19 August 2019
EMA/CHMP/463206/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda of CHMP written procedure* 19-22 August 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

*** Written Procedure - comments on the draft documents should be forwarded to the Product Lead (PL) as identified in the CHMP agenda.**

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Of note, this agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

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Novimmune B.V.; treatment of paediatric patients with primary haemophagocytic lymphohistiocytosis (HLH).

Scope: Letter from applicant dated 26 July 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in June 2019

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 13.12.2018.

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treatment of non-cystic fibrosis bronchiectasis (NCFBE) patients with chronic lung infection with Pseudomonas aeruginosa (P. aeruginosa)

Scope: Letter from applicant dated 06 August 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in March 2019

Adopted via written procedure on 14.08.2019

Action: For information

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 26.07.2018.

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Action: For adoption

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7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

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Genzyme Europe BV

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Eva A. Segovia

Scope: Request by the applicant for an extension to the clock stop to respond to the request for supplementary information adopted on 25.07.2019

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019.

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Applicant: various

Lead Rapporteur: Johann Lodewijk Hillege (NL)

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

Timetable

Action: For adoption

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Applicants: Nordic Group B.V. (Nordimet), Therakind Limited (Jylamvo), various

Referral PRAC Rapporteur: Martin Huber; Referral PRAC Co-rapporteur: Željana Margan Koletić

Jylamvo EMEA/H/C/003756 - Rapporteur: Bruno Sepodes, PRAC Rapporteur: Jan Neuhauser

Nordimet EMEA/H/C/003983 - Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber

Scope: CHMP opinion

Action: For adoption

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Action: For information

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Information related to GMP inspections will not be published as it undermines the purpose of such inspections

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Information related to GCP inspections will not be published as it undermines the purpose of such inspections

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Information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections

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Information related to GLP inspections will not be published as it undermines the purpose of such inspections

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B.1.1. Annual reassessment for products authorised under exceptional circumstances

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Epidyolex - cannabidiol - EMEA/H/C/004675, Orphan GW Pharma (International) B.V., Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Inbrija - levodopa - EMEA/H/C/004786 Acorda Therapeutics Ireland Limited, treatment of symptoms of OFF periods in Parkinson's disease, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

Nuceiva - botulinum toxin type a - EMEA/H/C/004587 Evolus Pharma Limited, temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Trogarzo - ibalizumab - EMEA/H/C/004961 Theratechnologies International Limited, treatment of adults infected with HIV-1 resistant to at least 1 agent in 3 different classes, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
VITRAKVI - larotrectinib - EMEA/H/C/004919, Orphan Bayer AG, treatment of adult and paediatric patients with locally advanced or metastatic solid tumours, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as these contain commercially confidential information.

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0007 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Opinion adopted on 09.08.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 09.08.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0093 AstraZeneca AB, Rapporteur: Bart Van der Schueren Opinion adopted on 09.08.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 09.08.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

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B.5.9. Information on withdrawn type II variation / WS procedure

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly." Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 15.11.2018. Withdrawal request submitted on 02.08.2019.	The MAH withdrew the procedure on 02.08.2019.

B.5.10. Information on type II variation / WS procedure with revised timetable

NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0106 Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 06.06.2019, 07.03.2019, 20.09.2018.	Request for an extension to the clock stop to respond to the Request for Supplementary Information adopted on 06.06.2019

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

B.6.1. Start of procedure for New Applications: timetables for information

arsenic trioxide - EMEA/H/C/005218 treatment of relapsed acute promyelocytic leukaemia (APL)
fampridine - EMEA/H/C/005359

treatment of Multiple Sclerosis
filgotinib - EMEA/H/C/005113 treatment of adult patients with moderately to severely active rheumatoid arthritis
budesonide / formoterol fumarate dihydrate - EMEA/H/C/004882 treatment of asthma and COPD
rilpivirine - EMEA/H/C/005060 treatment of human immunodeficiency virus type 1 (HIV-1)
rivaroxaban - EMEA/H/C/005279 prevention of atherothrombotic events
cabotegravir - EMEA/H/C/004976 treatment of human immunodeficiency virus type 1 (HIV-1)

