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Human Medicines Evaluation

Labelling exemption requests under article 63 of Directive 2001/83/EC examined by QRD group

See also ‘Recommendations for the implementation of the exemptions to the labelling and package leaflet obligations in the centralised procedure’ document.

***Rev.3 Changes since the last version:** Update with latest decisions taken by QRD Group

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Product name Active substance	Date of discussion	Company name	Company proposal	Outcome	Comments
Defitelio *defibrotide* Art. 63(1)	March 2017	Gentium S.r.l.	1/English only outer carton and vial label in 7 countries (CZ, HR, EL, SL, BG, HU, and PL). 2/English only package leaflet in 4 of those 7 countries, i.e. EL, SL, HR and PL.	1/Partially positive 2/No consensus	1/All MSs accepted the company's request with the exception of PL. 2/Since the translation exemption for the leaflet falls out of the scope of art. 63.1, the company should contact MSs directly. Nevertheless, HR and SL confirmed their acceptance of the leaflet in English.
Bronchitol *mannitol* Art. 63(1)	March 2017	Pharmaxis Pharmaceuticals Limited	Bilingual English/German pack in 13 countries (BG, CZ, ET, EL, HU, LV, LT, MT, PL, PT, RO, SK, SL)	Negative	The Group rejected the request based on a number of important warnings on the outer carton which should be translated. The Group requested the MAH to first look into the possibility of developing multilingual packs.
Cystadrops *mercaptamine* Art. 63(1)	March 2017	Orphan Europe S.A.R.L.	Bilingual French/Dutch outer carton in Belgium	Positive	
Sirturo bedaquiline Art. 63(1)	October 2016	Janssen-Cilag International NV	English only blister label	Positive	The Group accepted the request provided the month for the expiry date was expressed in numbers (in some languages abbreviations of months may have a different meaning, therefore confusion is possible).

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Venclyxto *venetoclax* Art. 63(1)	June 2016	AbbVie Ltd.	To supply with UK/Finland/Sweden blisters/cartons initial packs for Hungary/Poland, Bulgaria/Romania, Czech/Slovakia, Estonia/Lithuania/Latvia and Croatia/Slovenia markets only.	Positive	
Revlimid *lenalidomide* Art. 63(1)	June 2016	Celgene Europe Limited	English only blister label in Portugal (2.5 mg pack only)	Positive	
Zinplava *bezlotoxumab* Art. 63(3)	April 2016 (Written procedure)	Merck Sharp & Dohme Limited	Minimum particulars on vial label	Positive	Inclusion of the total content per total volume on the vial label and in section 4 of the outer carton label will be requested.
Brineura *cerliponase alfa* Art. 63(1) and 63(3)	March 2016	BioMarin International Limited	1/ English only vial and outer carton 2/English only package leaflet	1/ Positive 2/ No consensus	2/The applicant should submit this specific request separately to each Member State, in accordance with Art.63.3.

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EndolucinBeta *lutetium (177 Lu) chloride* Art. 63(3)	March 2016	ITG Isotope Technologies Garching GmbH	Omission of "For administration after *in vitro* radiolabelling" and pharmaceutical form from the vial label	Positive	
Imnovid *pomalidomide* Art. 63(1)	March 2016	Celgene Europe Limited	EN only outer carton in Poland	Positive	The exemption for 250 English packages to be marketed in Poland was confirmed by the Polish QRD member. This exemption is granted as a temporary measure, since the MAH confirmed that an outer carton in Polish was being developed and would be available shortly.
Vizamyl *flutemetamol (18F)* Art. 63(3)	March 2016	GE Healthcare Ltd	Simplification of package leaflet (omission of manufacturers)	Positive	The Group agreed, due to the particularities of this product (radiopharmaceutical), to the Company's request to include the manufacturer's details only on the vial label. It should be requested that the manufacturer is also displayed on the shield.
Dinutuximab beta Apeiron *dinutuximab beta* Art. 63(1)	October 2015	APEIRON Biologics AG	1/ English only vial label 2/ English only outer carton 3/ English only package leaflet	1/Positive 2/Negative 3/No consensus	2/ The applicant should first explore the possibility to accommodate as many languages as possible of those countries most affected by the disease. To this end, current text on the carton could be simplified. To be submitted nationally (as per Art.63.3).

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Pandemic influenza vaccine H5N1 MedImmune *pandemic influenza vaccine (H5N1) (live attenuated, nasal)* Art. 63(3)	October 2015	MedImmune	Omission of common name “Pandemic influenza vaccine” from the immediate packaging	Positive	
Wakix *pitolisant* Art. 63(1)	October 2015	Bioprojet Pharma	EN only outer carton and bottle label	Negative	First option should be the creation of multilingual packs.
Strimvelis *autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence* Art. 63(3)	October 2015	GSK	Minimum particulars on the label pouch	Positive	
Iclusig *ponatinib* Art. 63(1)	October 2015	Ariad Pharma	EN only blister and pouch label	Positive	Short term of the pharmaceutical form (tablets) should be used in the blister and pouch foil.

