpha | Treatment and prophylaxis of bleeding in patients with **haemophilia A (congenital factor VIII deficiency).** NovoEight can be used for all age groups. | 13/11/2013 | Novo Nordisk A/S |
| NOVOSEVEN | Human recombinant coagulation Factor VIIa<br>INN = Eptacog alpha (activated) | Treatment of bleeding episodes and for the prevention of bleeding in those undergoing surgery or invasive procedures in the following patient groups : in patients with congenital **haemophilia** with inhibitors to coagulation factors VIII or IX > 5 BU; in patients with congenital **haemophilia** who are expected to have a high anamnestic response to factor VIII or factor IX administration; in patients with **acquired haemophilia**; in patients with **congenital FVII deficiency**; in patients with **Glanzmann's thrombasthenia** with antibodies to GP IIb - IIIa and/or HLA, and with past or present refractoriness to platelet transfusions. | 23/02/1996 | Novo Nordisk A/S |
| NOVOTHIRTEEN | Catridecacog | Long term prophylactic treatment of bleeding in patients 6 years and above with **congenital factor XIII A-subunit deficiency.** | 03/09/2012 | Novo Nordisk A/S |
| NOXAFIL | Posaconazole | *Treatment of the fungal infections in adults:<br>- Invasive **aspergillosis** in patients with disease that is refractory to amphotericin B or itraconazole or in patients who are intolerant of these medicinal products,<br>- **Fusariosis** in patients with disease that is refractory to amphotericin B or in patients who are intolerant of amphotericin B.- **Chromoblastomycosis** and **mycetoma** in patients with disease that is refractory to itraconazole or in patients who are intolerant of itraconazole,<br>- **Coccidioidomycosis** in patients with disease that is refractory to amphotericin B, itraconazole or fluconazole or in patients who are intolerant of these medicinal products.<br>*Prophylaxis of invasive fungal infections in :<br>- Patients receiving remission-induction chemotherapy for acute myelogenous leukemia (AML) or myelodysplastic syndromes (MDS) expected to result in prolonged neutropenia and who are at high risk of developing invasive fungal infections,<br>- Hematopoietic stem cell transplant (HSCT) recipients who are undergoing high-dose immunosuppressive therapy for graft versus host disease and who are at high risk of developing invasive fungal infections. | 25/10/2005 | Merck Sharp & Dohme Ltd. |

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| NUEDEXTA | Dextromethorphan hydrobromide / Quinidine<br>INN = Dextromethorphan hydrobromide / Quinidine sulfate | For the symptomatic treatment of pseudobulbar affect (PBA) in adults. Efficacy has been studied in patients with underlying **Amyotrophic Lateral Sclerosis**. | 24/06/2013 | Jenson Pharmaceutical Services Limited |
| OMNITROPE | Somatropin | * Infants, children and adolescents:<br>- Growth disturbance due to **insufficient secretion of growth hormone** (GH),<br>- Growth disturbance associated with **Turner syndrome**,<br>- Growth disturbance (current height standard deviation score (SDS) < -2,5 and parental adjusted SDS < -1) in short children/adolescents born small for gestational age (SGA), with a birth weight and/or length below -2 standard deviation (SD), who failed to show catch-up growth (height velocity (HV) SDS < 0 during the last year) by 4 years of age or later,<br>- **Prader-Willi syndrome** (PWS), for improvement of growth and body composition. The diagnosis of PWS should be confirmed by appropriate genetic testing.<br>* Adults:<br>- Replacement therapy in adults with pronounced **growth hormone deficiency**. Patients with severe growth hormone deficiency in adulthood are defined as patients with known hypothalamic pituitary pathology and at least one known deficiency of a pituitary hormone not being prolactin. These patients should undergo a single dynamic test in order to diagnose or exclude a growth hormone deficiency. In patients with childhood onset isolated GH deficiency (no evidence of hypothalamic-pituitary disease or cranial irradiation), two dynamic tests should be recommended, except for those having low IGF-I concentrations (SDS < -2) who may be considered for one test. The cut-off point of the dynamic test should be strict. | 12/04/2006 | Sandoz GmbH |
| ORENCIA | Abatacept | In combination with methotrexate, for the treatment of moderate to severe active **polyarticular juvenile idiopathic arthritis** (JIA) in paediatric patients 6 years of age and older who have had an insufficient response to other DMARDs including at least one TNF inhibitor. | 21/05/2007 | Bristol-Myers Squibb Pharma EEIG |
| OZURDEX | Dexamethasone | For the treatment of adult patients with **inflammation of the posterior segment of the eye** presenting as **non-infectious uveitis.** | 27/07/2010 | Allergan Pharmaceuticals Ireland |

