



EURORDIS
Rare Diseases Europe

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**EURORDIS
THERAPEUTIC ACTIVITIES
REPORT**

Update on monthly activities related to therapeutic development and participation of patients' representatives in EMA activities

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General News

- ✦ **Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) has elected Lise Murphy as its new co-chair**



Lise Murphy, representing the EURORDIS and the Swedish Marfan Association has been a member of the PCWP since 2007. She will co-chair the Working Party for the next three years, together with Isabelle Moulon, Head of the Medical Information Sector at the European Medicines Agency. Dr Moulon has been renominated as co-chair for a further three-year term by the Agency's Executive Director, Thomas Lönnngren.

- ✦ **Tenth EMA Human Scientific Committee's Working Party with Patients' and Consumers' Organisations (PCWP) meeting**

The meeting was held in London at the European Medicines Agency on June 16, 2010 and covered the following topics: revision of the mandate and rules of procedure of the PCWP; the interaction between the Agency and health technology assessment bodies; the interaction between the Agency and patient & consumer organisations; direct reporting of adverse events by patients.

To access the documents from this meeting, please click [here](#).

- ✦ **European Medicines Agency publishes first review of orphan designation**

The European Medicines Agency has published the first of its 'review of orphan designation' documents. These documents summarise the review of the orphan designation carried out by the Committee for Orphan Medicinal Products (COMP) whenever an orphan medicine reaches marketing authorisation. The review is carried out to check that the criteria underpinning the medicine's orphan designation still apply.

The publication of these documents has been introduced in order to increase transparency over the Agency's orphan designation process. The documents summarise the COMP's

position on whether the orphan designation for a medicinal product that is receiving marketing authorisation should be maintained or revoked, and include a discussion on the justification of benefit over other authorized treatments.

The first review document concerns Vpriv (velaglucerase alfa), which was authorised for the treatment of Gaucher disease on 26 August 2010. The COMP concluded that Vpriv's orphan designation can be maintained on 8 July 2010.

The Agency will continue to publish these documents for all orphan medicinal products at the time of marketing authorisation, and for all extensions of indication approved for orphan medicines already on the market.

✦ **Reflection paper on clinical trials in third countries**

The European Medicines Agency published a draft "[Reflection paper on ethical and GCP aspects of clinical trials conducted in third countries for evaluation in marketing authorisation applications for medicines for human use submitted to the EMA...](#)" which was open for comments by 30th September 2010.

The reflection paper is part of the Agency's overall strategy on the acceptance of clinical trials conducted in third countries. Highlighting the need for cooperation between international regulatory authorities, the paper proposes a series of measures to ensure a robust framework for the oversight and conduct of clinical trials, no matter where in the world investigators' sites are located and patients are recruited.

Members of the EURORDIS community contributed comments to this reflection paper. A follow up workshop will be held on elaboration of a new document once all comments are collected and analysed.

✦ **European Medicines Agency holds first scientific workshop on nanomedicines**

On 2-3 September 2010, the European Medicines Agency (EMA) hosted the first international scientific workshop on nanomedicines. Some 200 European and international participants from 27 countries including Australia, Canada, India, Japan and the United States discussed benefits and challenges arising from the application of nanotechnologies to medicines. Participants included representatives from patients' organisations, health care professionals' organisations, academia, regulatory authorities and pharmaceutical industry.

The participants of the workshop shared experience, reviewed existing and emerging nanomedicines and discussed a number of specific aspects, including characterisation, biodistribution and interactions of nanomedicines with biological systems, to identify gaps in scientific knowledge and to prepare for the evaluation of future nanomedicines.

To read the press release, click [here](#).

✦ **Protecting patients: EU to upgrade medicine safety monitoring**

Patients will be better informed on how to use medicines, and enabled to report their adverse effects directly to national authorities, thanks to updates of EU laws agreed with the Council and endorsed by Parliament. The EU and Member States will set up pharmacovigilance web

sites, and medicines that need special monitoring after being placed on the market will be marked with a black symbol.

To read the European Commission press release, click [here](#).

