

# 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 30 June 2017)

| N° CHMP + opinions <sup>a</sup> | N° products <sup>b</sup> | Medicinal Product                                       | MA Sponsor                       | Authorised Therapeutic Indication  |      |
|---------------------------------|--------------------------|---|----------------------------------|--|------|
| 2001                            |                          |   |                                  |  |      |
| 1                               | 1                        | <b>Fabrazyme</b><br>(agalsidase beta)<br><b>EXPIRED</b> | Genzyme BV                       | Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency).   |      |
| 2                               | 2                        | <b>Replagal</b><br>(agalsidase alpha)<br><b>EXPIRED</b> | 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                        | <b>Glivec</b><br>(imatinib)<br><b>EXPIRED</b>           | Novartis<br>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                               |                          | <b>Glivec</b><br>(imatinib)<br><b>WITHDRAWN</b>         | Novartis<br>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                               |                          | <b>Glivec</b><br>(imatinib)<br><b>WITHDRAWN</b>         | Novartis<br>Europharm Limited    | Treatment of adult patients with unresectable recurrent and/or metastatic dermafibrosarcoma protuberans  | 2006 |
| 6                               |                          | <b>Glivec</b><br>(imatinib)<br><b>WITHDRAWN</b>         | Novartis<br>Europharm Limited    | Treatment of adult patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) as monotherapy   | 2006 |
| 7                               |                          | <b>Glivec</b><br>(imatinib)<br><b>WITHDRAWN</b>         | Novartis<br>Europharm Limited    | Treatment of adult patients with myelodysplastic/ myeloproliferative diseases (MDS/MPD) associated with PDGFR gene re-arrangement  | 2006 |
| 8                               |                          | <b>Glivec</b><br>(imatinib)<br><b>WITHDRAWN</b>         | Novartis<br>Europharm Limited    | Treatment of adult patients with hypereosinophilic syndrome (HES) and chronic eosinophilic leukaemia (CEL)   | 2006 |
| 2002                            |                          |   |                                  |  |      |
| 9                               | 4                        | <b>Trisenox</b><br>(arsenic trioxide)<br><b>EXPIRED</b> | 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.<br>The response rate of other acute myelogenous leukaemia subtypes to TRISENOX has not been examined."   |      |
| 10                             | 5                       | <b>Tracleer</b><br>(bosentan)<br><b>EXPIRED</b>       | Actelion<br>Registration<br>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:<br>- Primary (idiopathic and familial) 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." |      |
| 11                             |                         | <b>Tracleer</b><br>(bosentan)<br><b>WITHDRAWN</b>     | Actelion<br>Registration<br>Limited | Indicated to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease.  | 2007 |
| 12                             | 6                       | <b>Somavert</b><br>(pegvisomant)<br><b>EXPIRED</b>    | 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                       | <b>Zavesca</b><br>(miglustat)<br><b>EXPIRED</b>       | Actelion<br>Registration<br>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                             |                         | <b>Zavesca</b><br>(miglustat)                         | Actelion<br>Registration<br>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                       | <b>Carbaglu</b><br>(carglumic acid)<br><b>EXPIRED</b> | Orphan Europe<br>Sarl               | Treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency.   |      |
| 16                             |                         | <b>Carbaglu</b><br>(carglumic acid)                   | Orphan Europe<br>SARL - France      | This variation concerns an extension of indication of Carbaglu to add the treatment of hyperammonemia due to isovaleric acidemia, methylmalonic acidemia and propionic acidemia.   | 2011 |
| 17                             | 9                       | <b>Aldurazyme</b><br>(laronidase)<br><b>EXPIRED</b>   | Genzyme Europe<br>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                      | <b>Busilvex</b><br>(busulfan)<br><b>EXPIRED</b>       | Pierre Fabre<br>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.<br>Busilvex followed by cyclophosphamide (BuCy4) or melphalan (BuMel) is indicated as   |      |