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| PANRETIN | Alitretinoin | Topical treatment of cutaneous lesions in patients with AIDS-related **Kaposi's sarcoma** (KS) : when lesions are not ulcerated or lymphoedematous, and treatment of visceral KS is not required, and when lesions are not responding to systemic antiretroviral therapy, and radiotherapy or chemotherapy are not appropriate. | 11/10/2000 | Eisai Ltd |
| PIXUVRI | Pixantrone dimaleate | As monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive **non-Hodgkin B cell lymphomas** (NHL). The benefit of pixantrone treatment has not been established in patients when used as fifth line or greater chemotherapy in patients who are refractory to last therapy. | 10/05/2012 | CTI Life Sciences Ltd |
| PRIVIGEN | Human normal immunoglobulin (IVIg) | * Replacement therapy in adults, and children and adolescents (0-18 years) in:<br>- **Primary immunodeficiency** (PID) syndromes with impaired antibody production,<br>- **Hypogammaglobulinaemia** and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed,<br>- **Hypogammaglobulinaemia** and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunization,<br>- **Hypogammaglobulinaemia** in patients after allogeneic haematopoietic stem cell transplantation (HSCT),<br>* Immunomodulation in adults, and children and adolescents (0-18 years) in:<br>-**Primary immune thrombocytopenia** (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count,<br>- **Guillain-Barré syndrome**,<br>- **Kawasaki disease**,<br>- **Chronic inflammatory demyelinating polyneuropathy** (CIDP). Only limited experience is available of use of intravenous immunoglobulins in children with CIDP. | 25/04/2008 | CSL Behring GmbH |
| PUREGON | Follitropin beta | Treatment of deficient spermatogenesis due to **hypogonadotrophic hypogonadism.** | 03/05/1996 | NV Organon |
| RATIOGRASTIM | Filgrastim | In patients, children or adults, with **severe congenital, cyclic,** or **idiopathic neutropenia** with an absolute neutrophil count (ANC) of $\leq 0.5 \times 10^9$/l, and a history of severe or recurrent infections. | 15/09/2008 | Ratiopharm GmbH |
| REFACTO AF | Moroctocog alpha | Treatment and prophylaxis of bleeding in patients with **haemophilia A** (congenital factor VIII deficiency) in adults and children of all ages, including newborns. | 13/04/1999 | Pfizer Ltd |

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| REPLAGAL | Agalsidase alfa | Long-term enzyme replacement therapy in patients with a confirmed diagnosis of **Fabry Disease** (alpha-galactosidase A deficiency) | 03/08/2001 | Shire Human Genetic Therapies AB |
| REVOLADE | Eltrombopag | 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. | 11/03/2010 | Glaxo-SmithKline Trading Services Limited |
| RILUTEK | Riluzole | To extend life or the time to mechanical ventilation for patients with **amyotrophic lateral sclerosis** (ALS). | 10/06/1996 | Aventis Pharma S.A. |
| ROACTEMRA | Tocilizumab | Treatment of active **systemic juvenile idiopathic arthritis** (sJIA) in patients 2 years of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX. | 16/01/2009 | Roche Registration Ltd |
| RUCONEST | Conestat alfa | Treatment of acute angioedema attacks in adults with **hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency.** | 28/10/2010 | Pharming Group N.V. |
| SAMSCA | Tolvaptan | Treatment of adult patients with hyponatraemia secondary to **syndrome of inappropriate antidiuretic hormone secretion** (SIADH). | 03/08/2009 | Otsuka Pharmaceutical Europe Ltd |
| SOMAVERT | Pegvisomant | 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 tolerate. | 13/11/2002 | Pfizer Ltd |
| STAYVEER | Bosentan monohydrate | * For the treatment of **pulmonary arterial hypertension** (PAH) to improve exercise capacity and symptoms in patients with WHO functional class III. Efficacy has been shown in:<br>- Primary (idiopathic and heritable) PAH ;<br>- PAH secondary to scleroderma without significant interstitial pulmonary disease ;<br>- PAH associated with congenital systemic-to-pulmonary shunts and Eisenmenger's physiology.<br>Some improvements have also been shown in patients with PAH WHO functional class II.<br>* To reduce the number of new digital ulcers in patients with **systemic sclerosis** and ongoing digital ulcer disease. | 24/06/2013 | Marklas Nederland BV |