This month:

- ▶ **Four dossiers** were received from the Scientific Advice Working Party (SAWP) for **Protocol Assistance** and **no patients' representatives** were proposed as patient experts this month.
- ▶ **Fourteen products** received orphan drug status
- ▶ **No orphan products** received **marketing authorisation this month**

Committee for Orphan Medicinal Products (COMP)

✦ September Meeting – COMP update

(<http://www.emea.europa.eu/htms/general/contacts/COMP/COMP.html>)

Patient experts at COMP in September

Two patient experts were invited to the September meeting to give their opinion on medicinal products for Hereditary Angioedema and Fabry disease, respectively.

Positive opinions

The COMP adopted 14 positive opinions in September.

Negative opinion

The COMP adopted 1 negative opinion recommending the refusal of the orphan medicinal product designation for the following medicine:

Lentiviral vector expressing the truncated form of human tyrosine hydroxylase gene, human aromatic L amino-acid decarboxylase gene, human GTP-cyclohydrolase 1 gene for treatment of ‘OFF’-periods in adult patients with advanced Parkinson’s disease who are not responding adequately to L-DOPA treatment, Oxford Biomedica (UK) Ltd.

- ▶ **14** medicinal products received orphan designation during this COMP Plenary (See Table 1).
- ▶ Overview of Orphan Medicinal Product Designation Procedure since 2000 (See Table 2).
- ▶ No orphan medicinal product received marketing authorisation since the previous month (see Table 8)

Table 1: Fourteen orphan drugs designated in September 2010

Product	Sponsor	Indication
Methylthioninium	Dr Hans Moebius	behavioural variant frontotemporal dementia
Methylthioninium	Dr Hans Moebius	progressive non-fluent aphasia
Methylthioninium	Dr Hans Moebius	frontotemporal dementia with parkinsonism-17
Murine monoclonal antibody against CD26	Adienne S.r.l	graft-versus-host disease
Recombinant human von Willebrand factor	Baxter Innovations GmbH	von Willebrand disease
Sildenafil citrate	Pfizer Limited	postcardiotomy right ventricular failure
2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H,5H)-dione	Fulcrum Pharma (Europe) Ltd.	idiopathic pulmonary fibrosis
Chimeric monoclonal antibody against claudin-18 splice variant 2	GANYMED Pharmaceuticals AG	gastric cancer
Methylthioninium	Dr Hans Moebius	progressive supranuclear palsy
Nanoparticle albumin-bound paclitaxel	Abraxis BioScience Limited	pancreatic cancer
N-tert-butyl-3-[(5-methyl-2-[[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate	Dr Ulrich Granzer	post-polycythaemia vera myelofibrosis
N-tert-butyl-3-[(5-methyl-2-[[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate	Dr Ulrich Granzer	post-essential thrombocythaemia myelofibrosis
Recombinant fusion protein consisting of the extracellular portion of human activin receptor IIB linked to the human IgG1 Fc domain	INC Research	Duchenne muscular dystrophy
Recombinant human arylsulfatase A	Shire Pharmaceuticals Ireland Limited	metachromatic leukodystrophy

Table 2: Overview of Orphan Medicinal Product Designation Procedure since 2000

Year	Applications submitted	Positive COMP opinions	Applications withdrawn	Final negative COMP opinions	Designations granted by Commission
2010	125	90	37	3	69
2009	164	113	23	1	106
2008	119	86	31	1	73
2007	125	97	19	1	98
2006	104	81	20	2	80
2005	118	88	30	0	88
2004	108	75	22	4	72
2003	87	54	41	1	55
2002	80	43	30	3	49
2001	83	64	27	1	64
2000	72	26	6	0	14
Totals	1185	817	286	17	768

(as per COMP report at September 2010)

Paediatric Committee (PDCO)

✦ September meeting – PDCO update

(<http://www.emea.europa.eu/htms/general/contacts/PDCO/PDCO.html>)

▶ **Priority list of off-patent medicines**

Further to information presented in the July Therapeutic Report describing the initiative in the 7th Framework Programme of the European Commission to fund studies into off-patent medicinal products (i.e. those not covered by a patent or supplementary protection certificate) is available; a revised priority list can be found [here](#).