B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information

Darzalex - daratumumab - EMEA/H/C/004077/X/0032, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (1800 mg) and a new route of administration (subcutaneous route). The RMP version 7.0 was updated in accordance.”
Jorveza - budesonide - EMEA/H/C/004655/X/0007/G, Orphan Dr. Falk Pharma GmbH, Rapporteur: Martina Weise, Co-Rapporteur: Tomas Boran, PRAC Rapporteur: Zane Neikena, “Extension application to add a new strength of 0.5 mg for budesonide orodispersible tablets, grouped with: - A type II variation (C.I.6) - Extension of indication to include the maintenance of remission for Jorveza (0.5 mg and 1 mg orodispersible tablets); as a consequence, sections 4.2, 4.8 and 5.1 of the SmPC are updated to reflect the recommended daily dose and duration of treatment of Jorveza for the maintenance of remission, to update the list of adverse reactions and the clinical efficacy and safety information based on the results of the

phase III clinical study BUL-2/EER. The relevant sections of the PL are updated accordingly. In addition, a revised RMP (version 2.0) has been submitted to reflect the results of this study and to align with the GVP Module V (rev 2) template. The MAH also took the opportunity to bring the product information in line with the latest QRD template (version 10.1). - A type IB variation (B.II.e.5.a.2) – To add a new pack-size of 200 x 1 orodispersible tablets (unit dose) in a blister for Jorveza 1 mg orodispersible tablet (EU/1/17/1254/006)"	

B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information

adalimumab - EMEA/H/C/004879 treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis, adolescent hidradenitis suppurativa List of Questions adopted on 28.03.2019.	
azacitidine - EMEA/H/C/005147 Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) and AML with >30% marrow blasts according to the WHO classification List of Questions adopted on 29.05.2019.	
azacitidine - EMEA/H/C/005075 Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) List of Questions adopted on 29.05.2019.	
brolucizumab - EMEA/H/C/004913 treatment of neovascular (wet) age-related macular degeneration (AMD) List of Questions adopted on 27.06.2019.	
cinacalcet - EMEA/H/C/005236 treatment of secondary hyperparathyroidism and hypercalcaemia List of Questions adopted on 29.05.2019.	
Dificlir - fidaxomicin -	

EMEA/H/C/002087/X/0034/G

Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to introduce a new pharmaceutical form associated with new strength (40 mg/ml granules for oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use of Dificlir in children from birth to less than 18 years of age.
The RMP (version 11.0) is updated in accordance.
Consequential updates have been made to the SmPC of Dificlir200 mg Film-coated tablet.
The labelling and package leaflet (PL) are updated accordingly.
The PL is also being amended to include a statement that Dificlir is essentially ‘sodium-free' (in accordance with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'). The details of the local representative of the MAH in the Czech Republic are also updated.”
List of Questions adopted on 29.05.2019.

Emgality - galcanezumab - EMEA/H/C/004648/X/0004

Eli Lilly Nederland B.V., Rapporteur: Daniela Melchiorri (IT) (MNAT with IT for Clinical Efficacy, IT for Clinical Pharmacology, IT for Clinical Safety, IT for Coordination, IT for Non-Clinical, ES for Quality), Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, “Extension application to add a new strength of 100 mg/ml solution for injection in pre-filled syringe for Emgality, associated with a new indication (episodic cluster headache).”
List of Questions adopted on 27.06.2019.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

entrectinib - EMEA/H/C/004936

treatment of adult and paediatric patients with neurotrophic tyrosine receptor kinase (NTRK) fusion-positive locally advanced or metastatic solid tumours and treatment of patients with ROS1-positive, advanced non-small cell lung cancer (NSCLC)
List of Questions adopted on 29.05.2019.

recombinant vesicular stomatitis virus -

zaire ebolavirus vaccine (live) -
EMEA/H/C/004554
Ebola Vaccine
List of Questions adopted on 25.06.2019.

imipenem / cilastatin / relebactam -
EMEA/H/C/004808
indicated for the treatment of bacterial infections due to gram-negative microorganisms
List of Questions adopted on 28.03.2019.

cholera vaccine, oral, live -
EMEA/H/C/003876
indicated for active immunisation against disease caused by Vibrio cholerae serogroup O1 in adults and children aged 6 years and older
List of Questions adopted on 29.05.2019.