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| SUTENT | Sunitinib | *Treatment of unresectable and/or metastatic malignant **gastrointestinal stromal tumour** (GIST) after failure of imatinib mesilate treatment due to resistance or intolerance.<br>*Treatment of advanced/metastatic **renal cell carcinoma** (MRCC) in adults.<br>*Treatment of unresectable or metastatic, well-differentiated **pancreatic neuroendocrine tumours** (pNET) with disease progression in adults<br>Experience with SUTENT as first-line treatment is limited. | 19/07/2006 | Pfizer Limited |
| TARCEVA | Erlotinib | In combination with gemcitabine, for the treatment of patients with metastatic **pancreatic cancer**.<br>When prescribing Tarceva, factors associated with prolonged survival should be taken into account.<br>No survival advantage could be shown for patients with locally advanced disease. | 19/09/2005 | Roche Registration Limited |
| TARGRETIN | Bexarotene | Treatment of skin manifestations of advanced stage **cutaneous T-cell lymphoma** (CTCL) patients refractory to at least one systemic treatment. | 29/03/2001 | Eisai Ltd |
| TAXOTERE | Docetaxel | *In combination with cisplatin and 5-fluorouracil for the treatment of patients with metastatic **gastric adenocarcinoma**, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for metastatic disease<br>*In combination with cisplatin and 5-fluorouracil for the induction treatment of patients with locally advanced **squamous cell carcinoma of the head and neck.** | 27/11/1995 | Aventis Pharma S.A. |
| TEMODAL | Temozolomide | *Treatment of adult patients with newly-diagnosed **glioblastoma** multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment.<br>*Treatment of children from the age of three years, adolescents and adult patients with **malignant glioma**, such as **glioblastoma** multiforme or anaplastic **astrocytoma**, showing recurrence or progression after standard therapy. | 26/01/1999 | Merck Sharp & Dohme Ltd. |
| TEVAGRASTIM | Filgrastim | In patients, children or adults, with **severe congenital, cyclic,** or **idiopathic neutropenia** with an absolute neutrophil count (ANC) of $\leq 0.5 \times 10^9$/l, and a history of severe or recurrent infections. | 15/09/2008 | Teva Generics GmbH |
| TEYSUNO | Tegafur/Gimeracil /Oteracil | In adults for the treatment of advanced **gastric cancer** when given in combination with cisplatin. | 14/03/2011 | Nordic Group BV |

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| THYROGEN | Thyrotropin alfa | For use with serum thyroglobulin (Tg) testing with or without radioiodine imaging for the detection of thyroid remnants and **well-differentiated thyroid cancer** in post-thyroidectomy patients maintained on hormone suppression therapy (THST).<br>Low-risk patients with well-differentiated thyroid carcinoma who have undetectable serum Tg levels on THST and no rh (recombinant human) TSH-stimulated increase of Tg levels may be followed-up by assaying rh TSH-stimulated Tg levels.<br>For pre-therapeutic stimulation in combination with a range of 30 mCi (1.1 GBq) to 100 mCi (3.7 GBq) radioiodine for ablation of thyroid tissue remnants in patients who have undergone a near-total or total thyroidectomy for **well-differentiated thyroid cancer** and who do not have evidence of distant metastatic thyroid cancer. | 09/03/2000 | Genzyme Europe B.V. |
| TRISENOX | Arsenic trioxide | Induction of remission and consolidation in adult patients with relapsed/refactory **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 should have included a retinoid and chemotherapy. | 05/03/2002 | Cephalon Europe |
| VEDROP | Tocofersolan | Indicated in vitamin E deficiency due to digestive malabsorption in paediatric patients with **congenital chronic cholestasis** or **hereditary chronic cholestasis**, from birth (full term newborns) up to 18 years of age. | 24/07/2009 | Orphan Europe S.A.R.L |
| VELCADE | Bortezomib | * As monotherapy is indicated for the treatment of adult patients with progressive **multiple myeloma** who have received at least 1 prior therapy and who have already undergone or are unsuitable for bone marrow transplantation.<br>* In combination with melphalan and prednisone is indicated for the treatment of adult patients with previously untreated **multiple myeloma** who are not eligible for high-dose chemotherapy with bone marrow transplant.<br>* In combination with dexamethasone, or with dexamethasone and thalidomide, is indicated for the induction treatment of adult patients with previously untreated **multiple myeloma** who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. | 26/04/2004 | Janssen-Cilag International NV |
| VENTAVIS | Iloprost | Treatment of patients with **primary pulmonary hypertension**, classified as NYHA functional class III, to improve exercise capacity and symptoms. | 16/09/2003 | Bayer Pharma AG |