▶ **Congratulations to Dr. Brasseur for his second mandate as PDCO chair**

On 8 September, the Committee elected Dr Daniel Brasseur as its Chair for a second term of three years, and Dr Dirk Mentzer as Vice-Chair replacing Professor Gerard Pons who completed his term as Vice-Chair.

▶ **Cooperation with FDA**

At the September meeting, the PDCO welcomed two representative(s) of the US Food and Drug Administration (FDA), who attended within the framework of the ‘Principles of interaction between the Agency and FDA paediatric therapeutics’. According to the terms of these principles, the Agency’s staff may attend the FDA’s Pediatric Implementation Team meetings and FDA staff may attend the Agency’s Paediatric Committee meetings, to enable regulators from either agency to observe operational activities, and to optimise mechanisms and timing of information exchanges.

The objective of the cooperation between the Agency and FDA in the field of paediatric medicines is to facilitate the framework for global paediatric development plans, compatible for both agencies, with the aim of avoiding exposing children to unnecessary trials.

▶ **Opinions on product-specific waivers**

The PDCO adopted positive opinions for product-specific waivers, recommending that the obligation to submit data obtained through clinical studies with children be waived in all subsets of the paediatric population, for the following medicines:

- ❖ **Ingenol mebutate**, from LEO Pharma A/S, in the therapeutic area of dermatology / oncology;
- ❖ **Tropicamide, Phenylephrine hydrochloride, Lidocaine hydrochloride**, from Laboratoires THEA, in the therapeutic area of ophthalmology;
- ❖ **1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-[methyl[(4-methyl-1-piperazinyl)acetyl] amino]phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)-, monoethanesulfonate**, from Boehringer Ingelheim International GmbH, in the therapeutic area of pneumology – allergology;
- ❖ **Phentermine/topiramate**, from Vivus BV, in the therapeutic area of endocrinology-gynaecologyfertility-metabolism;
- ❖ **Dronabinol**, from Bionorica AG, in the therapeutic area of pain;
- ❖ **Fampridine**, from Acorda Therapeutics Inc, in the therapeutic area of neurology;
- ❖ **Derivative of 4,4'-(1-methylene)-bisbenzotrile**, from Novartis Europharm Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

Waivers can be issued if there is evidence that the medicine concerned is likely to be ineffective or unsafe in the paediatric population, or that the disease or condition targeted occurs only in adult populations, or that the medicine, or the performance of trials, does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

A **Paediatric Investigation Plan (PIP)** sets out a programme for the development of a medicine in the paediatric population. The PIP aims to generate the necessary quality, safety and efficacy data through studies to support the authorisation of the medicine for use in children of all ages. These data have to be submitted to the European Medicines Agency, or national competent authorities, as part of an application for a marketing authorisation for a new medicine, or for one covered by a patent. In some cases, a PIP may include a waiver of the studies in one or more paediatric subsets, or a deferral.

Table 3: September PDCO adopted opinions agreeing paediatric investigation plans (PIPs)

Product	Sponsor	Therapeutic area
Riociguat	Bayer Schering Pharma AG	cardiovascular diseases
Prucalopride succinate,	Movetis NV	gastroenterology-hepatology
Everolimus Orphan	Novartis Europharm Limited	Immunology-rheumatology-transplantation
Eculizumab Orphan	Alexion Europe SAS	immunology-rheumatologytransplantation
Pagibaximab Orphan	Biosynexus, Incorporated	neonatology – paediatric intensive care
L-asparaginase encapsulated in erythrocytes Orphan	ERYtech Pharma	oncology
12 Grass Pollen Extract and Cultivated Rye Pollen Extract (oromucosal solution)	Allergy Therapeutics (UK) Ltd	pneumology – allergology
12 Grass Pollen Extract and Cultivated Rye Pollen Extract (suspension for injection)	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Dermatophagoides farinae and Dermatophagoides pteronyssinus extracts (oromucosal solution)	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Dermatophagoides farinae and Dermatophagoides pteronyssinus extracts (suspension for injection),	Allergy Therapeutics (UK) Ltd,	pneumology –allergology
Birch, hazel and alder pollen extracts	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Birch pollen extract	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Birch / alder / hazel pollen extract,	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Grass pollen extract, cultivated rye pollen extract and birch pollen extract	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Grass pollen extract, cultivated rye pollen extract and birch / alder / hazel pollen extract,	Allergy Therapeutics (UK) Ltd	pneumology – allergology
Grass pollen extract, cultivated rye pollen extract and mugwort pollen extract	Allergy Therapeutics (UK) Ltd	pneumology – allergology