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|--------------------------------|-------------------------|--|-------------------------------|---|
|                                |                         |  |                               | conditioning treatment prior to conventional haematopoietic progenitor cell transplantation in paediatric patients.   |
| 19                             | 11                      | <b>Ventavis</b><br>(iloprost)<br><b>EXPIRED</b>                                    | Schering AG                   | Treatment of patients with primary pulmonary hypertension, classified as NYHA functional class III, to improve exercise capacity and symptoms.  |
| 20                             | 12                      | <b>Onsenal</b><br>(celecoxib)<br><b>WITHDRAWN FROM THE MARKET - SAFETY</b>         | 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                      | <b>Photobarr</b><br>(porfimer sodium)<br><b>WITHDRAWN FROM THE MARKET - SAFETY</b> | 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                      | <b>Litak</b><br>(cladribine,B)<br><b>EXPIRED</b>                                   | Lipomed GmbH                  | Treatment of hairy cell leukaemia   |
| 23                             | 15                      | <b>Lysodren</b><br>(mitotane)<br><b>EXPIRED</b>                                    | 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                      | <b>Pedea</b><br>(ibuprofen)<br><b>EXPIRED</b>                                      | Orphan Europe SARL            | Indicated to close a patent ductus arteriosus in preterm newborn infants  |
| 25                             | 17                      | <b>Wilzin</b><br>(zinc-acetate dihydrate)<br><b>EXPIRED</b>                        | Orphan Europe SARL            | Treatment of Wilson's disease   |
| 26                             | 18                      | <b>Xagrid</b><br>(anegrelide hydrochloride)<br><b>EXPIRED</b>                      | Shire Pharmaceuticals 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                      | <b>Prialt</b><br>(ziconotide)<br><b>EXPIRED</b>                                    | 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                      | <b>Orfadin</b><br>(nitisinone)<br><b>EXPIRED</b>                                   | 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                      | <b>Xyrem</b><br>(sodium oxybate)<br><b>WITHDRAWN</b>                               | UCB Pharma Ltd                | Treatment of narcolepsy with cataplexy in adult patients.   |
| 30                             | 22                      | <b>Revatio</b><br>(sildenafil citrate)   | Pfizer limited                | Treatment of pulmonary arterial hypertension. Revatio has been shown to improve exercise ability and to reduce mean   |

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|--------------------------------|-------------------------|--|-----------------------------|--|------|
|                                |                         | <b>EXPIRED</b>   |                             | pulmonary arterial pressure  |      |
| 2006                           |                         |  |                             |  |      |
| 31                             | 23                      | <b>Naglazyme</b><br>(N-acetylgalactosamine 4-sulfatase,A)<br><b>EXPIRED</b>                          | 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                      | <b>Myozyme</b><br>(recombinant human acid alpha-glucosidase)<br><b>EXPIRED</b>                       | 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).<br><br>Myozyme is indicated in adults and paediatric patients of all ages.<br><br>In patients with late-onset Pompe disease the evidence of efficacy is limited.                            |      |
| 33                             | 25                      | <b>Evoltra</b><br>(clofarabine)<br><b>EXPIRED</b>  | 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                      | <b>Nexavar</b><br>(sorafenib tosylate)<br><b>EXPIRED</b>   | 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                             |                         | <b>Nexavar</b><br>(sorafenib tosylate)   | Bayer Healthcare AG         | Extension of Indication to include treatment of hepatocellular carcinoma   | 2007 |
| 36                             |                         | <b>Nexavar</b><br>(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                      | <b>Savene</b><br>(dexrazoxane)<br><b>EXPIRED</b>   | SpePharm Holding BV         | Treatment of anthracycline extravasation   |      |
| 38                             | 28                      | <b>Exjade</b><br>(4-(3,5-Bis(hydroxyphenyl) - 1,2,4) triazol-1-yl)benzoic acid, B)<br><b>EXPIRED</b> | Novartis Europharm Limited  | Treatment of chronic iron overload due to blood transfusions (transfusion haemosiderosis) in adult and paediatric patients (aged 2 years and over)   |      |
| 39                             | 29                      | <b>Sprycel</b><br>(dasatinib)<br><b>EXPIRED</b>  | 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.<br><br>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                      | <b>Sutent</b><br>(sunitinib)   | Pfizer Ltd.                 | Sutent is indicated for the treatment of advanced and/or metastatic renal cell   |      |