Vyndaqel - tafamidis -
EMEA/H/C/002294/X/0049/G, Orphan
Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ghania Chamouni, “Extension application to:
- introduce a new strength (tafamidis 61 mg soft capsules, pack-size of 30 and 90 capsules) including a new indication "treatment of transthyretin amyloidosis in adult patients with wild-type or hereditary cardiomyopathy to reduce all-cause mortality and cardiovascular-related hospitalisation (ATTR-CM)"
- introduce qualitative change in declared active substance (tafamidis) not defined as a new active substance;
grouped with a type II variation (C.I.4) to update section 4.6 of the Vyndaqel (tafamidis meglumine) 20 mg soft capsules SmPC to add wording pertaining to the Tafamidis Enhanced Surveillance for Pregnancy Outcomes (TESPO) programme.
Submission of an updated RMP version 9.0 in order to include the proposed new dosage/indication, review of the additional data collected from the ATTR-CM clinical program and post marketing reporting, reclassify of the safety concerns, remove of HCP educational leaflet. Relevant changes are proposed for Annex II.
In addition, the MAH is proposing an update to Section 16 Information in Braille of Annex IIIa - Labelling (carton) to differentiate between the dosage forms.)”

List of Questions adopted on 29.05.2019.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

selinexor - EMEA/H/C/005127, Orphan
Karyopharm Europe GmbH, treatment of patients with relapsed refractory multiple myeloma (RRMM)
List of Questions adopted on 24.04.2019.

B.6.4. Annual Re-assessments: timetables for adoption

Brineura - cerliponase alfa - EMEA/H/C/004065/S/0018, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga

IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMEA/H/C/002596/S/0041
Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Lojuxta - lomitapide - EMEA/H/C/002578/S/0036
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

Mepsevii - vestronidase alfa - EMEA/H/C/004438/S/0007, Orphan
Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Naglazyme - galsulfase - EMEA/H/C/000640/S/0078
BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins

B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed

Caprelsa - vandetanib - EMEA/H/C/002315/R/0041
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

CRYSVITA - burosumab - EMEA/H/C/004275/R/0009, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/R/0035
MSD Vaccins, Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0026, Orphan, ATMP
Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, CHMP Coordinators: Jan Mueller-Berghaus and Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald

Jinarc - tolvaptan - EMEA/H/C/002788/R/0027
Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Amelia Cupelli

Prolia - denosumab - EMEA/H/C/001120/R/0082
Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Synjardy - empagliflozin / metformin - EMEA/H/C/003770/R/0044
Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva A. Segovia

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.7. Type II Variations scope of the Variations: Extension of indication

Brilique - ticagrelor - EMEA/H/C/001241/II/0047/G
AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto

Yerro, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) without a history of myocardial infarction who have undergone percutaneous coronary intervention (PCI) based on the final results of study D513BC00001 (THEMIS), a phase III multinational, randomised, double-blind, placebo controlled study to evaluate the effect of ticagrelor twice daily on the incidence of cardiovascular death, myocardial infarction or stroke in patients with T2DM; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. Update of section 4.8 of the SmPC regarding with new safety information on traumatic haemorrhages based on the final results from study D513BC00001 (THEMIS) and data from the ticagrelor clinical development programme and post-marketing data. The Package Leaflet is updated in accordance. The RMP version 12 has also been submitted."	
Invokana - canagliflozin - EMEA/H/C/002649/II/0046 Janssen-Cilag International NV, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber, "Update of sections 4.1, 4.2, 4.8 and 5.1 of the Summary of Product Characteristics to add a new therapeutic indication for Invokana (canagliflozin) for the treatment of stage 2 or 3 chronic kidney disease and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus. The proposed new indication is based upon new clinical efficacy and safety data from the Phase 3 study: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation Trial (CREDENCE) (DNE3001). The Package Leaflet is updated in accordance. The RMP version 8.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	

Ultomiris - ravulizumab -
EMEA/H/C/004954/II/0002, Orphan
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include the treatment of patients with atypical hemolytic uremic syndrome (aHUS) for Ultomiris; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, Annex II.D is proposed to be updated to include the risk of thrombotic microangiopathy (TMA) with the new indication in the educational materials. The RMP version 1.6 has also been submitted."