Table 4: Paediatric Committee (PDCO) opinions since 2008

Number of PDCO opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	44	159
Positive on PIP, including potential deferral	81	122	80	283
Negative opinions adopted	4	13	5	22
Positive opinions adopted on modification of a PIP	8	51	81	140
Negative opinions adopted on modification of a PIP	0	0	4	4
Positive opinions on compliance with a PIP	5	8	7	20
Negative opinions on compliance with a PIP	0	1	0	1

Committee for Advanced Therapies (CAT)

✦ September meeting – CAT update

(<http://www.emea.europa.eu/htms/general/contacts/CAT/CAT.html>)

* ATMP = Advanced Therapy Medicinal Product

▶ **Hearing with Interested Parties to the CAT**

On 16th June 2010, CAT held a hearing with representatives of associations representing mainly Academia (ESGCT, EGBMT, EATRIS, CliniGene, TERMIS, Andalusian Initiative for Advanced Therapies, Spanish Association of Haematology and Haemotherapy, BCRT, ISCT). The CAT discussed topics identified by the stakeholders such as: cGMP and ATMP development, ATMP manufacturing process and QC tests, potency assay for ATMPs, Risk based approach, future CAT interactions with Interested Parties, CAT cooperation with other Regulatory agencies (e.g. FDA), implementation of the ‘hospital exemption clause’ at member state level, conduct of clinical trials for ATMPs.

Where possible questions were addressed during the hearing and remaining answers will be sent in a written response.

Future hearings with other interested parties will be conducted in November-December 2010 in the margins of CAT Plenary meetings.

Organisations which have not yet registered to become an interested party to the CAT can still do so by completing the form that can be found on the Agency’s Website:

http://www.ema.europa.eu/htms/human/advanced_therapies/interested_parties.htm

▶ **Scientific recommendation on advanced therapy classification**

Further to consultation with the European Commission, the CAT finalised **three** scientific recommendations on the following classifications of advanced therapy medicinal products (ATMPs).

The following products were classified as **tissue engineered** products:

- **Frozen, cultured allogeneic keratinocytes on a silicone dressing material**, intended for the treatment of acute burn wounds.
- **Autologous human keratinocytes**, intended for the treatment of superficial, partial and full thickness burns.
- **Allogeneic mesenchymal precursor cells**, intended for the treatment of cardiovascular disease.
- **Umbilical cord blood cells expanded ex vivo using allogeneic mesenchymal precursor cells**, intended for treatment of diseases in haematology-oncology therapeutic area.

Table 5: Initial evaluation and Marketing Authorisation applications for Advanced Therapy Medicinal Products

Initial evaluation of MAA for ATMP			
	2009	2010	Total
Submitted	3	1	4
Positive draft Opinion	1	0	1
Negative draft Opinion	1	0	1
Withdrawals	1	1	2

Table 6: Scientific recommendation on advanced therapy classification

Scientific recommendation on advanced therapy classification			
	2009	2010	Total
Submitted	22	16	38
Adopted	12	21	33

Further information on the ATMP classification procedure can be found at:

http://www.ema.europa.eu/htms/human/advanced_therapies/atmp_classification.htm

Table 7: Scientific recommendation on advanced therapy classification

Certification of quality and non-clinical data for small and medium-sized enterprises developing ATMPs			
	2009	2010	Total
Submitted	1	0	1
Adopted	0	1	1