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| VFEND | Voriconazole | In adults and children aged 2 years and above as follows:<br>- treatment of invasive **aspergillosis**.<br>- treatment of **serious fungal infections** caused by *Scedosporium spp*. and *Fusarium spp*.<br>Vfend should be administered primarily to patients with progressive, possibly life-threatening infections. | 19/03/2002 | Pfizer Limited |
| VONCENTO | Human coagulation factor VIII / Von Willebrand factor | * Treatment of haemorrhage or prevention and treatment of surgical bleeding in patients with **von Willebrand disease (VWD)**, when desmopressin (DDAVP) treatment alone is ineffective or contraindicated.<br>* Prophylaxis and treatment of bleeding in patients with **haemophilia A (congenital FVIII deficiency)**. | 12/08/2013 | CSL BEHRING GMBH |
| VOTRIENT | Pazopanib | *In adults for the first-line treatment of advanced **renal cell carcinoma** (RCC) and for patients who have received prior cytokine therapy for advanced disease.<br>*For the treatment of adult patients with selective subtypes of advanced **soft-tissue sarcoma** (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo)-adjuvant therapy.<br>Efficacy and safety have only been established in certain STS histological tumour subtypes. | 14/06/2010 | Glaxo Group Ltd |
| XELODA | Capecitabine | First-line treatment of advanced **gastric cancer** in combination with a platinum-based regimen | 02/02/2001 | Roche Registration Limited |
| XYREM | Sodium oxybate | Treatment of **narcolepsy with cataplexy** in adult patients. | 13/10/2005 | UCB Pharma Ltd |
| ZARZIO | Filgrastim | In children and adults with **severe congenital, cyclic, or idiopathic neutropenia** with an absolute neutrophil count (ANC) of $\leq 0.5 \times 10^9$/l, and a history of severe or recurrent infections, long term administration of filgrastim is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events. | 06/02/2009 | Sandoz GmbH |
| ZEVALIN | Ibritumomab tiuxetan | *Consolidation therapy after remission induction in previously untreated patients with **follicular lymphoma.**<br>***Treatment of adult patients with rituximab relapsed or refractory CD20+ **follicular B-cell non-Hodgkin's lymphoma** (NHL). | 16/01/2004 | Spectrum Pharmaceuticals B.V. |
| ZUTECTRA | Human Hepatitis B Immunoglobulin | Prevention of **hepatitis B virus** (HBV) **re-infection** in HBV-DNA negative patients over 6 months **after liver transplantation for hepatitis B induced liver failure**. Zutectra is indicated in adults only. The concomitant use of adequate virostatic agents should be considered, if appropriate, as standard of hepatitis B re-infection prophylaxis. | 30/11/2009 | Biotest Pharma GmbH |

# Classification par date décroissante d'AMM

| 2013 |
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| GRASTOFIL |
| HYQVIA |
| NOVOEIGHT |
| NUEDEXTA |
| STAYVEER |
| VONCENTO |
| **2012** |
| CAPRELSA |
| COLOBREATHE |
| INLYTA |
| NOVOTHIRTEEN |
| PIXUVRI |
| **2011** |
| BUCCOLAM |
| CINRYZE |
| EURARTESIM |
| HIZENTRA |
| TEYSUNO |
| **2010** |
| NIVESTIM |
| OZURDEX |
| REVOLADE |
| RUCONEST |
| VOTRIENT |