Vokanamet - canagliflozin / metformin -
EMEA/H/C/002656/II/0051
Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.1, 4.2, 4.8 and 5.1 of the Summary of Product Characteristics to add a new therapeutic indication for Vokanamet (canagliflozin/metformin) for the treatment of stage 2 or 3 chronic kidney disease and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus. The proposed new indication is based upon new clinical efficacy and safety data from the Phase 3 study: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation Trial (CREDENCE) (DNE3001).
The Package Leaflet is updated in accordance. The RMP version 8.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

AMGEVITA - adalimumab -
EMEA/H/C/004212/II/0019/G
Amgen Europe B.V., Rapporteur: Kristina Dunder

Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) -
EMEA/H/C/002333/II/0079/G

GSK Vaccines S.r.l, Rapporteur: Kristina Dunder

Cresemba - isavuconazole -
EMEA/H/C/002734/II/0024/G, Orphan
Basilea Pharmaceutica Deutschland GmbH,
Rapporteur: Johann Lodewijk Hillege

Empliciti - elotuzumab -
EMEA/H/C/003967/II/0019/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur:
Paula Boudewina van Hennik

Empliciti - elotuzumab -
EMEA/H/C/003967/II/0020/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur:
Paula Boudewina van Hennik

GONAL-f - follitropin alfa -
EMEA/H/C/000071/II/0145/G
Merck Europe B.V., Rapporteur: Johann Lodewijk
Hillege

Kevzara - sarilumab -
EMEA/H/C/004254/II/0015/G
sanofi-aventis groupe, Rapporteur: Jan
Mueller-Berghaus

Privigen - human normal immunoglobulin -
EMEA/H/C/000831/II/0154/G
CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus

Simulect - basiliximab -
EMEA/H/C/000207/II/0101/G
Novartis Europharm Limited, Rapporteur: Jan
Mueller-Berghaus

Viramune - nevirapine -
EMEA/H/C/000183/II/0141/G
Boehringer Ingelheim International GmbH,
Rapporteur: Bruno Sepodes

B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

Afstyla - lonoctocog alfa -
EMEA/H/C/004075/II/0024
CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus, “Update of sections 4.4 and
4.8 of the SmPC with safety information
regarding the development of factor VIII
inhibitors in patients treated with Afstyla based
on clinical trial and post-marketing data reviewed
recently with data lock point 03 January 2019.
The PL is updated accordingly. Additionally, local

representatives' details for Bulgaria and Croatia have been updated."

Baraclude - entecavir - EMEA/H/C/000623/II/0063

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Submission of responses to the final clinical study report (CSR) from a Paediatric Safety and Efficacy Study (AI463189), a comparative study of the antiviral efficacy and safety of Entecavir (ETV) versus placebo in paediatric subjects with chronic Hepatitis B Virus (HBV) infection who are HBeAg positive, in order to provide additional clarification regarding the on-treatment and long-term follow-up haematology findings. The final CSR for AI463189 was already submitted and assessed within the context of procedure EMEA/H/C/000623/P46/010."

Empliciti - elotuzumab - EMEA/H/C/003967/II/0018

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the SmPC with final overall survival data from study CA204004 (A Phase 3, Randomized, Open Label Trial of lenalidomide/dexamethasone With or Without Elotuzumab in Relapsed or Refractory Multiple Myeloma)."

EVOTAZ - atazanavir / cobicistat - EMEA/H/C/003904/II/0030

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Update of sections 4.3 and 4.5 of the SmPC in order to add as contraindications the concomitant administration of dabigatran or lomitapide with Evotaz, and to add drug-drug interaction recommendations between Evotaz with direct oral anticoagulants and lomitapide (lipid modifying agent), based on already updated information in other marketing authorisations. Section 4.6 of the SmPC is also updated to reflect the accumulated information on the use of cobicistat during pregnancy, based on published literature. The package leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Glivec - imatinib - EMEA/H/C/000406/II/0117

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, “Update of section 4.6 of the SmPC to include that women of childbearing potential must be advised to use effective contraception for at least 15 days after stopping treatment with imatinib, based on a company review of the company Core Data Sheet. The PL has been updated accordingly.”

Herzuma - trastuzumab - EMEA/H/C/002575/II/0023

Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus, “C.I.13: Submission of the final report from study CT-P6 3.2. This is a phase 3, double blind, randomized, parallel-group, active-controlled study to compare the efficacy and safety of CT-P6 and Herceptin as Neoadjuvant and Adjuvant treatment in patients with HER2 positive early breast cancer.”

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0110/G

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include the number of PID patients, to include prescriber information and tolerability information for manual push infusion, to update prescriber information on device-assisted infusion and to include safety information, based on final results from study IgPro20_4004, an open-label study to evaluate the safety and tolerability of higher infusion parameters of Hizentra infused manually or with pump assistance in PID patients.
Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update the number of PID patients and to include safety information based on final results from study IgPro_4005, a phase 4, open-label, single-sequence, crossover study to investigate the tolerability, safety and efficacy of biweekly Hizentra dosing in PID patients.
The Package Leaflet is updated accordingly.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representative in the Package Leaflet, to make some editorial updates in sections 4.2, 5.1 and 5.2 of the SmPC and to bring the PI in line with the latest QRD template version 10.1.”