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Zerbaxa *ceftolozane / tazobactam* Art. 63(3)	July 2015 (written procedure)	Cubist Pharmaceuticals	Minimum particulars on vial label (20 ml)	Positive	The short term for the pharmaceutical form should be 'Powder for concentrate' and the route of administration "For iv. use after reconstitution and dilution".
ZEPATIER *grazoprevir/Elbasvir* Art. 63(1)	June 2015	Merck Sharp & Dohme Limited	1/ English only blister label 2/ Omission of EXP and Lot from the wallet label 3/Braille on inner side of the wallet carton 4/ EXP and Lot in English only on the outer carton	1/Positive 2/Positive 3/Positive 4/ Positive	1/ The QRD Group accepted the request to have the blister label in English only with the following information to be displayed on the blister label: Invented name, INN (English and latin), EXP, Lot and 2D code.
Praxbind *idarucizumab* Art. 63(3)	June 2015	Boehringer Ingelheim International GmbH	Simplification of vial label (50 ml)	Positive	The excipients and the 'single-use' statement should be part of the vial label. The MAH details can be removed to gain space and the overall design of the label will need to be addressed. The abbreviation for the route of administration can also be used in case of space constraints.
Coagadex *human coagulation factor X* Art. 63(1)	June 2015	BIO PRODUCTS LABORATORY	English only outer and inner label, and package leaflet	Negative	The QRD Group suggested to explore first simplification of the labelling to allow the combination of several languages; if the assessment of the multilingual packs is not satisfactory, then the request of English only packaging may be reconsidered. The Group suggested to apply nationally to those MSs that could accept an English

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					only package leaflet.
Zalviso *sufentanil* Art. 63(3)	June 2015	Grunenthal GmbH	Omission of particulars (expiry date) from cartridge label	Positive	
Sirturo *bedaquiline* Art. 63(1)	March 2015	Janssen-Cilag	English only labelling	Negative	The Group rejected the request. Despite the orphan status, an English only label for a medicine to be handled directly by the patient raised concerns for a number of Member States. The Group suggested exploring multilingual labelling in order to cover as many markets as possible. **Decision after appeal by MAH (written procedure in March 2015):** Following an appeal by the MAH to the above decision the Group concluded that they would be inclined to accept the request provided the MAH explores first the option of multilingual labelling.
Kyprolis *carfilzomib* Art. 63(3)	March 2015	Amgen	Minimum particulars on vial label	Negative	The request was rejected and the applicant will be asked to look into alternative options to fit the full set of particulars (e.g. concertina labels).

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Strensiq *asfotase alfa* Art. 63(1)	March 2015	Alexion	Partial translation exemption of labelling and leaflet UK/FR/ES/IT/DE: National language BG/CZ/DK/EE/EL/HR/CY/ LV/LT/HU/IE/MT/PL/RO/ SL/SK/FI/SV: EN only AT: German language BE/NL/LU: trilingual with French, Dutch and German languages	Negative	The request was rejected and the applicant will be asked to attempt multilingual combinations first for the outer carton and vial label. The applicant will be offered the option of using article 63.3 on the basis of severe availability issues and, therefore, could approach each Member State at national level.
Signifor *pasireotide* Art. 63(3)	March 2015	Novartis Europharm Ltd	Omission of certain particulars on intermediate label (blister tray)	Negative	The Group concluded that the applicant's proposal to display the invented name along with EXP and Lot of the injection kit is misleading and, therefore, not acceptable. Deletion of all particulars from the plastic tray foil would be acceptable, as an alternative solution.
Revlimid, Thalidomide, Imnovid *lenalidomide, thalidomide, pomalidomide*	March 2015	Celgene Europe Ltd	English only outer carton in Baltic States	Negative	The Group rejected the request. Multilingual outer carton was recommended due to important warnings and self-administration by patients, but certain translation exceptions could be allowed (e.g. INN).

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Art. 63(1)					
Zavicefta *ceftazidime / avibactam* Art. 63(3)	March 2015	AstraZeneca	Minimum particulars on 20 ml vial label	Positive	
Evarrest *human fibrinogen / human thrombin* Art. 63(3)	December 2014 (written procedure)	Omrix Biopharmaceuticals N. V.	Minimum particulars on foil pouch label	Partially positive	QRD members were in agreement with a reduced set of information as proposed, however they also requested the inclusion of the amount of active substance per cm^2 to be added to the pouch label.
Lenvima *lenvatinib* Art. 63(1)	October 2014	Eisai Ltd.	1/English only outer carton 2/Simplification of blister label (omission of pharmaceutical form to have an English only label)	1/Negative 2/Partially positive	1/The justification was not considered strong enough and, on the other hand, the product was meant to be handled directly by patients. Multilingual packs could be an option provided readability is not compromised. 2/The Group was in agreement to have an English only blister that includes the pharmaceutical form.