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|--------------------------------|-------------------------|---|---|--|------|
|                                |                         | <b>WITHDRAWN</b>  |   | carcinoma.<br><br>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                      | <b>Thelin</b><br>(sitaxentan sodium)<br><b>WITHDRAWN FROM THE MARKET - SAFETY</b> | 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                      | <b>Diacomit</b><br>(stiripentol)<br><b>EXPIRED</b>                                | 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                      | <b>Elaprase</b><br>(iduronate-2-sulfatase)<br><b>EXPIRED</b>                      | Shire Human Genetic Therapies AB - Sweden | "Elaprase is indicated for the long-term treatment of patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II).<br><br>Heterozygous females were not studied in the clinical trials."  |      |
| 44                             | 34                      | <b>Inovelon</b><br>(rufinamide)   | Esai Limited                              | Adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients 4 years and older  |      |
| 45                             | 35                      | <b>Cystadane</b><br>(betaine anhydrous A)<br><b>EXPIRED</b>                       | Orphan Europe                             | Adjunctive treatment of homocystinuria, involving deficiencies or defects in:<br><br>- cystathionine beta-synthase (CBS),<br>- 5,10-methylene-tetrahydrofolate reductase (MTHFR),<br>- cobalamin cofactor metabolism (cbl).<br><br>Cystadane should be used as supplement to other therapies such as vitamin B6 (pyridoxine), vitamin B12 (cobalamin), folate and a specific diet. |      |
| 46                             | 36                      | <b>Revlimid</b><br>(lenalidomide)   | Celgene Europe Ltd                        | Revlimid is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.<br><br>Revlimid in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.   |      |
| 47                             |                         | <b>Revlimid</b><br>(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.   | 2013 |
| 48                             | 37                      | <b>Soliris</b><br>(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  |      |

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|--------------------------------|-------------------------|---|-----------------------------|---|------|
|                                |                         |   |                             | with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history   |      |
| 49                             |                         | <b>Soliris</b><br>(eculizumab)                            | Alexion Europe SAS - France | Extension Of Indication for atypical haemolytic uremic syndrome (aHUS)  | 2011 |
| 50                             | 38                      | <b>Siklos</b><br>(hydroxyurea)                            | 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                      | <b>Increlex</b><br>(mecasermin)                           | Ipsen Pharma                | <p>Long-term treatment of growth failure in children and adolescents with severe primary insulin like growth factor-1 deficiency (Primary IGFD).</p> <p>Severe Primary IGFD is defined by:</p> <ul style="list-style-type: none"> <li>• height standard deviation score <math>\leq -3.0</math> and</li> <li>• basal IGF-1 levels below the 2.5th percentile for age and gender and</li> <li>• GH sufficiency.</li> </ul> <p>• Exclusion of secondary forms of IGF-1 deficiency, such as malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids.</p> <p>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.</p> |      |
| 52                             | 40                      | <b>Atriance</b><br>(nelarabine)                           | Glaxo Group Ltd             | <p>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.</p> <p>Due to the small patient populations in these disease settings, the information to support these indications is based on limited data.</p>  |      |
| 53                             | 41                      | <b>Gliolan</b><br>(5 aminolevulinic acid hydrochloride L) | Medac GmbH                  | Visualisation of malignant tissue during surgery for malignant glioma   |      |
| 54                             | 42                      | <b>Yondelis</b><br>(trabectedin)                          | 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 data are based mainly on liposarcoma and leiomyosarcoma patients   |      |
| 55                             |                         | <b>Yondelis</b><br>(trabectedin)                          | PharmaMar SA                | <p>EXTENSION OF INDICATION</p> <p>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.</p> <p>In combination with pegylated liposomal doxorubicin (PLD) is indicated for the treatment of patients with relapsed platinum-sensitive ovarian cancer.</p>   | 2009 |