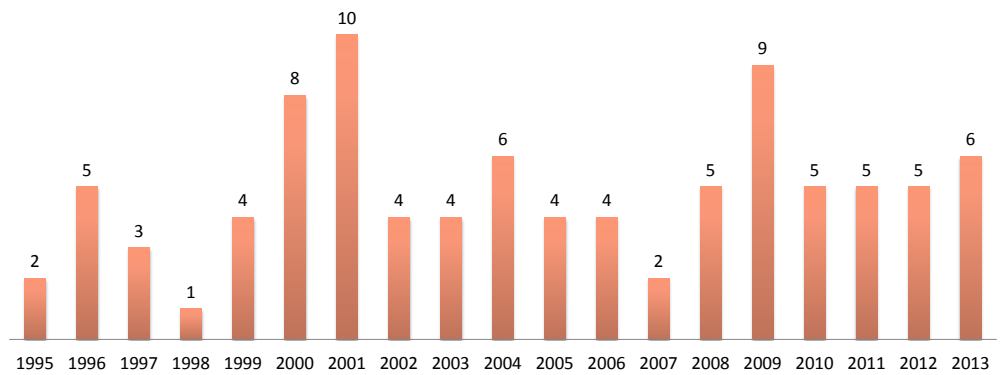
| 2009 |
|---|
| AFINITOR |
| FILGRASTIM HEXAL |
| ILARIS |
| IXIARO |
| ROACTEMRA |
| SAMSCA |
| VEDROP |
| ZARZIO |
| ZUTECTRA |
| **2008** |
| ADCIRCA |
| BIOGRASTIM |
| PRIVIGEN |
| RATIOGRASTIM |
| TEVAGRASTIM |
| **2007** |
| FLEBOGAMMA DIF |
| ORENCIA |
| **2006** |
| ATRYN |
| KIOVIG |
| OMNITROPE |
| SUTENT |

| 2005 |
|---|
| AVASTIN |
| NOXAFIL |
| TARCEVA |
| XYREM |
| **2004** |
| ADVATE |
| ALIMTA |
| DUKORAL |
| ERBITUX |
| VELCADE |
| ZEVALIN |
| **2003** |
| ALDURAZYME |
| BUSILVEX |
| HUMIRA |
| VENTAVIS |
| **2002** |
| KINERET |
| SOMAVERT |
| TRISENOX |
| VFEND |

| 2001 |
|---|
| CANCIDAS |
| CEPROTIN |
| DEPOCYTE |
| FABRAZYME |
| GLIVEC |
| INOMAX |
| NONAFACT |
| REPLAGAL |
| TARGRETIN |
| XELODA |
| **2000** |
| ENBREL |
| HELIXATE NEXGEN |
| HERCEPTIN |
| INTRONA |
| KEPPRA |
| KOGENATE BAYER |
| PANRETIN |
| THYROGEN |
| **1999** |
| AMMONAPS |
| FERRIPROX |
| REFACTO AF |
| TEMODAL |

| 1998 |
|---|
| MABTHERA |
| **1997** |
| BENEFIX |
| CEREZYME |
| CYSTAGON |
| **1996** |
| CAELYX |
| HYCAMTIN |
| NOVOSEVEN |
| PUREGON |
| RILUTEK |
| **1995** |
| GONAL-F |
| TAXOTERE |

**Nombre de médicaments orphelins en Europe avec autorisation de mise sur le marché européenne sans désignation orpheline par date d'AMM**



# Classification par classe ATC

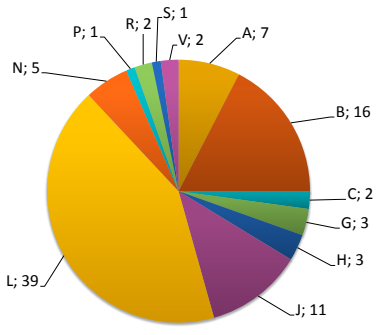
| A- ALIMENTARY TRACT AND METABOLISM |
|---|
| ALDURAZYME |
| AMMONAPS |
| CEREZYME |
| CYSTAGON |
| FABRAZYME |
| REPLAGAL |
| VEDROP |
| **B- BLOOD AND BLOOD FORMING ORGANS** |
| ADVATE |
| ATRYN |
| BENEFIX |
| CEPROTIN |
| CINRYZE |
| HELIXATE NEXGEN |
| KOGENATE BAYER |
| NONAFACT |
| NOVOEIGHT |
| NOVOSEVEN |
| NOVOTHIRTEEN |
| REFACTO AF |
| REVOLADE |
| RUCONEST |
| VENTAVIS |
| VONCENTO |
| **C- CARDIOVASCULAR SYSTEM** |
| SAMSCA |
| STAYVEER |