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0053, Orphan

Janssen-Cilag International NV, Rapporteur: Filip Josephson, “the submission of final report on PFS by investigator assessment in study PCYC-1112-CA, including PFS2 and overall survival data until study closure per protocol (ANX_003)”

Instanyl - fentanyl - EMEA/H/C/000959/II/0051

Takeda Pharma A/S, Rapporteur: Alexandre Moreau, “Update of section 4.8 to include dyspnoea. The MAH has also taken the opportunity to include editorial changes in Patient Leaflet.”

Invanz - ertapenem - EMEA/H/C/000389/II/0060

Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, “To update sections 4.8 and 5.1 of the SmPC to update the safety information with the addition of a new post-marketing adverse reaction term: acute generalized exanthematous pustulosis (AGEP) and to update the breakpoints table with the most recent EUCAST recommendation (v 9.0, Jan 2019) on clinical breakpoints for ertapenem. Section 4 of the Package Leaflet is updated accordingly. The MAH is also updating the labelling section and the rest of the Product Information according to the latest QRD requirements and is updating List of Local Representatives.”

Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0008, Orphan

Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, “Update of section 5.3 of the SmPC based on the final results from study UX003-PC010 a Developmental and Perinatal/Postnatal reproduction non-clinical study in rats including a Post-natal Behavioural/Functional Evaluation.
In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1.”

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0010/G, Orphan

Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, “A group of two type II variations, to submit the non-clinical in vitro study reports PFZ-07 and 6000572 relating to the effects of gemtuzumab ozogamicin on platelet

development as well as on human platelet function."

PREVYMIS - letermovir - EMEA/H/C/004536/II/0013, Orphan

Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update the viral resistance profile that may be associated with a change in susceptibility to letermovir considering new intro pharmacology data based on the analysis of the patients' samples included in the study MK-8228. This study is a Phase III Randomized, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of MK-8228 (Letermovir) for the Prevention of Clinically Significant Human Cytomegalovirus (CMV) Infection in Adult, CMV Seropositive Allogeneic Hematopoietic Stem Cell. This variation follows the recommendation dated 9th November 2017 that asked for the submission when available of the results to update the CMV phenotypic resistance analyses of all clinical isolates for subjects failing letermovir treatment and to explore the possibility to obtain additional pre-failure CMV genotypic data from available samples."

Xarelto - rivaroxaban - EMEA/H/C/000944/II/0068

Bayer AG, Rapporteur: Kristina Dunder, "Update of section 5.1, of the SmPC based on results from the pantoprazole/placebo randomization part of the COMPASS study; this is part of a double-blind, double-dummy randomized trial in which pantoprazole is being compared with placebo in patients participating in the trial who are not receiving a proton-pump inhibitor. In addition, an amendment to the COMPASS Clinical Study Report is submitted to correct values caused by a programming error in the statistical outputs in this study. No changes on the approved label are proposed due to this correction."

Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0058

Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, "To update section 5.1 of the SmPC based on final results from study PCR3011 (Lattitude); this is a randomized, double-blind, placebo-controlled study designed

to determine the efficacy of abiraterone acetate and low-dose prednisone in men with metastatic hormone-naive prostate cancer."

Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0059

Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, "To update sections 4.4 and 4.8 of the SmPC with safety information on QT prolongation and Torsades de Pointes following a cumulative review of QT Prolongation/Torsades de pointes occurrence."

WS1636/G
Mekinist-EMEA/H/C/002643/WS1636/0035/G
Tafinlar-EMEA/H/C/002604/WS1636/0040/G

Novartis Europharm Limited, Lead Rapporteur: Filip Josephson, "Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 5-years overall survival (OS) results from study MEK115306 (COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma and the 5-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma."