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|--------------------------------|-------------------------|---|------------------------------------|---|------|
| 56                             | 43                      | <b>Torisel</b><br>(temsirolimus)              | Pfizer Limited                     | First-line treatment of patients with advanced renal cell carcinoma who have at least three of six prognostic risk factors.   |      |
| 57                             |                         | <b>Torisel</b><br>(temsirolimus)              | Pfizer Limited                     | EXTENSION OF INDICATION to include treatment of adult patients with relapsed and/or refractory mantle cell lymphoma.  | 2009 |
| 58                             | 44                      | <b>Tasigna</b><br>(nilotinib)                 | Novartis<br>Europharm Ltd          | Treatment of Philadelphia chromosome positive chronic myelogenous leukaemia (CML)   |      |
| 2008                           |                         |   |                                    |   |      |
| 59                             | 45                      | <b>Thalidomide Celgene</b><br>(thalidomide)   | 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                      | <b>Volibris</b><br>(ambrisentan)              | 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                      | <b>Firazyr</b><br>(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).  |      |
| 62                             | 48                      | <b>Ceplene</b><br>(histamine dihydrochloride) | 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                      | <b>Kuvan</b><br>(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.   |      |
| 64                             | 50                      | <b>Vidaza</b><br>(azacitidine)                | Celgene Europe Ltd- United Kingdom | Treatment of adult patients who are not eligible for haematopoietic stem cell transplantation with: <ul style="list-style-type: none"> <li>• intermediate-2 and high-risk myelodysplastic syndromes (MDS) according to the International Prognostic Scoring System (IPSS),</li> <li>• chronic myelomonocytic leukaemia (CMML) with 10-29% marrow blasts without myeloproliferative disorder,</li> <li>• acute myeloid leukaemia (AML) with 20-30% blasts and multi-lineage dysplasia, according to World Health Organisation (WHO) classification.</li> </ul> |      |
| 2009                           |                         |   |                                    |   |      |
| 65                             | 51                      | <b>Nplate</b><br>(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   |      |

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|--------------------------------|-------------------------|---|--|--|--|
|                                |                         |   |  | contra-indicated.  |  |
| 66                             | 52                      | <b>Mepact</b><br>(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.  |  |
| 67                             | 53                      | <b>Peyona</b><br>(previously Nymusa, caffeine citrate)  | Chiesi Farmaceutici S.P.A. - Italy                 | Treatment of primary apnoea of premature newborns.   |  |
| 68                             | 54                      | <b>Mozobil</b><br>(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.  |  |
| 69                             | 55                      | <b>Cayston</b><br>(aztreonam lysinate inhalation use)   | Gilead Sciences International Ltd – UK             | Suppressive therapy of chronic pulmonary infections due to <i>Pseudomonas aeruginosa</i> in patients with cystic fibrosis (CF) aged 18 years and older.  |  |
| 70                             | 56                      | <b>Rilonacept</b><br><b>Regeneron</b><br>(formerly Arcalyst; rilonacept)<br><b>WITHDRAWN FROM THE MARKET – SAFETY</b> | 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                      | <b>Firdapse</b><br>(amifampridine)  | BioMarin Europe Ltd                                | Symptomatic treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.   |  |
| 72                             | 58                      | <b>Revolade</b><br>(eltrombopag)<br><b>WITHDRAWN</b>  | 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.   |  |
| 73                             | 59                      | <b>Afinitor</b><br>(everolimus)<br><b>WITHDRAWN</b>   | 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                      | <b>Ilaris</b><br>(canakinumab)<br><b>WITHDRAWN</b>  | 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                      | <b>Tepadina</b><br>(thiotepa)   | Adienne S.r.l - Italy                              | Indicated, in combination with other chemotherapy medicinal products:<br>1) with or without total body irradiation (TBI), as conditioning treatment prior to   |  |