Further information on the advanced therapy medicinal products (ATMP) certification procedure can be found at:

http://www.emea.europa.eu/htms/human/advanced_therapies/certification.htm

Orphan drugs with marketing authorisation

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

Table 8: List of Orphan Drugs with Marketing Authorisation (as of September 2010)

N° CHMP + opinions <i>a</i>	N° products <i>b</i>	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication
1	1	Fabrazyme	Genzyme BV	Fabrazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α -galactosidase A deficiency).
2	2	Replagal	TKT Europe AS	Replagal is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α -galactosidase A deficiency).
3	3	Trisenox	Cell Therapeutics (UK) Ltd	TRISENOX is indicated 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-Receptoralpha (PML/RAR-alpha) gene. Previous treatment should have included a retinoid and chemotherapy.
4		Tracleer (Bosentan)	Actelion	Treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity and symptoms in patients with grade III functional status. Efficacy has been shown in: Primary PAH PAH secondary to scleroderma without significant interstitial pulmonary disease
5	4	Tracleer (Bosentan)	Actelion	Treatment of new digital ulcers in patients with systemic sclerosis and active digital ulcers
6		Tracleer (Bosentan)	Actelion	EXTENSION OF INDICATION to treat patients with a mildly symptomatic PAH categorised as WHO functional class II
7	5	Glivec	Novartis Europharm Limited	Treatment of adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcrabl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment. Glivec is also indicated for the treatment of adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis. The effect of Glivec on the outcome of bone marrow transplantation has not been determined.
8		Glivec	Novartis Europharm Limited	Glivec is also indicated for the treatment of adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST).
9		Glivec	Novartis Europharm Limited	Treatment of adult patients with unresectable recurrent and/or metastatic dermatofibrosarcoma protuberans
10		Glivec	Novartis Europharm Limited	Treatment of adult patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) as monotherapy
11		Glivec	Novartis Europharm Limited	Treatment of adult patients with myelodysplastic/ myeloproliferative diseases (MDS/MPD) associated with PDGFR gene re-

N° CHMP + opinions <i>a</i>	N° products <i>b</i>	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication
				arrangement
12		Glivec	Novartis Europharm Limited	Treatment of adult patients with hypereosinophilic syndrome (HES) and chronic eosinophilic leukaemia (CEL)
13	6	Somavert (Pegvisomant)	Pharmacia Enterprises SA	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.
14	7	Zavesca (Miglustat) 1,5-(Butylimino)-1,5-dideoxy, D-glucitol	Oxford GlycoSciences (UK) Ltd (transferred to Actelion)	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.
15		Zavesca (Miglustat) 1,5-(Butylimino)-1,5-dideoxy, D-glucitol)		Extension of Indication – to include the treatment of progressive neurological manifestations in adult patients and paediatric patients with Niemann-Pick type C disease.
16	8	Carbaglu	Orphan Europe Sarl	Treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency.
17	9	Aldurazyme (Laronidase)	Genzyme Europe BV	Aldurazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis I (MPSI; a [alpha]-L-iduronidase deficiency) to treat the non-neurological manifestations of the disease
18	10	Busilvex (Busulfan)	Pierre Fabre Medicament	Conditioning treatment prior to hematopoietic progenitor cell transplantation in adult patients.
19	11	Ventavis (Iloprost)	Schering AG	Treatment of patients with primary pulmonary hypertension, classified as NYHA functional class III, to improve exercise capacity and symptoms.
20	12	Onsenal (Colecixib)	Pharmacia-Pfizer EEIG	Reduction of the number of adenomatous intestinal polyps in familial adenomatous polyposis (FAP) as an adjunction to surgery and further endoscopic surveillance.
21	13	Photobarr	Axcan Pharma International BV	Photodynamic therapy (PDT) with porfimer sodium is indicated for: Ablation of high grade dysplasia (HGD) in patients with Barrett's Esophagus (BE)
22	14	Litak (Cladribine,B)	Lipomed GmbH	Treatment of hairy cell leukaemia
23	15	Lysodren (Mitotane)	Laboratoire HRA Pharma	Symptomatic treatment of advanced (unresectable, metastatic or relapsed) adrenal cortical carcinoma. The effect of Lysodren on non-functional adrenal cortical carcinoma is not established.
24	16	Pedea (Ibuprofen),M	Orphan Europe SARL	Indicated to close a patent ductus arteriosus in preterm newborn infants
25	17	Wilzin (Zinc-acetate dihydrate),M	Orphan Europe SARL	Treatment of Wilson's disease
26	18	Xagrid (Anegrelide Hydrochloride)	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.
27	19	Orfadin (Nitisinone)	Swedish Orphan Int.	Hereditary tyrosinemia type 1