WS1683
Elebrato Ellipta-EMEA/H/C/004781/WS1683/0012
Temybric Ellipta-EMEA/H/C/005254/WS1683/0001
Trelegy Ellipta-EMEA/H/C/004363/WS1683/0010

GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely, "Update of SmPC in order to add information in section 5.1 on survival data from the IMPACT study"

B.6.10. CHMP-PRAC assessed procedures

Eliquis - apixaban -

EMEA/H/C/002148/II/0063

Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.9, of the SmPC in order to reflect the availability of a reversal agent for apixaban following the recent approval of andexanet alfa in the EU; the Package Leaflet and labelling are updated accordingly. The RMP version 20 has also been submitted, with updates due to the availability of a reversal agent and implement the revised GVP template Rev.2. As a result, the list of safety concerns has been updated and a number of safety concerns listed as missing information have been reclassified and have been removed from the RMP.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to update the information in the SmPC and Package Leaflet in accordance with the most recent guidance on labelling of excipients of medicinal products for human use."

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0033

MSD Vaccins, Rapporteur: Kristina Dunder, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.2, 4.6, 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study V503-P004 listed as a category 3 study in the RMP (MEA007); this is an open-label phase III clinical trial to study the immunogenicity and tolerability of Gardasil 9 in adult women (27 to 45 year-olds) compared to young adult women (16 to 26 year-olds); the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC according to the Guideline on quality aspects included in the product information for vaccines for human use (EMA/CHMP/BWP/133540/2017), and to include editorial changes in Section 5.1 of the SmPC"

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0052, Orphan

Janssen-Cilag International NV, Rapporteur: Filip

Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, “submission of the final report on the long term safety study PAM 3038-1, which assessed long term safety data collected from predefined cohorts of subjects treated with ibrutinib for up to 5 years or until disease progression or unacceptable toxicity at the recommended daily doses of 420 mg/day for CLL/SLL and 560 mg/day for MCL. This final report fulfils the milestone for the Post Approval Measure MEA025”	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0080 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, “To update sections 4.2, 4.4 and 4.8 of the SmPC on the safety information for immune-related endocrinopathies following a safety review for Addison’s disease/Primary adrenal insufficiency. The updated RMP version 26.1 has also been submitted. The MAH also took the opportunity to include the changes in Annex II related to the new EMA QRD template version 10.1 and to update the List of Local Representatives of Portugal in the Package Leaflet.”	
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0075 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, “Update of sections 4.4 and 5.1 of the Summary of Product Characteristics in order to reflect change in the existing warning on immunogenicity and immunomodulation and add new clinical information on infantile onset patients (IOPD) immune tolerance induction based on data on use of immune tolerance induction in infantile onset Pompe disease patients from two exploratory Phase 4 studies (AGLU03707 / MSC12817 and companion study AGLU03807/ MSC12892) and the Duke Center of Excellence Observational Study (01562). The updated RMP version 9.0 has also been submitted.”	
Raxone - idebenone - EMEA/H/C/003834/II/0016, Orphan Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli, “C.I.11 for SOB studies:	

Submission of the final report from study SNT-CRS-002 listed as a Specific Obligation (SOB10, former SOB2) in the Annex II of the Product Information. This is a historical case record survey (CRS) of visual acuity data from patients with Leber's hereditary optic neuropathy (LHON). The goal is to generate a natural history group to serve as a comparator group of idebenone-naïve patients for the open-label study SNT-IV-005 which will assess long-term efficacy and safety in patients with LHON treated with Raxone. Annex II is modified accordingly. Submission of an updated RMP version 1.8 accordingly."

Tamiflu - oseltamivir - EMEA/H/C/000402/II/0142

Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC following completion of the paediatric studies NV25719 and NV20234 and downstream population PK and PK/PD analysis, listed in the approved Tamiflu Paediatric Investigation Plan (PIP) (EMEA-000365-PIP01-08-M10); the study NV25719 was a prospective, open-label, randomized study which investigated PK and PD of two weight adjusted oseltamivir doses for the treatment of influenza-infected immunocompromised (IC) children less than 13 years of age. The study NV20234 was a prospective, double-blind, randomized trial which investigated safety and viral resistance to oseltamivir treatment in influenza-infected IC adults, adolescents and children. The purpose of this variation is to establish a dose recommendation for the treatment of paediatric IC patients.
The Package Leaflet and Labelling are updated accordingly.
The updated RMP version 19 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led

Accofil - filgrastim - EMEA/H/C/003956/II/0037

Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka,

PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of an updated RMP version 4.0 in order to update the section of additional pharmacovigilance activities (removal of SCNIR and EBMT registry) following the conclusion of Accofil Severe Chronic Neutropenia International Registry (SCNIR) and European Group for Blood and Marrow Transplantation (EBMT) Combined Analysis Report. The MAH has taken the occasion also to implement the RMP template based on GVP revision 2 guideline."

