



Republic of the Philippines
Department of Health

FOOD AND DRUG ADMINISTRATION



13 March 2015

FDA CIRCULAR No. 2015-004

SUBJECT: List of Reference Biotherapeutic Products (RBPs) for Head-to-Head Comparability Studies of Similar Biotherapeutic Products (SBPs)

For the effective implementation of Administrative Order No. 2014-0016, “Adoption of the World Health Organization “Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs)” for the Registration of Biosimilar Products”, particularly on the provision requiring head-to-head comparability studies for the registration of SBPs, the Food and Drug Administration (FDA) hereby provides the following listing of RBPs for use in comparability exercises of SBPs to establish similarity:

A. Non-Insulin Products

	Active Ingredient	Dosage Strength and Form	Brand Name	Marketing Authorization Holder	Registration Number
1.	Aflibercept	40 mg/mL Solution for Intravitreal Injection	Eylea	Bayer Philippines, Inc.	BR-912
2.	Alglucosidase alfa	50 mg Lyophilized Powder for Concentrate for Solution for IV Infusion	Myozyme	Sanofi-Aventis Philippines Inc.	BR-893
3.	Basiliximab	20 mg Freeze Dried Powder for IV Infusion	Simulect	Novartis Healthcare Phils., Inc.	BR-1051
4.	Belimumab	80 mg/mL Powder for Solution for IV Infusion	Benlysta	GlaxoSmithKline Philippines Inc	BR-862
5.	Bevacizumab	400 mg/16mL (25 mg/mL) Concentrate for Solution for IV Infusion	Avastin	Roche Philippines, Inc.	BR-739
6.	Canakinumab	150 mg/mL Lyophilized Powder for Solution (SC)	Ilaris	Novartis Healthcare Phils Inc	BR-1052
7.	Cetuximab	5 mg/mL Solution for IV Infusion	Erbitux	Merck, Inc.	BR-1050
8.	Choriogonadot	250 mcg/0.5 mL	Ovidrel	Merck, Inc.	BR-916



	ropin alfa	Solution for Injection (SC)			
9.	Corifollitropin alfa	150 mg/0.5 mL Solution for Subcutaneous Injection	Elonva	Merck Sharp & Dohme (I.A.) Corporation	BR-979
		100 mcg/0.5 mL Solution for Subcutaneous Injection	Elonva	Merck Sharp & Dohme (I.A.) Corporation	BR-978
10.	Darbepoetin alfa	10 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1017
		20 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1018
		30 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1019
		40 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1020
		60 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1021
		120 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1022
		180 mcg/0.5 mL Solution for Injection (IV/SC)	Nesp	Zuellig Pharma Coporation	BR-1023
11.	Denosumab	70 mg/mL Solution for Injection (SC)	Xgeva	GlaxoSmithKline Philippines Inc	BR-853
12.	Epoetin alfa (Recombinant Human Erythropoietin)	2,000 IU/0.5 mL Solution for Injection (IV/SC)	Eprex	Johnson & Johnson (Philippines), Inc.	BR-703
		4,000 IU/0.4 mL Solution for Injection (IV/SC)	Eprex	Johnson & Johnson (Philippines), Inc.	BR-701
		10,000 IU/mL Solution for Injection (IV/SC)	Eprex	Johnson & Johnson (Philippines), Inc.	BR-702
		40,000 IU/mL Solution for Injection (IV/SC)	Eprex	Johnson & Johnson (Philippines), Inc.	BR-704
13.	Etanercept	25 mg/0.5 mL Solution for Injection (SC) (Pre-filled Syringe)	Enbrel	Pfizer Inc	BR-1070