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Unituxin *dinutuximab* Art. 63(1) and 63(3)	June 2014, October 2014 and June 2015	United Therapeutics Europe	1/ English only labelling (outer and inner) 2/ English only package leaflet	1/ Positive 2/Negative	2/ The applicant should apply for the translation exemption individually at each NCA based on art 63.3.
Amyvid *florbetapir (18F)* Art. 63(3)	June 2014	Avid Radiopharmaceuticals	Simplification of package leaflet (omission of manufacturers)	Positive	The Group agreed, due to the particularities of this product (radiopharmaceutical), to the Company's request to include the manufacturer's details only on the vial label. It should be requested that the manufacturer is also displayed on the shield.
Uptravi *selexipag* Art. 63(1)	June 2014	Actelion Registration Ltd.	English only blister	Positive	The Group considered the proposal acceptable if the unit is spelt out.
Raplixa *human fibrinogen / human thrombin* Art. 63(3)	June 2014	ProFibrix BV	Simplification of vial label	Negative	The Group concluded that more elements should be included on the label, i.e. active substance, strength and pharmaceutical form.
Quinsair *levofloxacin* Art. 63(1)	June 2014	Aptalis Pharma	English only ampoule label	Positive	

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Procysbi *mercaptamine* Art. 63(1)	June 2014	Raptor Pharmaceuticals Europe BV	Translation exemption of 'EXP' and 'Lot' on outer carton and inner label	Partially positive	BG, LV, ES, IT, LT and PL accepted to use EXP and Lot on both the outer carton and bottle label on the grounds of its orphan status. DE only accepted to use EXP and Lot on the bottle label, but not on the outer carton.
Vimizim *elosulfase alfa* Art. 63(1)	October 2013	BioMarin	English only vial label	Positive	No concerns were raised
Entyvio *vedolizumab* Art. 63(3)	June 2013	Takeda Pharma	Minimum particulars for the 20 mL vial label	Positive	No concerns were raised
Xofigo *radium Ra223 dichloride* Art. 63(3)	June 2013	Bayer Pharma	EN only vial label	Positive	With regards to the proposal from the company to have multi-layered label for the lead pot, the QRD Group agreed in principle to this concept, but with the following comments: - The first and last language of the booklet should be English, so that the immediate attached label is in English (in case the other languages are lost); - The label should be printed on one side only (one language per page); - There should not be any sticky part on the label.

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Zevalin *ibritumomab tiuxetan* Art. 63(3)	June 2013	Spectrum pharmaceutical	EN only for outer carton and vial label	Positive	The Group accepted the request. However, due to the prevalence of the disease in Germany, the company should consider providing a German outer carton and vial label for this market.
Imnovid *pomalidomide* Art. 63(1)	June 2013	Celgene	EN only for blister foil	Positive	No concerns were raised.
Ceplene *histamine dihydrochloride* Art. 63(1)	June 2013	Meda AB	EN only for outer carton and vial label	Positive	
Spherox *spheroids of human autologous matrix-associated chondrocytes* Art. 63(3)	March 2013	CO.DON AG	Simplification of labelling	Positive	a) The applicant's proposal to only include batch number and number of spheroids in the immediate container (application system or syringe) was agreed by the Group. b) Proposal to only include the patients' ID in the secondary packaging (tube) was agreed by the Group. C) Proposal to omit both statements 'Keep out of the sight and reach of children' and 'Read the package leaflet before use' on the outer packaging (pouch) was agreed by the Group.

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Granupas *para-aminosalicylic acid* Art. 63(1)	March 2013	Lucane Pharma	EN only sachet labelling	Positive	The Group agreed to have the main particulars in English only (pharmaceutical form, INN, EXP and Lot) and requested to include the full warning translated in all languages on the sachet '*Do not use if sachet is swollen or the granules have lost their light brown colour and are dark brown or purple*' together with the warning '*Do not chew*'.
Naglazyme *galsulfase* Art. 63(1)	March 2013	BioMarin	EN only for vial label	Positive	No concerns were raised.
Vantobra *tobramycin* Art. 63(1)	March 2013	Pari Pharma	1/ EN only ampoule labelling 2/ Simplification of ampoule labelling	Positive for both requests	
Lucentis *ranibizumab* Art. 63(3)	May 2012	Novartis	To omit the route of administration 'intravitreal use' from the pre-filled syringe label in all languages	Negative	The QRD Group felt the current information provided on the pre-filled syringe label could be re-arranged in order to gain some space to fit the route of administration; e.g. by decreasing the importance given to the trade name and company name.

