INFORMATION CENTRE FOR RARE DISEASES AND ORPHAN DRUGS
ИНФОРМАЦИОНЕН ЦЕНТЪР ЗА РЕДКИ БОЛЕСТИ И ЛЕКАРСТВА СИРАЦИ

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# ORPHAN DRUGS IN BULGARIA

***PERIODIC REVIEW OF THE ACCESS TO MEDICINES FOR RARE DISEASES IN BULGARIA***

## *Methodology*

**1. Orphan drug is a medical product if its sponsor can establish:**
**(a) that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand persons in the Community when the application is made, or**
**that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the Community and that without incentives it is unlikely that the marketing of the medicinal product in the Community would generate sufficient return to justify the necessary investment;**
**and**
**(b) that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.**

**The orphan drugs, included in this report, have been designated under the Regulation (EC) No 141/2000 and have marketing authorization and positive evaluation of significant benefits.**

**The list is arranged by tradename in alphabetical order, for each orphan drug its ATC code, active substance, marketing authorization holder and date of marketing authorization are shown. The conditions which are treated with the orphan drug are indicated, as well the information about the presence of the medicine in the Positive drug list (PDL) of Bulgaria and Regulation 34 of 25 November 2005, concerning the procedure of payment from the state budget for the medical treatment of Bulgarian citizens, outside the compulsory health insurance.**

**Used sources and links:**

- Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products
- **European medicines agency (EMA) –** Registry of human medicines
- **Ministry of health (MoH) –** Positive drug list
- **Ministry of health (MoH) –** Regulation 34/25.11.2005
- **Bulgarian drug agency –** Registry of medicines

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# SUMMARY

By June 2010, 60 orphan drugs have market authorization by the centralized procedure under Regulation (EC) № 726/2004 of the European Parliament and the Council of 31 March 2004. Market authorizations are valid for use in all European Union member states, including Bulgaria. 18 of them are included in the Bulgarian PDL (appendices 3 and 4) and 11 are reimbursed by Regulation 34 (see diagram 1). Average time from EMA market authorization to PDL inclusion is about 44 months (see table 1).

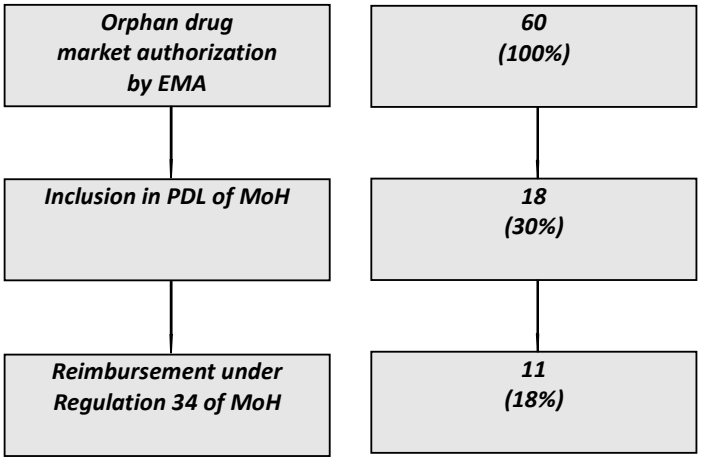


***Diagram 1. Access to orphan drugs in Bulgaria***

***Table 1*. Time from orphan drug market authorization to PDL inclusion***

| *Tradename* | *Date of market authorization by EMA* | *Date of inclusion in PLM* | *Delay (in months)* |
|---|---|---|---|
| **Elaprase** | 08/01/2007 | 24/06/2009 | 29 months |
| **Exjade** | 28/08/2006 | 24/06/2009 | 34 months |
| **Naglazyme** | 24/01/2006 | 24/06/2009 | 41 months |
| **Nplate** | 04/02/2009 | 09/02/2010 | 12 месеца |
| **Somavert** | 13/11/2002 | 24/06/2009 | 79 months |
| **Torisel** | 19/11/2007 | 21/08/2009 | 21 months |
| **Tracleer** | 15/05/2002 | 08/04/2010 | 95 months |
| | | ***Average:*** | **44 months** |