N° CHMP + opinions <i>a</i>	N° products <i>b</i>	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication
28	20	Prialt® (Ziconotide)	Elan Pharma Int.	Ziconotide is indicated for the 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
29	21	Revatio (sildenafil citrate)	Pfizer limited	Treatment of pulmonary arterial hypertension. Revatio has been shown to improve exercise ability and to reduce mean pulmonary arterial pressure.
30	22	Naglazyme (N-acetylgalactosamine 4-sulfatase,A)	BioMarin Europe	Naglazyme is indicated for long term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis VI (MPS VI; (N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux Lamy syndrome) to treat the clinical manifestations of the diseases.
31	23	Myozyme (recombinant human acid alpha-glucosidase)	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)
32	24	Evoltra (2-chloro-9-[2-deoxy-2-Fluoro-β-D-Arabinofuranosyl]adeniteL)	Bioenvision Ltd	Treatment of acute lymphoblastic and acute myeloid leukaemia
33	25	Nexavar (sorafenib tosylate)	Bayer Healthcare AG	Treatment of advanced renal cell carcinoma
34		Nexavar (sorafenib tosylate)	Bayer Healthcare AG	Extension of Indication to include treatment of hepatocellular carcinoma
35	26	Savene (dexrazoxane)	Topo Target A/S	Treatment of anthracycline extravasation
36	27	Thelin (sitaxentan sodium)	Encysive (UK)	Treatment of idiopathic pulmonary arterial hypertension (IPAH) or pulmonary arterial hypertension
37	28	Exjade (4-(3,5-Bis (hydroxiphenyl)-1,2,4) triazol-1-yl)benzoic acid, 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)
38	29	Sprycel (dasatinib)	Bristol-Myers Squibb Pharma	Treatment of chronic myeloid leukaemia (CML) and philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL)
39		Sprycel (dasatinib)	Bristol-Myers Squibb Pharma	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	Inovelon (Rufinamide)	Esai Limited	Adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients 4 years and older
41	31	Diacomit (Stiripentol)	BIOCODEX	Treatment of severe myoclonic epilepsy in infancy
42	32	Elaprase (iduronate-2-sulfatase)	TKT UK	Treatment of Hunter syndrome (Mucopolysaccharidosis II)
43	33	Cystadane (betaine anhydrous A)	Ophan Europe	Treatment of homocystinuria
44	34	Revlimid	Celgene Europe Ltd	Treatment in combination with dexamethasone of multiple myeloma patients who have received at least one prior therapy
45	35	Soliris (Eculizumab)	Alexion Europe	Treatment if paroxysmal nocturnal hemoglobinuria (PNH)