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NovoThirteen *catridecacog* Art. 63(1)	November 2011	NovoNordisk	EN only for outer carton and vial label	Positive	No concerns were raised.
Tysabri *natalizumab* Art. 63(3)	June 2011	Elan Pharma International Ltd	Minimum particulars on the 15 ml vial label	Positive	No concerns were raised.
Nexavar *sorafenib* Art. 63(1)	March 2011	Bayer	INN in EN only for the blister foil	Positive	No concerns were raised.
Zinforo *ceftaroline fosamil* Art. 63(3)	November 2010	AstraZeneca	Vial (20ml) label simplification	Positive	The group agreed to implement the minimum particulars for the vial label of Zinforo.
Xofigo *radium Ra223 dichloride* Art 63(3)	November 2010	Bayer Pharma AG	1/ EN only and simplification of vial (10ml) labelling 2/ EN only labelling for the lead container	1.Positive 2. Negative	1. The request from the company to have the particulars set out in Art.66 on the vial label in EN only has been accepted by the Group. 2. However, the Group would allow the exclusion of certain particulars considered not critical in order to gain space.

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Bronchitol Art 63(1)	September 2010	Pharmaxis	EN only and simplification of blister labelling	Positive for the EN only. Negative for the simplificati on	The full pharmaceutical form (inhalation powder, hard capsules) should be displayed on the labelling.
Glybera Art 63(1)	March 2010	Diamond Biopharm Ltd	EN only labelling for vial and protective casing	Positive	No concerns were raised.
Scintimun Art 63(3)	November 2009	CIS bio international	EN only labelling for certain MS (considered as small markets) and FR & NL only labelling for BE pack.	Positive	By law, all three languages (NL, FR and DE) have to be included on the label for BE. However, in BE for radiopharmaceuticals kits, an exception for small immediate packs is possible and therefore an EN only label could be accepted.
Tracleer (paediatric formulation) Art 63(1)	September 2009	Actelion Pharmaceutic als Ltd	Multi-lingual blister foil DE/ES/FR/IT/PT/EN for the 6 bigger markets (AT, DE, ES, FR, IT, PT) EN only for outer carton and blister foil for the rest of the Member States	Positive	With reservation of EL to be included as the 7th biggest market.

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Firdapse (previously Zenas) Art 63(1)	June 2009	EUSA Pharma SAS	EN only ampoule label	Positive	No concerns were raised.
Pedea Art 63(1)	June 2009	Orphan Europe	EN only ampoule label	Positive	No concerns were raised.
Ixiaro (withdrawal of orphan designation) Review of QRD decision made at June 2008 plenary. Now the orphan designation has been withdrawn, company's justification falls under 63.3. Therefore, translation exemptions can still be applied to the package leaflet but not to the labelling anymore.	June 2009	Intercell	EN syringe label Tri-lingual outer carton (EN/ES/IT, DE/FR/NL, SE/FI/NO) Tri-lingual package leaflet (EN/ES/IT, DE/FR/NL, SE/FI/NO)	Negative	The Group suggested to have another combination of 3 languages for the package leaflet (including Greek) and to translate the labelling in all languages. Moreover, the company should ensure, and, if necessary, consult with the relevant national authorities, that the combination supplied in a given MS is the preferred one by the respective national authority.
Insuman	March 2009	Sanofi-	EN/FR labelling (outer carton, label and	Positive	Provided that: a sentence, translated in all relevant languages, is

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Art 63(3)		Aventis	package leaflet)		included in the bilingual FR/EN Package Leaflet informing the patient that the package leaflet is available in their language on the EMA website; the company will provide on request the package leaflet to the patient concerned in their own language; and the company will inform EMA in case of change in the sales status for this product, as the current decision will then need to be reassessed by the QRD group.
Treprostinil sodium Art 63(1)	September 2008	United therapeutics Europe Ltd	EN only labelling	Positive	Request in principle acceptable, however, the request to delete the INN in the immediate packaging due to readability concerns was rejected, since other particulars such as the name of the MAH could be left out instead.
Ixiaro Art 63(1)	June 2008	Intercell	EN only syringe label Tri-lingual outer carton: EN/ES/IT, DE/FR/NL and DK/FI/NO. Tri-lingual package leaflet: EN/ES/IT, DE/FR/NL and DK/FI/NO.	Positive	Labelling in EN only was considered acceptable. For the package leaflet in the national language, the A4 format in all national languages would be delivered by the company, separate from the pack.
Evicel Art 63(3)	June 2008	OMRIX Biopharmace	EN only vial label	Positive	

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Cayston Art 63(1)	June 2008	Gilead Sciences International Ltd	EN only diluent label	Positive	Provided that an appropriate explanation is provided in the package leaflet.