PRAC Led

Caprelsa - vandetanib -

EMEA/H/C/002315/II/0040

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 13 in order to remove the Health Care Professionals survey from the list of additional Pharmacovigilance Activities and to remove several safety concerns from the list of important identified and potential risks and missing information to follow revised guidance in the GVP Module V Rev.2 as requested during variation procedure no. EMEA/H/C/002315/II/0028."

PRAC Led

Edurant - rilpivirine -

EMEA/H/C/002264/II/0037

Janssen-Cilag International NV, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from a Drug Utilization Study (DUS), with register number EUPAS5766, in the EuroSIDA cohort listed as a category 3 study in the RMP.
This is an Observational Cohort Study to assess rilpivirine (RPV) utilization according to the European SmPC.
The RMP version 9.0 has also been submitted."

PRAC Led

EXJADE - deferasirox -

EMEA/H/C/000670/II/0068

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report related to the Physician Survey (NO6987) conducted for

Exjade to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate use of both formulations (Dispersible Tablets and Film-Coated tablets). The updated RMP version 17.1 is submitted as well."

PRAC Led

Glivec - imatinib - EMEA/H/C/000406/II/0115

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 12 in order to revise the lists of safety concerns in EU RMP and align with the current GVP Rev 2 based on the PRAC advice received on the latest PSUR (11-May-2015 to 10-May-2018)."

PRAC Led

Jakavi - ruxolitinib - EMEA/H/C/002464/II/0043

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from a safety study (INC424AIC01T) of ruxolitinib in myelofibrosis (MF) listed as a category 3 study in the RMP. This is a non-interventional, observational post-authorisation safety study (PASS) intended to provide real-world safety data on patients with MF who were exposed and non-exposed to ruxolitinib and thereby provide insights into disease management and the safety profile of ruxolitinib.
The RMP version 11 has also been submitted. The updated RMP v11 reflects the completion of additional pharmacovigilance studies including the above-mentioned PASS (INC424AIC01T, Category 3) as well as the RESPONSE study (INC424B2301, Category 1). This RMP is incorporated in this variation and will be cross-referred in the variation forthcoming submission for the RESPONSE study within a month of this submission."

PRAC Led

Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0015,

Orphan

Les Laboratoires Servier, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Ingrid Wang, "Submission of an updated RMP version 2.7 in order to update the RMP further to the last PSUSA procedures (PSUSA/00010534/201804 and (PSUSA/00010534/201810) and in accordance with GVP Module V Rev.2."

PRAC Led

WS1614

Enbrel-EMEA/H/C/000262/WS1614/0227

LIFMIOR-EMEA/H/C/004167/WS1614/0021

Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the final report from study (B1801035; PURPOSE) listed as a category 3 study in the RMP. This is a non-interventional, multi-centre, prospective, observational, cohort study conducted to evaluate the long-term safety and effectiveness of etanercept prescribed by dermatologists to paediatric patients for the treatment of plaque psoriasis."

PRAC Led

WS1651

Idacio-EMEA/H/C/004475/WS1651/0003

Kromeya-EMEA/H/C/005158/WS1651/0003

Fresenius Kabi Deutschland GmbH, Lead PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "To update the risk management plans (RMP) for Idacio and Kromeya in order to align it with the parent product Humira one.
The Risk Minimization Measures in Annex II.D of the PI are also updated.
Minor linguistic changes/corrections to the Product Information in German, French, Hungarian (Idacio only) and Slovenian have been included."

PRAC Led

WS1663/G

Exviera-EMEA/H/C/003837/WS1663/0046/G

Viekirax-EMEA/H/C/003839/WS1663/0055/G

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “C.I.13 To submit the final report from study P15-421, listed as a category 3 study in the RMP. This was a prospective, observational cohort study utilizing the Hepatitis C Therapeutic Registry and Research Network (HCV-TARGET) data to evaluate the clinical impact and real world frequency of Grade 3+ ALT elevations in patients being treated for Hepatitis C with paritaprevir with ritonavir (paritaprevir/r), ombitasvir and dasabuvir (3-DAA regimen) or paritaprevir/r and ombitasvir (2-DAA regimen) with or without ribavirin for Hepatitis C Infection (HCV) C.I.11.Z (Type IB): To change the final due date for the prospective safety study report in order to evaluate the recurrence of hepatocellular carcinoma associated with Viekirax and Exviera from Q2 2021 to Q2 2023. Annex II of the Product Information is updated accordingly.
An updated RMP version 5.0 has also been submitted.”