| N° CHMP + opinions<br><i>a</i> | N° products<br><i>b</i> | Medicinal Product   | MA Sponsor                                      | Authorised Therapeutic Indication  |      |
|--------------------------------|-------------------------|---|---|--|------|
|                                |                         |   |   | 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." |      |
| 76                             | 62                      | <b>Arzerra</b><br>(ofatumumab)  | Glaxo Group Limited - UK                        | Refractory chronic lymphocytic leukaemia (CLL):<br>Arzerra is indicated for the treatment of CLL in patients who are refractory to fludarabine and alemtuzumab.  |      |
| 77                             |                         | <b>Arzerra</b><br>(ofatumumab)  | Glaxo Group Limited - UK                        | Previously untreated chronic lymphocytic leukaemia (CLL):<br>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                      | <b>VPRIV</b><br>(velaglucerase alfa)  | Shire Pharmaceuticals Ireland Limited – Ireland | Treatment of type 1 Gaucher disease  |      |
| 2011                           |                         |   |   |  |      |
| 79                             | 64                      | <b>Esbriet</b><br>(perfenidone)   | InterMune UK Ltd.                               | Treatment of idiopathic pulmonary fibrosis   |      |
| 80                             | 65                      | <b>TOBI podhaler</b><br>(tobramycin)  | Novartis Europharm Limited                      | Suppressive therapy of chronic pulmonary infection due to <i>Pseudomonas aeruginosa</i> in adults and children aged 6 years and older with cystic fibrosis   |      |
| 81                             | 66                      | <b>Votubia</b><br>(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   |      |
| 82                             | 67                      | <b>Plenadren</b><br>(hydrocortisone (modified release tablet))                            | ViroPharma SPRL                                 | Treatment of adrenal insufficiency   |      |
| 83                             | 68                      | <b>Vyndaqel</b><br>(tafamidis)  | Pfizer Limited - UK                             | Treatment of transthyretin amyloidosis in patients with symptomatic polyneuropathy   |      |
| 2012                           |                         |   |   |  |      |
| 84                             | 69                      | <b>Xaluprine</b><br>(previously known as Mercaptopurine Nova Laboratories and Novapurine) | Nova Laboratories Limited - UK                  | Treatment of acute lymphoblastic leukaemia   |      |
| 85                             | 70                      | <b>Bronchitol</b><br>(manitolium)   | Pharmaxis Pharmaceuticals                       | Treatment of cystic fibrosis   |      |
| 86                             | 71                      | <b>Signifor</b><br>(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  |      |