****Note.: Precise information is available only for medicines, which are included in the new PDL after 1 June 2009.***

# Orphan Drugs in European Union and Bulgaria

***(by tradename in alphabetical order)***

| Tradename | Active substance and ATC code | Indication | Marketing authorisation holder | **Marketing authorisa-tion date** | **Included in PDL (Append.)** | **Included in Reg. 34** |
|---|---|---|---|---|---|---|
| AFINITOR | Everolimus L01XE10 | Renal cell carcinoma | Novartis Europharm Ltd | 03/08/2009 | | |
| ALDURAZYME | Laronidase A16AB05 | Mucopolysaccharidosis I | Genzyme B.V. | 10/06/2003 | YES (A4) | N0 |
| ARCALYST | Rilonacept L04AC08 | Cryopyrin-Associated Periodic Syndromes (CAPS) | Regeneron UK Limited | 23/10/2009 | | |
| ARZERRA | Ofatumumab L01XC10 | T-cell acute lymphoblastic leukemia | Glaxo Group Ltd. | 19/04/2010 | | |
| ATRIANCE | Nelarabine L01BB07 | T-cell acute lymphoblastic leukemia<br>T-cell lymphoblastic lymphoma | GlaxoSmith-Kline Research & Development Limited | 22/08/2007 | YES (A3) | YES |
| BUSILVEX | Busulfan L01AB01 | Hematopoietic progenitor cell transplantation | Pierre Fabre Médicament | 09/07/2003 | | |
| CARBAGLU | N-carbamyl-L-glutamic acid A16AA05 | Hyperammonemia due to N-acetylglutamate synthase deficiency | Orphan Europe | 24/01/2003 | | |
| CAYSTON | Aztreonam J01DF01 | Cystic fibrosis | Gilead Sciences International Limited | 21/09/2009 | | |
| CEPLENE | Histamine dihydrochloride L03AX14 | Acute myeloid leukemia | EpiCept GmbH | 07/10/2008 | | |
| CYSTADANE | Betaine anhydrous A16AA06 | Homocystinuria | Orphan Europe | 15/02/2007 | | |
| DIACOMIT | Stiripentol N03AX17 | Severe myoclonic epilepsy | Biocodex | 04/01/2007 | | |
| ELAPRASE | Idursulfase A16AB09 | Mucopolysaccharidosis II | TKT UK Ltd | 08/01/2007 | YES (A4) | YES |
| EVOLTRA | Clofarabine L01BB06 | Acute lymphoblastic leukemia | Bioenvision Limited | 29/05/2006 | | |
| EXJADE | Deferasirox V03AC03 | Chronic iron overload | Novartis Euro-pharm Limited | 28/08/2006 | YES (A3, A4) | YES |
| FABRAZYME | Alpha-Galactosidase A A16AB04 | Fabry disease | Genzyme B.V. | 03/08/2001 | YES (A4) | YES |
| | | Hereditary angioedema | | | | |