PRAC Led

WS1671

Afinitor-EMEA/H/C/001038/WS1671/0063

Votubia-EMEA/H/C/002311/WS1671/0059

Novartis Europharm Limited, Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, “To update the RMP for Afinitor and Votubia to version 14.0 to change the safety concerns, to reflect the completion of pharmacovigilance studies [CRAD001Y2201 (Afinitor II/0058), CRAD001M2304 (Votubia II/0051), CRAD001J2301 (Afinitor II/0051G), CRAD00W2301 (Afinitor II/0051G)] and to implement the latest GVP module V rev.2 template. The change has been agreed by the PRAC in the outcome of a PSUR assessment (EMEA/H/C/PSUSA/00010268/201703).”

PRAC Led

WS1680

Actos-EMEA/H/C/000285/WS1680/0082

Competact-EMEA/H/C/000655/WS1680/0074

Glubrava-EMEA/H/C/000893/WS1680/0060
Glustin-EMEA/H/C/000286/WS1680/0081
Tandemact-EMEA/H/C/000680/WS1680/0060
Takeda Pharma A/S, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP (version 27) in order to update and consolidate within a single RMP the RMPs for Pioglitazone, Pioglitazone/Metformin fixed dose combination (FDC) and Pioglitazone/Glimepiride FDC. The list of safety concerns has also been reviewed and consolidated RMP version updated with information agreed/approved as part of the PSUR procedure (EMEA/H/C/PSUSA/00002417/201807) with regards to discontinuation of pioglitazone aRMMs."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

B.6.15. Unclassified procedures and worksharing procedures of type I variations

WS1676/G
Exelon-EMEA/H/C/000169/WS1676/0124/G
Prometax-EMEA/H/C/000255/WS1676/0125/G
Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau

WS1681
Esperoct-EMEA/H/C/004883/WS1681/0001
NovoEight-EMEA/H/C/002719/WS1681/0032
Novo Nordisk A/S, Lead Rapporteur: Jan Mueller-Berghaus

WS1687
Fiasp-EMEA/H/C/004046/WS1687/0017
NovoMix-EMEA/H/C/000308/WS1687/0100
NovoRapid-EMEA/H/C/000258/WS1687/0130
Ryzodeg-EMEA/H/C/002499/WS1687/

0037

Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

B.7.1. Yearly Line listing for Type I and II variations

B.7.2. Monthly Line listing for Type I variations

B.7.3. Opinion on Marketing Authorisation transfer (MMD only)

B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)

B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)

B.7.6. Notifications of Type I Variations (MMD only)

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver

F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended

F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health

G. ANNEX G

H. ANNEX H - Product Shared Mailboxes – e-mail address

Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 2)*

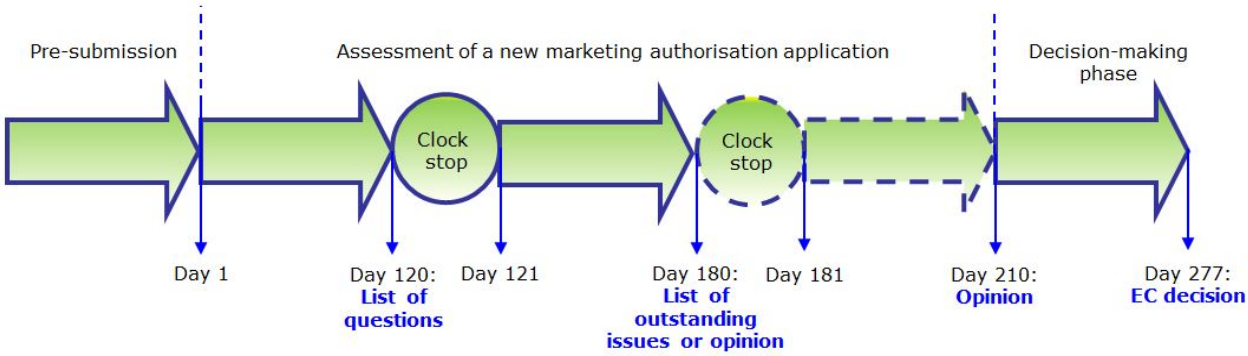
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

Initial applications *(section 3)*

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 4)*

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 5)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 6)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 3.5)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section5.3)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 3.7)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 8)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 9)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 12)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 13)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 14.3.1)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 14.2)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 14.3)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/