| G- GENITO URINARY SYSTEM AND SEX HORMONES |
|---|
| ADCIRCA |
| GONAL-F |
| PUREGON |
| **H- SYSTEMIC HORMONAL PREPARATIONS, EXCL, SEX HORMONES AND INSULINS** |
| OMNITROPE |
| SOMAVERT |
| THYROGEN |
| **J- GENERAL ANTIINFECTIVES FOR SYSTEMIC USE** |
| CANCIDAS |
| DUKORAL |
| FLEBOGAMMA DIF |
| HIZENTRA |
| HYQVIA |
| IXIARO |
| KIOVIG |
| NOXAFIL |
| PRIVIGEN |
| VFEND |
| ZUTECTRA |
| **L- ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS** |
| AFINITOR |
| ALIMTA |
| AVASTIN |

| BIOGRASTIM |
|---|
| BUSILVEX |
| CAELYX |
| CAPRELSA |
| DEPOCYTE |
| ENBREL |
| ERBITUX |
| FILGRASTIM HEXAL |
| GLIVEC |
| GRASTOFIL |
| HERCEPTIN |
| HUMIRA |
| HYCAMTIN |
| ILARIS |
| INLYTA |
| INTRONA |
| KINERET |
| MABTHERA |
| NIVESTIM |
| ORENCIA |
| PANRETIN |
| PIXUVRI |
| RATIOGRASTIM |
| ROACTEMRA |
| SUTENT |
| TARCEVA |
| TARGRETIN |
| TAXOTERE |
| TEMODAL |

| TEVAGRASTIM |
|---|
| TEYSUNO |
| TRISENOX |
| VELCADE |
| VOTRIENT |
| XELODA |
| ZARZIO |
| **N- NERVOUS SYSTEM** |
| BUCCOLAM |
| KEPPRA |
| NUEDEXTA |
| RILUTEK |
| XYREM |
| **P- ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS** |
| EURARTESIM |
| **R- RESPIRATORY SYSTEM** |
| COLOBREATHE |
| INOMAX |
| **S- SENSORY ORGANS** |
| OZURDEX |
| **V- VARIOUS** |
| FERRIPROX |
| ZEVALIN |

**Nombre de médicaments orphelins en Europe avec autorisation de mise sur le marché européenne sans désignation orpheline par catégorie ATC**



# Classification par titulaire d'AMM

| |
|---|
| **ABBOTT LABORATORIES LTD** |
| HUMIRA |
| **ALLERGAN PHARMACEUTICALS IRELAND** |
| OZURDEX |
| **APOTEX EUROPE B.V.** |
| FERRIPROX |
| GRASTOFIL |
| **ASTRAZENECA AB** |
| CAPRELSA |
| **AVENTIS PHARMA S.A.** |
| RILUTEK |
| TAXOTERE |
| **BAXTER AG** |
| ADVATE |
| CEPROTIN |
| KIOVIG |
| **BAXTER INNOVATIONS GMBH** |
| HYQVIA |
| **BAYER PHARMA AG** |
| HELIXATE NEXGEN |
| KOGENATE BAYER |
| VENTAVIS |
| **BIOTEST PHARMA GMBH** |
| ZUTECTRA |
| **BRISTOL-MYERS SQUIBB PHARMA EEIG** |
| ORENCIA |
| **CEPHALON EUROPE** |
| TRISENOX |
| **CRUCELL SWEDEN AB** |
| DUKORAL |
| **CSL BEHRING GMBH** |
| HIZENTRA |
| PRIVIGEN |
| VONCENTO |
| **CT ARZNEIMITTEL GMBH** |
| BIOGRASTIM |
| **CTI LIFE SCIENCES LTD** |
| PIXUVRI |
| **EISAI LTD** |
| PANRETIN |
| TARGRETIN |

