20 April 2018
EMA/COMP/145093/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for Orphan Medicinal Products (COMP) meeting report on the review of applications for orphan designation

April 2018

The Committee for Orphan Medicinal Products held its 199th plenary meeting on 17-19 April 2018.

## Orphan medicinal product designation

### Positive opinions

The COMP adopted 14 positive opinions recommending the following medicines for designation as orphan medicinal products to the European Commission:

1. Opinions adopted at the second COMP discussion, following the sponsor's response to the COMP list of questions:

- Autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor for treatment of follicular lymphoma, Celgene Europe Limited;
- Equine immunoglobulin F(ab')$_2$ fragments targeting Shiga toxin for prevention of haemolytic uraemic syndrome, Chemo Research S.L.;
- H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met($O_2$)-$NH_2$-DOTA-225-actinium for treatment of glioma, Dr. Regenold GmbH;
- Itraconazole for prevention of invasive aspergillosis, Galephar M/F.

2. Opinions adopted at the first COMP discussion:

- 1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one for treatment of Stargardt's disease, IQVIA RDS Ireland Limited;
- Three human monoclonal antibodies against the Ebola virus glycoprotein for treatment of Ebola virus disease, Regeneron Ireland U.C.;

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- Adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII for treatment of haemophilia A, Baxalta Innovations GmbH;
- Adeno-associated viral vector serotype 9 containing the human *CLN1* gene for treatment of neuronal ceroid lipofuscinosis, Abeona Therapeutics Europe SL;
- Ambroxol hydrochloride for treatment of amyotrophic lateral sclerosis, Spedding Research Solutions SAS;
- Bardoxolone methyl for treatment of Alport syndrome, Dr Stefan Blesse;
- Daratumumab for treatment of AL amyloidosis, Janssen-Cilag International N.V.;
- Glucagon analogue linked to a human immunoglobulin Fc fragment for treatment of congenital hyperinsulinism, Hanmi Europe Limited;
- Modified mRNA encoding human methylmalonyl-coenzyme A mutase encapsulated into lipid nanoparticles for treatment of methylmalonic acidaemia, Pharma Gateway AB;
- Synthetic double-stranded siRNA oligonucleotide targeted against transthyretin mRNA, with six phosphorothioate linkages in the backbone, and nine 2'-fluoro and thirty-five 2'-O-methyl nucleoside residues in the sequence, which is covalently linked via a phosphodiester group to a ligand containing three N-acetylgalactosamine residues for treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis), Alnylam UK Limited.

3. Opinion(s) following appeal procedures:

None

Public summaries of opinions will be available on the EMA website following adoption of the respective decisions on orphan designation[1] by the European Commission. Please also refer to the Community Register of orphan medicinal products for human use.

## Negative opinion

1. Opinion adopted following the sponsor's response to the COMP list of questions:

None

2. Opinion following appeal procedures:

None

## Lists of questions

The COMP adopted 12 lists of questions on initial applications. These applications will be discussed again at the next COMP meeting prior to the adoption of an opinion.

## Oral hearings

7 oral hearings took place.

[1] Details of all orphan designations granted to date by the European Commission are entered in the EU Register of Orphan Medicinal Products

### Withdrawals of applications for orphan medicinal product designation

The COMP noted that 5 applications for orphan medicinal product designation were withdrawn by the sponsor before adoption of the COMP opinion.

### Detailed information on the orphan designation procedures

An overview of orphan designation procedures since 2000 is provided in Annex 1.

The list of medicinal products for which decisions on orphan designation have been granted by the European Commission since the last COMP meeting is provided in Annex 2.

## Re-assessment of orphan designation at time of marketing authorisation

(Article 5(12) (b) of Regulation (EC) No 141/2000 of the European Parliament and of the Council)

When a designated orphan medicinal product receives a positive opinion for marketing authorisation from EMA's Committee for Medicinal Products for Human Use (CHMP), the COMP has the responsibility to review whether or not the medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation.

1. Opinion(s) adopted at time of CHMP opinion:

- Rubraca (rucaparib) for treatment of ovarian cancer, Clovis Oncology UK Ltd (EU/3/12/1049). The opinion was adopted by written procedure after the March meeting.

2. Opinion(s) following appeal procedures:

None

Details of the designated orphan medicinal products that have been subject of a new European Union (EU) marketing authorisation application since the last COMP monthly report are provided in Annex 3.

Details on the authorised orphan medicinal products can be found on the EMA website.

## Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

## Upcoming meetings

- The 200th meeting of the COMP will be held on 22-24 May 2018.