| N° CHMP + opinions<br><i>a</i> | N° products<br><i>b</i> | Medicinal Product  | MA Sponsor  | Authorised Therapeutic Indication  |      |
|--------------------------------|-------------------------|--|---|--|------|
| 87                             |                         | <b>Signifor</b><br>(pasireotide)   | Novartis<br>Europharm Limited<br>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                      | <b>Kalydeco</b><br>ivacaftor   | Vertex<br>Pharmaceuticals<br>(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                      | <b>Jakavi</b><br>(ruxolitinib)<br><b>WITHDRAWN</b>                             | Novartis<br>Europharm Limited<br>- 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                      | <b>Revestive</b><br>(teduglutide)  | NPS Pharma<br>Holdings Limited  | Treatment of adult patients with Short Bowel Syndrome. Patients should be stable following a period of intestinal adaptation after surgery.  |      |
| 91                             | 75                      | <b>NovoThirteen</b><br>(catridecacog)<br><b>WITHDRAWN</b>                      | 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                      | <b>Dacogen</b><br>(decitabine)   | Janssen-Cilag<br>International NV -<br>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                      | <b>Glybera</b><br>(adeno-associated viral vector expressing lipoprotein lipase | uniQure biopharma<br>B.V. - The<br>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   |      |
| 94                             | 78                      | <b>Adcetris</b><br>(brentuximab vedotin)                                       | Takeda Global<br>Research and<br>Development<br>Centre (Europe) Ltd<br>- UK | Adcetris is indicated for the treatment of adult patients with relapsed or refractory CD30+ H83 (Hodgkin's lymphoma):<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>Adcetris is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL). |      |
| 95                             | 79                      | <b>NexoBrid</b><br>(concentrate of proteolytic enzymes enriched in bromelain)  | MediWound<br>Germany GmbH   | NexoBrid is indicated for removal of eschar in adults with deep partial- and full-thickness thermal burns.   |      |
| 2013                           |                         |  |   |  |      |
| 96                             | 80                      | <b>Bosulif</b><br>(bosutinib)  | Pfizer Limited<br>United Kingdom  | Treatment of chronic myeloid leukaemia   |      |
| 97                             | 81                      | <b>Iclusig</b><br>(ponatinib)  | ARIAD Pharma Ltd<br>- UK  | Iclusig is indicated in adult patients with:<br>1) chronic-phase, accelerated-phase or blast-phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib, who  |      |

| N° CHMP + opinions <i>a</i> | N° products <i>b</i> | Medicinal Product   | MA Sponsor   | Authorised Therapeutic Indication   |
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|                             |                      |   |  | are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate, or who have the T315I mutation;<br>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                   | <b>Imnovid</b><br>(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                   | <b>Procysbi</b><br>(cysteamine bitartrate)                        | Raptor Pharmaceuticals Europe BV - The Netherlands | Procysbi 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                   | <b>Orphacol</b><br>(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                   | <b>Defitelio</b><br>(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 transplantation (HSCT) therapy.   |
| 102                         | 86                   | <b>Opsumit</b><br>(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                   | <b>Jinarc</b><br>(tolvaptan)<br><b>WITHDRAWN</b>                  | Otsuka Pharmaceutical Europe Ltd                   | Autosomal dominant polycystic kidney disease  |
| 2014                        |                      |   |  |   |
| 104                         | 88                   | <b>Sirturo</b><br>(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                   | <b>Cometriq</b><br>(cabozantinib)                                 | TMC Pharma   | Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma   |
| 106                         | 90                   | <b>Adempas</b><br>(riociguat)                                     | Bayer Pharma AG                                    | Treatment of Chronic thromboembolic pulmonary hypertension (CTEPH) and Pulmonary arterial hypertension (PAH)  |

| N° CHMP + opinions<br><i>a</i> | N° products<br><i>b</i> | Medicinal Product  | MA Sponsor                               | Authorised Therapeutic Indication   |      |
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| 107                            | 91                      | <b>Kolbam</b><br>(cholic acid)<br><b>WITHDRAWN</b>                           | FGK Representative Service GmbH, Germany | Inborn errors in primary bile-acid synthesis  |      |
|                                |                         | Kolbam<br>(cholic acid)  | Retrophin Europe Ltd                     | Inborn errors in primary bile-acid synthesis  | 2015 |
| 108                            | 92                      | <b>Granupas</b><br>(previously para-aminosalicylic acid<br>Lucane or PAS-GR) | Lucane Pharma SA - France                | Treatment of tuberculosis   |      |
| 109                            | 93                      | <b>Deltyba</b><br>(delamanid)  | Otsuka Novel Products GmbH - Germany     | Treatment of multidrug-resistant tuberculosis (MDR-TB)  |      |
| 110                            | 94                      | <b>Vimizim</b><br>(elosulfase alfa)  | BioMarin Europe Ltd                      | Treatment of mucopolysaccharidosis, type IVA (Morquio A Syndrome, MPS IVA) in patients of all ages.   |      |
| 111                            | 95                      | <b>Sylvant</b><br>(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                      | <b>Gazyvaro</b><br>(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                      | <b>Translarna</b><br>(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 dystrophin gene should be determined by genetic testing. |      |
| 114                            | 98                      | <b>Imbruvica</b><br>(ibrutinib)  | Janssen-Cilag International NV           | Imbruvica is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).  |      |
| 115                            |                         | <b>Imbruvica</b><br>(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                      | <b>Ketoconazole HRA</b><br>(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                     | <b>Lynparza</b><br>(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                     | <b>Cyramza</b><br>(ramucirumab)  | Eli Lilly Nederland                      | In combination with paclitaxel is indicated for the treatment of adult patients with  |      |