| |
|---|
| **ELI LILLY NEDERLAND B.V.** |
| ADCIRCA |
| ALIMTA |
| **FOREST LABORATORIES UK LTD** |
| COLOBREATHE |
| **GENZYME EUROPE B.V.** |
| ALDURAZYME |
| CEREZYME |
| FABRAZYME |
| THYROGEN |
| **GLAXO GROUP LTD** |
| VOTRIENT |
| **GLAXOSMITHKLINE TRADING SERVICES LIMITED** |
| REVOLADE |
| **GTC BIOTHERAPEUTICS UK LIMITED** |
| ATRYN |
| **HEXAL AG** |
| FILGRASTIM HEXAL |
| **HOSPIRA UK LTD** |
| NIVESTIM |
| **INO THERAPEUTICS AB** |
| INOMAX |
| **INSTITUTO GRIFOLS S.A.** |
| FLEBOGAMMA DIF |
| **INTERCELL AG** |
| IXIARO |
| **JANSSEN-CILAG INTERNATIONAL NV** |
| CAELYX |
| VELCADE |
| **JENSON PHARMACEUTICALS SERVICES LIMITED** |
| NUEDEXTA |
| **MARKLAS NEDERLAND BV** |
| STAYVEER |
| **MERCK KGAA** |
| ERBITUX |

| |
|---|
| **MERCK SERONO EUROPE LTD** |
| GONAL-F |
| **MERCK SHARP & DOHME LTD** |
| CANCIDAS |
| INTRONA |
| NOXAFIL |
| TEMODAL |
| **NORDIC GROUP BV** |
| TEYSUNO |
| **NOVARTIS EUROPHARM LTD** |
| AFINITOR |
| GLIVEC |
| ILARIS |
| **NOVO NORDISK A/S** |
| NOVOEIGHT |
| NOVOSEVEN |
| NOVOTHIRTEEN |
| **NV ORGANON** |
| PUREGON |
| **ORPHAN EUROPE S.A.R.L.** |
| CYSTAGON |
| VEDROP |
| **OTSUKA PHARMACEUTICAL EUROPE LTD** |
| SAMSCA |
| **PACIRA LIMITED** |
| DEPOCYTE |
| **PFIZER LTD** |
| BENEFIX |
| ENBREL |
| INLYTA |
| REFACTO AF |
| SOMAVERT |
| SUTENT |
| VFEND |
| **PHARMING GROUP N.V.** |
| RUCONEST |
| **PIERRE FABRE MÉDICAMENTS** |
| BUSILVEX |

| |
|---|
| **RATIOPHARM GMBH** |
| RATIOGRASTIM |
| **ROCHE REGISTRATION LTD** |
| AVASTIN |
| HERCEPTIN |
| MABTHERA |
| ROACTEMRA |
| TARCEVA |
| XELODA |
| **SANDOZ GMBH** |
| OMNITROPE |
| ZARZIO |
| **SANQUIN** |
| NONAFACT |
| **SHIRE HUMAN GENETIC THERAPIES AB** |
| REPLAGAL |
| **SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.P.A** |
| EURARTESIM |
| **SMITHKLINE BEECHAM LTD** |
| HYCAMTIN |
| **SPECTRUM PHARMACEUTICALS B.V.** |
| ZEVALIN |
| **SWEDISH ORPHAN BIOVITRUM INTERNATIONAL AB** |
| AMMONAPS |
| KINERET |
| **TEVA GENERICS GMBH** |
| TEVAGRASTIM |
| **UCB PHARMA LTD** |
| XYREM |
| **UCB PHARMA SA** |
| KEPPRA |
| **VIROPHARMA SPRL** |
| BUCCOLAM |
| CINRYZE |

Rédacteurs du cahier : Virginie Hivert & Marie-Pierre Bécas-Garro ● Conception visuelle : Julie Christ ● Photographie : M. Depardieu/Inserm

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« Lists of medicinal products for rare diseases in Europe », Les Cahiers d'Orphanet, Série *Médicaments Orphelins*, Janvier 2014,
http://www.orpha.net/orphacom/cahiers/docs/FR/liste_des_medicaments_orphelins_en_europe.pdf