**Note**

This monthly report, together with other information on the work of the European Medicines Agency, can be found on the EMA website: www.ema.europa.eu

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# Annex 1

**Overview for orphan medicinal product designation procedure since 2000**

Please also refer to the Community Register of orphan medicinal products for human use.

| Year | Applications submitted | Applications discussed in reporting year | Positive COMP opinions | Applications withdrawn[2] | Negative COMP opinions | EC designations | Orphan medicinal products[3] authorised | Orphan designations included in authorised therapeutic indication[4] |
|---|---|---|---|---|---|---|---|---|
| 2018 | 70 | 92 | 56 (61%) | 34 (37%) | 2 (2%) | 59 | 5 | 5 |
| 2017 | 260 | 245 | 144 (59%) | 100 (41%) | 2 (1%) | 147 | 14 | 15 |
| 2016 | 330 | 304 | 220 (72%) | 82 (27%) | 2 (1%) | 209 | 14 | 14 |
| 2015 | 258 | 272 | 177 (65%) | 94 (35%) | 1 (1%) | 190 | 14 | 21 |
| 2014 | 329 | 259 | 196 (76%) | 62 (24%) | 2 (1%) | 187 | 15 | 16 |
| 2013 | 201 | 197 | 136 (69%) | 60 (30%) | 1 (1%) | 136 | 7 | 8 |
| 2012 | 197 | 192 | 139 (72%) | 52 (27%) | 1 (1%) | 148 | 10 | 12 |
| 2011 | 166 | 158 | 111 (70%) | 45 (29%) | 2 (1%) | 107 | 5 | 5 |
| 2010 | 174 | 176 | 123 (70%) | 51 (29%) | 2 (1%) | 128 | 4 | 4 |
| 2009 | 164 | 136 | 113 (83%) | 23 (17%) | 0 (0%) | 106 | 9 | 9 |
| 2008 | 119 | 118 | 86 (73%) | 31 (26%) | 1 (1%) | 73 | 6 | 7 |
| 2007 | 125 | 117 | 97 (83%) | 19 (16%) | 1 (1%) | 98 | 13 | 13 |
| 2006 | 104 | 103 | 81 (79%) | 20 (19%) | 2 (2%) | 80 | 9 | 11 |
| 2005 | 118 | 118 | 88 (75%) | 30 (25%) | 0 (0%) | 88 | 4 | 4 |
| 2004 | 108 | 101 | 75 (74%) | 22 (22%) | 4 (4%) | 73 | 6 | 6 |
| 2003 | 87 | 96 | 54 (56%) | 37 (40%) | 1 (1%) | 55 | 5 | 5 |

[2] Revision of the figures for 2015, 2014, 2003, 2002, 2001 and 2000
[3] The number of orphan medicinal products authorised includes the products for which the market exclusivity has expired.
[4] The market authorisation of an orphan medicinal product may cover more than one orphan designation.

| Year | Applications submitted | Applications discussed in reporting year | Positive COMP opinions | Applications withdrawn | Final negative COMP opinions | EC designations | Orphan medicinal products authorised | Orphan designations included in authorised therapeutic indication |
|---|---|---|---|---|---|---|---|---|
| 2002 | 80 | 75 | 43 (57%) | 32 (42%) | 2 (3%) | 49 | 4 | 4 |
| 2001 | 83 | 90 | 62 (70%) | 26 (29%) | 1 (1%) | 64 | 3 | 3 |
| 2000 | 72 | 32 | 26 (81%) | 3 (10%) | 0 (0%) | 14 | 0 | 0 |
| **Total** | **3045** | **2877** | **2027 (70%)** | **823 (29%)** | **27 (1%)** | **2011** | **147** | **162** |

# Annex 2

**Designations granted by the European Commission following COMP opinion on the fulfilment of the orphan designation criteria since last COMP plenary meeting**

Please also refer to the Community Register of orphan medicinal product for human use.

The list includes designation decisions that were revised following the amendment of an existing designated condition (identified by * when applicable)

| Active substance | Orphan indication | Sponsor | COMP opinion date | EC designation date |
|---|---|---|---|---|
| (2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide | Treatment of C3 glomerulopathy | FGK Representative Service GmbH | 15 February 2018 | 21 March 2018 |
| Adeno-associated viral vector serotype 8 containing the human acid alpha-glucosidase gene | Treatment of glycogen storage disease type II (Pompe's disease) | Dr Philippe Moullier | 15 March 2018 | 16 April 2018 |
| Adeno-associated viral vector serotype 9 encoding miRNA against human superoxide dismutase 1 | Treatment of amyotrophic lateral sclerosis | Stolmár & Partner Patentanwälte PartG mbB | 15 March 2018 | 16 April 2018 |
| Autologous dendritic cells pulsed with killed ovarian cancer cells and matured by TLR3 ligand ex vivo | Treatment of ovarian cancer | SOTIO a.s | 15 March 2018 | 16 April 2018 |
| Branaplam | Treatment of spinal muscular atrophy | Novartis Europharm Limited | 15 March 2018 | 16 April 2018 |
| Burosumab | Treatment of phosphaturic mesenchymal tumour | Ultragenyx Germany GmbH | 15 March 2018 | 16 April 2018 |
| Dimethyl fumarate | Treatment of Friedreich's ataxia | PharmaBio Consulting | 15 February 2018 | 21 March 2018 |