| Tradename | Active substance and ATC code | Indication | Marketing authorisation holder | **Marketing authorisation date** | **Included in PDL (Append.)** | **Included in Reg. 34** |
|---|---|---|---|---|---|---|
| FIRAZYR | Icatibant acetate C01EB19 | | Jerini AG | 11/07/2008 | | |
| FIRDAPSE (ex-ZENAS) | Amifampridine N07XX05 | Lambert-Eaton myasthenic syndrome | EUSA Pharma SAS | 23/12/2009 | | |
| GLIOLAN | 5-aminolevulinic acid hydrochloride L01XD04 | Malignant glioma | MEDAC GESELLSCHAFT FÜR KLINISCHE SPEZIALPRÄPARATE MBH | 07/09/2007 | | |
| GLIVEC | Imatinib mesilate L01XX28 | Chronic myeloid leukemia<br>Acute lymphoblastic leukemia<br>Myelodysplastic/myeloproliferative diseases<br>Hypereosinophilic syndrome<br>Chronic eosinophilic leukemia<br>Gastrointestinal stromal tumours<br>Dermatofibrosarcoma protuberans | NOVARTIS EUROPHARM LIMITED | 07/11/2001 | YES (A3, A4) | YES |
| ILARIS | Canakinumab L04AC08 | Cryopyrin-associated periodic syndromes | NOVARTIS EUROPHARM LTD | 23/10/2009 | | |
| INCRELEX | Mecasermin H01AC03 | Primary insulin-like growth factor 1 deficiency | TERCICA EUROPE LIMITED | 03/08/2007 | | |
| INOVELON | Rufinamide N03AF03 | Lennox Gastaut syndrome | EISAI LIMITED | 16/01/2007 | | |
| KUVAN | Sapropterin dihydrochloride A16AX07 | Hyperphenylalaninemia | MERCK KGAA | 02/12/2008 | | |
| LITAK | Cladribine L01BB04 | Hairy cell leukemia | LIPOMED GMBH | 14/04/2004 | YES (A3) | YES |
| LYSODREN | Mitotane L01XX23 | Adrenal cortical carcinoma | Laboratoire HRA Pharma | 28/04/2004 | | |
| MEPACT | Mifamurtide L03AX15 | Osteosarcoma | IDM Pharma S.A. | 06/03/2009 | | |
| MOZOBIL | Plerixafor L03AX16 | Lymphoma<br>Multiple myeloma | Genzyme Europe B.V. | 31/07/2009 | | |
| MYOZYME | Recombinant human acid alpha glucosidase A16AB07 | Pompe disease | Genzyme Europe B.V. | 29/03/2006 | YES (A4) | NO |
| NAGLAZYME | N-acetylgalactosamine-4- sulfatase A16AB08 | Mucopolysaccharidosis VI | BioMarin Europe Ltd | 24/01/2006 | YES (A4) | NO |

| Tradename | Active substance and ATC code | Indication | Marketing authorisation holder | **Marketing authorisation date** | **Included in PDL (Append.)** | **Included in Reg. 34** |
|---|---|---|---|---|---|---|
| NEXAVAR | Sorafenib L01XE05 | Hepatocellular carcinoma<br>Renal cell carcinoma | Bayer Healthcare AG | 19/07/2006 | YES (A3) | YES |
| NPLATE | Romiplostim B02BX04 | Immune (idiopathic) thrombocytopenic purpura | Amgen Europe B.V. | 04/02/2009 | YES (A4) | NO |
| NYMUSA | Caffeine citrate N06BC01 | Primary apnea | Chiesi Farmaceutici SpA | 02/07/2009 | | |
| ONSENAL | Celecoxib L01XX33 | Familial adenomatous polyposis | Pharmacia-Pfizer EEIG | 17/10/2006 | | |
| ORFADIN | Nitisinone A16A X04 | Tyrosinemia type 1 | SWEDISH ORPHAN INTERNATIONAL AB | 21/02/2005 | | |
| PEDEA | Ibuprofen C01EB16 | Patent ductus arteriosus | ORPHAN EUROPE | 29/07/2004 | | |
| PHOTOBARR | Porfimer sodium L01XD01 | Barrett's Oesophagus | AXCAN PHARMA INTERNATIONAL BV | 25/03/2004 | | |
| PRIALT | Ziconotide N02BG08 | Chronic pain who require intrathecal analgesia | Elan Pharma International Ltd. | 21/02/2005 | | |
| REPLAGAL | Alpha-Galactosidase A A16AB03 | Fabry Disease | TKT UK Ltd. | 03/08/2001 | | |
| REVATIO | Sildenafil citrate G04B E03 | Pulmonary arterial hypertension | PFIZER LIMITED | 28/10/2005 | YES (A4) | NO |
| REVLIMID | Lenalidomide L04AX04 | Multiple myeloma | Celgene Europe Limited | 14/06/2007 | | |
| REVOLADE | Eltrombopag B02BX05 | Immune (idiopathic) thrombocytopenic purpura | GlaxoSmithKline TRADING SERVICES LIMITED | 11/03/2010 | | |
| SAVENE | Dexrazoxane V03AF02 | Anthracycline extravasation | TopoTarget A/S | 28/07/2006 | | |
| SIKLOS | Hydroxycarbamide L01XX05 | Sickle cell syndrome | OTL Pharma | 29/06/2007 | | |
| SOLIRIS | Eculizumab L04AA25 | Paroxysmal nocturnal hemoglobinuria | QUADRAMED LIMITED | 20/06/2007 | | |
| SOMAVERT | Pegvisomant H01AX01 | Acromegaly | Pfizer Limited | 13/11/2002 | YES (A4) | YES |
| SPRYCEL | Dasatinib L01XE06 | Chronic myeloid leukemia<br>Acute lymphoblastic leukemia | Bristol-Myers Squibb Pharma EEIG | 20/11/2006 | YES (A3) | YES |