N° CHMP + opinions a	N° products b	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication
46	36	Siklos (hydroxyurea)	Addmedica	Prevention of vaso-occlusive crises in patients with symptomatic Sickle Cell Syndrome
47	37	Increlex (Mecasermin)	Tercica Europe Ltd	Treatment of growth failure
48	38	Atriance (Nelarabine)	Glaxo Group Ltd	Treatment of T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL)
49	39	Gliolan (5 aminolevulinic acid hydrochloride L)	Medac GmbH	Visualisation of malignant tissue during surgery for malignant glioma
50	40	Yondelis (Ecteinascidin 743 L)	PharmaMar SA	Treatment of advanced soft tissue sarcoma
51		Yondelis (Trabectedin L01CX01)	PharmaMar SA	Extension of Indication to include Yondelis in combination with pegylated liposomal doxorubicin (PLD) in the treatment of patients with relapsed platinum sensitive ovarian cancer.
52	41	Tasigna (Nilotinib)	Novartis Europharm Ltd	Treatment of Philadelphia chromosome positive chronic myelogenous leukaemia (CML)
53	42	Torisel (Temsirolimus L)	Wyeth Europa Ltd	Treatment of advanced renal cell carcinoma
54		Torisel (Temsiroliums L)	Wyeth Europa	Extension of Indication to include treatment of relapsed and/or refractory mantle cell lymphoma
55	43	Thalidomide Celgene (50 mg hard capsules)	Pharmion Ltd	Treatment of myeloma
56	44	Volibris (Ambrisentan)	Glaxo Group Ltd	Treatment of pulmonary arterial hypertension (PAH)
57	45	Firazyr (Icatibant acetate L)	Jerini AG	Treatment of hereditary angioedema
58	46	Ceplene (Histamine dihydrochloride L)	EpiCept GmbH	Treatment of acute myeloid leukaemia
59	47	Kuvan (Tetrahydrobiopterin)	Merck KGaA	Treatment of hyperphenylalaninemia
60	48	Vidaza (Azacitidine)	Celgene EU	Treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia
61	49	Nplate (Recombinant magakaryopoiesis stimulating protein)	Amgen Europe - BV	Treatment of idiopathic thrombocytopenic purpura
62	50	Mepact Muramyl tripeptide phosphatidyl ethanolamine L	Immuno-designed Molecules (IDM), SA - France	Treatment of osteosarcoma
63	51	Nymusa Caffeine citrate 06BC01	Chiesi Farmaceutici S.P.A. - Italy	Prevention of Japanese encephalitis
64	52	Mozobil 1,1'[1,4-phenylenebis (methylene)]-bis-1,4,8,11-tetraazacyclotetradecane	Genzyme BV The Netherlands	Treatment of lymphoma and multiple myeloma
65	53	Afinitor Everolimus	Novartis Europharm Ltd	Treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy
66	54	Cayston Aztreonam lysinate (inhalation use)	Gilead Sciences International Ltd - UK	Treatment of Gram-negative bacterial lung infections in cystic fibrosis

N° CHMP + opinions <i>a</i>	N° products <i>b</i>	Medicinal Product	MA Sponsor	Authorised Therapeutic Indication
67	55	Arcalyst Rilonacept M	Regeneron UK	Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
68	56	Ilaris Recombinant human monoclonal antibody to human IL- β of the IgG1/K class L/immuno	Novartis Europharm Limited UK	Treatment of Cryopyrin Associated Periodic Syndromes (CAPS), Familial Cold Urticaria Syndrome (FCUS), Muckle Wells Syndrome (MWS) and Neonatal Onset Multisystem Inflammatory Disease (NOMID) also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA).
69	57	Firdapse 3,4 diaminopyridine phosphate	EUSA Pharma SAS	Treatment of Lambert-Eaton Myasthenic Syndrome
70	58	Revolade (Eltrombopag olamine L/immuno)	GlaxoSmithKline Trading Services Limited - Ireland	Treatment of idiopathic thrombocytopenic purpura
71	59	Tepadina (thiotepa)	Adienne S.r.l - Italy	Conditioning treatment prior to conventional haematopoietic progenitor cell transplantation (HPCT)
72	60	Arzerra (Ofatumumab L-onco)	Glaxo Group Limited - UK	Treatment of chronic lymphocytic leukaemia (CLL or B-CLL), follicular non-Hodgkin's lymphoma (FL), diffuse large B-cell lymphoma (DLBCL), rheumatoid arthritis (RA) and multiple sclerosis (MS)

a = Number of positive CHMP opinions; **b** = Number of *different* products

Please note that Sutent and Xyrem were formerly orphan drugs but have been removed from the orphan drug register. This explains discrepancies between this list and that of the EMA.



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