| Active substance | Orphan indication | Sponsor | COMP opinion date | EC designation date |
|---|---|---|---|---|
| Docosahexaenoic acid ethyl ester | Treatment of sickle cell disease | TurnKey PharmaConsulting Ireland Limited | 15 February 2018 | 21 March 2018 |
| Efgartigimod alfa | Treatment of myasthenia gravis | argenx BVBA | 15 February 2018 | 21 March 2018 |
| Gemfibrozil | Treatment of neuronal ceroid lipofuscinosis | Quintiles Ireland Limited | 15 February 2018 | 21 March 2018 |
| Genetically modified replication-incompetent herpes simplex virus-1 expressing collagen VII | Treatment of epidermolysis bullosa | IDEA Innovative Drug European Associates Limited | 15 March 2018 | 16 April 2018 |
| Ivosidenib | Treatment of biliary tract cancer | QRC Consultants Ltd | 15 February 2018 | 21 March 2018 |
| Larotrectinib | Treatment of salivary gland cancer | Loxo Oncology Limited | 15 February 2018 | 21 March 2018 |
| Melatonin | Treatment of neonatal encephalopathy | Therapicon Srl | 15 February 2018 | 21 March 2018 |
| Miransertib | Treatment of Proteus syndrome | QRC Consultants Ltd | 15 February 2018 | 21 March 2018 |
| Patidegib | Treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome) | Blue-Reg Europe | 15 February 2018 | 21 March 2018 |
| Polatuzumab vedotin | Treatment of diffuse large B-cell lymphoma | Roche Registration Limited | 15 March 2018 | 16 April 2018 |
| Recombinant adeno-associated viral vector containing a codon-optimized Padua derivative of human coagulation factor IX cDNA | Treatment of haemophilia B | uniQure biopharma B.V. | 15 February 2018 | 21 March 2018 |
| Recombinant human acid alpha-glucosidase | Treatment of glycogen storage disease type II (Pompe's disease) | Amicus Therapeutics UK Ltd | 15 February 2018 | 21 March 2018 |
| Recombinant modified ricin toxin A-chain subunit | Prevention of ricin poisoning | Soligenix UK Ltd. | 15 February 2018 | 21 March 2018 |

| Active substance | Orphan indication | Sponsor | COMP opinion date | EC designation date |
|---|---|---|---|---|
| Ribavirin | Treatment of Crimean-Congo haemorrhagic fever | Pharmadev Healthcare Ltd | 15 February 2018 | 21 March 2018 |
| Ribavirin | Treatment of Lassa fever | Pharmadev Healthcare Ltd | 15 February 2018 | 21 March 2018 |
| Tazemetostat | for treatment of diffuse large B-cell lymphoma, | Quintiles Ireland Limited | 15 February 2018 | 21 March 2018 |
| Tazemetostat | Treatment of follicular lymphoma | Quintiles Ireland Limited | 15 February 2018 | 21 March 2018 |
| Tazemetostat | Treatment of malignant mesothelioma | Quintiles Ireland Limited. | 15 February 2018 | 21 March 2018 |

# Annex 3

**Designated orphan medicinal products that have been subject of a new European Union marketing authorisation application under the centralised procedure since the last COMP monthly report**

Please also refer to the Community Register of orphan medicinal products for human use.

| Active substance | Designated orphan indication | Sponsor/applicant | EU designation number |
|---|---|---|---|
| Pegvaliase | Treatment of hyperphenylalaninaemia | BioMarin International Limited | EU/3/09/708 |
| Pegylated recombinant factor VIII | Treatment of haemophilia A | Novo Nordisk A/S | EU/3/12/995 |
| Recombinant human IgG1 kappa light chain monoclonal antibody targeting plasma kallikrein | Treatment of hereditary angioedema | Shire Pharmaceuticals Ireland Limited | EU/3/15/1551 |
| Treprostinil sodium | Treatment of chronic thromboembolic pulmonary hypertension | SciPharm Sarl | EU/3/13/1103 |