| Tradename | Active substance and ATC code | Indication | Marketing authorisation holder | **Marketing authorisation date** | **Included in PDL (Append.)** | **Included in Reg. 34** |
|---|---|---|---|---|---|---|
| TASIGNA | Nilotinib L01XE08 | Chronic myeloid leukemia | Novartis Europharm Limited | 19/11/2007 | YES (A3, A4) | YES |
| TEPADINA | Thiotepa L01AC01 | Transplantation of hematopoietic progenitor cells | ADIENNE S.R.L. | 15/03/2010 | | |
| THALIDOMIDE CELGENE | Thalidomide L04AX02 | Multiple myeloma | Celgene Europe Ltd | 16/04/2008 | | |
| THELIN | Sitaxentan sodium C02KX03 | Pulmonary arterial hypertension | ENCYSIVE (UK) LIMITED | 10/08/2006 | | |
| TORISEL | Temsirolimus L01XE09 | Renal cell carcinoma<br>Mantle cell lymphoma | WYETH EUROPA LIMITED | 19/11/2007 | YES (A3) | YES |
| TRACLEER | Bosentan monohydrate C02KX01 | Pulmonary arterial hypertension | Actelion Registration Limited | 15/05/2002 | YES (A4) | NO |
| TRISENOX | Arsenic Trioxide LO1XX27 | Acute promyelocytic leukemia | Cell Therapeutics (UK) Limited | 05/03/2002 | | |
| VENTAVIS | Iloprost B01AC11 | Primary pulmonary hypertension | SCHERING AG | 16/09/2003 | YES (A4) | YES |
| VIDAZA | Azacitidine L01BC07 | Myelodysplastic syndromes<br>Chronic myelomonocytic leukemia<br>Acute myeloid leukemia | CELGENE EUROPE LTD | 17/12/2008 | | |
| VOLIBRIS | Ambrisentan CO2KX02 | Pulmonary arterial hypertension | Glaxo Group Ltd | 21/04/2008 | | |
| WILZIN | Zinc acetate dihydrate A16AX05 | Wilson's disease | Orphan Europe | 13/10/2004 | | |
| XAGRID | Anagrelide Hydrochloride L01XX35 | Essential thrombocythaemia | SHIRE PHARMACEUTICAL DEVELOPMENT LTD | 16/11/2004 | | |
| YONDELIS | Trabectedin L01CX01 | Soft tissue sarcoma | PHARMA MAR SA | 17/09/2007 | | |
| ZAVESCA | Miglustat A16AX06 | Type 1 Gaucher disease<br>Niemann-Pick type C disease | Actelion Registration Limited | 20/11/2002 | | |