| N° CHMP + opinions<br><i>a</i> | N° products<br><i>b</i> | Medicinal Product   | MA Sponsor                                | Authorised Therapeutic Indication   |
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|                                |                         | <b>WITHDRAWN</b>  | B.V.                                      | advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy.<br><br>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                     | <b>Scenesse</b><br>(afamelanotide)  | Clinuvel UK Limited                       | Prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP).   |
| 2015                           |                         |   |   |   |
| 120                            | 103                     | <b>Ofev</b><br>(nibtedanib)   | Boehringer Ingelheim Pharma GmbH & Co. KG | Ofev is indicated in adults for the treatment of Idiopathic Pulmonary Fibrosis (IPF).   |
| 121                            | 104                     | <b>Cerdelga</b><br>(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                     | <b>Holoclar</b><br>( <i>ex vivo</i> 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 mm <sup>2</sup> of undamaged limbus is required for biopsy.   |
| 123                            | 106                     | <b>Lenvima</b><br>(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                     | <b>Hetlioz</b><br>(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                     | <b>Unituxin</b><br>(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                     | <b>Kanuma</b><br>(sebelipase alfa)  | Synageva BioPharma Ltd                    | Kanuma is used to treat patients of all ages with lysosomal acid lipase deficiency.   |
| 127                            | 110                     | <b>Farydak</b><br>(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   |

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|                                |                         |   |  | immunomodulatory agent.  |
| 128                            | 111                     | <b>Strensiq</b><br>(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                     | <b>Raxone</b><br>(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                     | <b>Cresemba</b><br>(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                     | <b>Kyprolis</b><br>(carfilzomib)  | Amgen Europe BV                          | Kyprolis is indicated for the treatment of multiple myeloma  |
| 132                            | 115                     | <b>Orkambi</b><br>(lumacaftor/<br>ivacaftor)<br><b>WITHDRAWN</b>                                | Vertex Pharmaceuticals                   | Orkambi is indicated for the treatment of cystic fibrosis  |
| 133                            | 116                     | <b>Obizur</b><br>(susoctog alfa)<br><b>WITHDRAWN</b>  | Baxalta Innovations GmbH                 | Obizur is indicated for the treatment of haemophilia A   |
| 134                            | 117                     | <b>Elocta</b><br>(efmorotocog alfa)<br><b>WITHDRAWN</b>   | Biogen Idec Ltd                          | Elocta is indicated for the treatment of haemophilia A   |
| 135                            | 118                     | <b>Blincyto</b><br>(blinatumomab)   | Amgen Europe B.V.                        | Blincyto is indicated for the treatment of precursor cell lymphoblastic leukemia-lymphoma  |
| 136                            | 119                     | <b>Ravicti</b><br>(glycerol phenylbutyrate)   | Horizon Therapeutics Limited             | Ravicti is indicated for the treatment of inborn urea cycle disorders  |
| 137                            | 120                     | <b>Quinsair</b><br>(levofloxacin)<br><b>WITHDRAWN</b>   | Regintel                                 | Cystic fibrosis  |
| 2016                           |                         |   |  |  |
| 138                            | 121                     | <b>Coagadex</b><br>(human coagulation factor X)   | Bio Products Laboratory limited          | Factor X deficiency  |
| 139                            | 122                     | <b>Wakix</b><br>(pitolisant)  | Bioprojet Pharma                         | Narcolepsy   |
| 140                            | 123                     | <b>Idelvion</b><br>(albutrepenonacog alfa)  | CSL Behring GmbH                         | Haemophilia B  |
| 141                            | 124                     | <b>Uptravi</b><br>(selexipag)<br><b>WITHDRAWN</b>   | Actelion Registration Ltd                | Pulmonary arterial hypertension  |
| 142                            | 125                     | <b>Alprolix</b><br>(eftrenacog alfa)  | Biogen Idec Ltd                          | Haemophilia B  |
| 143                            | 126                     | <b>Darzalex</b><br>(daratumumab)  | Janssen-Cilag International N.V.         | Multiple myeloma   |
| 144                            | 127                     | <b>Galafold</b><br>(migalastat hydrochloride)   | Amicus Therapeutics UK Ltd               | Fabry disease  |
| 145                            | 128                     | <b>Strimvelis</b><br>(autologous CD34+ cells transduced with retroviral vector encoding for the | GlaxoSmithKline Trading Services Limited | Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)  |



| N° CHMP + opinions <i>a</i> | N° products <i>b</i> | Medicinal Product  | MA Sponsor                        | Authorised Therapeutic Indication  |
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|                             |                      | human adenosine deaminase (ADA))   |                                   |  |
| 146                         | 129                  | <b>Zalmoxis</b><br>(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                  | <b>Onivyde</b><br>(irinotecan hydrochloride trihydrate)  | Baxalta Innovations GmbH          | Metastatic adenocarcinoma of the pancreas  |
| 148                         | 131                  | <b>Lartruvo</b><br>(olaratumab)  | Eli Lilly Nederland B.V.          | Advanced soft tissue sarcoma   |
| 149                         | 132                  | <b>Ninlaro</b><br>(ixazomib)   | Takeda Pharma A/S                 | Multiple myeloma   |
| 150                         | 133                  | <b>Venclyxto</b><br>(venetoclax)   | AbbVie Ltd                        | Chronic lymphocytic leukemia   |
| 151                         | 134                  | <b>Ocaliva</b><br>(obeticholic acid)   | Intercept Pharma Ltd              | Primary biliary cholangitis  |
| 152                         | 135                  | <b>SomaKit TOC</b><br>(edotreotide)  | Advanced Accelerator Applications | Gastroenteropancreatic neuroendocrine tumours  |
| 2017                        |                      |  |                                   |  |
| 153                         | 136                  | <b>Cystadrops</b><br>(mercaptamine)  | Orphan Europe S.A.R.L.            | Cystinosis   |
| 154                         | 137                  | <b>Ledaga</b><br>(chlormethine)  | Actelion Registration Ltd         | Mycosis fungoides-type cutaneous T-cell lymphoma   |
| 155                         | 138                  | <b>Natpar</b><br>(parathyroid hormone)   | Shire Pharmaceuticals Ireland Ltd | Hypoparathyroidism   |
| 156                         | 139                  | <b>Dinutuximab beta Apeiron</b><br>(dinutuximab beta)  | Apeiron Biologics AG              | Neuroblastoma (in patients over 1 year of age)   |
| 157                         | 140                  | <b>Spinraza</b><br>(nusinersen)  | Biogen Idec Ltd                   | Spinal muscular atrophy  |
| 158                         | 141                  | <b>Brineura</b><br>(cerliponase alfa)  | Biomarin International Limited    | Neuronal ceroid lipofuscinosis type 2  |

*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



*This publication (or activity) has been funded with support from the European Union's Health Programme. This material only reflects the views of the author, and funders cannot be held responsible for any use which may be made of the information contained herein.*