		50 mg/mL Solution for Subcutaneous Injection (pre-filled Syringe)	Enbrel	Pfizer Inc	BR-1071
14.	Epoetin beta	10,000 IU/0.6 mL Solution for Injection (IV/SC)	Recormon	Roche Philippines, Inc.	BR-1062
		30,000 IU/0.6 mL Solution for Injection (IV/SC)	Recormon	Roche Philippines, Inc.	BR-1060
		5,000 IU/0.3 mL Solution for Injection (SC/IV)	Recormon	Roche Philippines, Inc.	BR-1061
15.	Filgrastim	300 mcg/mL Solution for Injection (SC/IV)	Neupogen	Roche Philippines, Inc.	BR-1063
16.	Follitropin alfa	75 IU (5.5 mcg) Lyophilized Powder for Solution for Subcutaneous Injection	Gonal-F	Merck, Inc.	BR-1049
		900 IU/1.5 mL (66 mcg/1.5 mL) Solution for Injection (SC)	Gonal-F	Merck, Inc.	BR-831
		450 IU/0.75 mL (33 mcg/7.5 mL)	Gonal-F	Merck, Inc.	BR-829
		300 IU/0.5 mL (22 mcg/0.5 mL) Solution for Injection (SC)	Gonal-F	Merck, Inc.	BR-830
		1,050 IU/1.75 mL (77 mcg/1.75 mL) Lyophilized Powder for Solution for Injection (SC)	Gonal-F	Merck, Inc.	BR-871
17.	Follitropin beta	50 IU/0.5 mL Solution for Injection (IM/SC)	Puregon	Merck Sharp & Dohme (I.A.) Corporation	BR-1041
		100 IU/0.5 mL Solution for Injection (IM/SC)	Puregon	Merck Sharp & Dohme (I.A.) Corporation	BR-1040
		150 IU/0.5 mL Solution for Injection (IM/SC)	Puregon	Merck Sharp & Dohme (I.A.) Corporation	BR-1039
		600 IU/0.72 mL Solution for Injection (SC)	Puregon	Merck Sharp & Dohme (I.A.) Corporation	BR-1038
18.	Golimumab	50 mg/0.5 mL Solution for Injection (SC)	Simponi	Johnson & Johnson (Philippines), Inc.	BR-906
19.	Infliximab	100 mg Lyophilized	Remicade	Johnson & Johnson	BR-759

		Powder for Concentrate for Solution for Infusion (IV)		(Phils.), Inc.	
20.	Interferon alfa 2A	3 M IU Solution for Injection (SC/IM)	Roferon-A	Roche Inc.	BR-1064
21.	Interferon alfa 2B	15 M IU/mL Solution for Injection (SC)	Intron A	Merck Sharp & Dohme (I.A.) Corporation	BR-1037
		25 M IU/mL Solution for Injection (SC)	Intron A	Merck Sharp & Dohme (I.A.) Corporation	BR-1036
		50 M IU/mL Solution for Injection (SC)	Intron A	Merck Sharp & Dohme (I.A.) Corporation	BR-1035
22.	Interferon beta-1A (human)	132 mcg (36 M IU)/1.5 mL Solution for Injection (SC)	Rebif	Merck, Inc.	BR-774
23.	Interferon beta-1B	250 mcg (8 M IU)/mL Lyophilized Powder for Injection (SC)	Betaferon	Bayer Philippines, Inc.	BR-846
24.	Laronidase	580 mcg/mL (2.9 mg/5 mL Concentrated Solution for IV Infusion	Aldurazyme	Sanofi-Aventis Phils Inc	BR-1026
25.	Lutropin alfa	75 IU (3.7 mcg/mL) Lyophilized Powder for Injection (SC)	Luveris	Merck, Inc.	BR-824
26.	Methoxy Polyethylene Glycol-Epoetin beta	50 mcg/0.3 mL Solution for Injection (IV/SC)	Mircera	Roche Philippines, Inc.	BR-638
27.	Omalizumab	202.5 mg Lyophilized Powder for Injection (SC) (150 mg/ 1.2 mL Reconstituted Solution)	Xolair	Novartis Healthcare Phils., (Inc.)	BR-987
28.	Panitumumab	20 mg/mL Concentrate for Solution for Intravenous Infusion	Vectibix	GlaxoSmithKline Philippines Inc	BR-896
29.	Pegfilgrastim	6 mg/0.6 mL Solution for Injection (SC)	Neulastim	Roche Philippines, Inc.	BR-1065
30.	Peginterferon alfa-2a	180 mcg/0.5 mL Solution for Injection (SC)	Pegasys	Roche Phils Inc	BR-1066
		135 mcg/0.5 mL Solution for Injection	Pegasys	Roche Phils Inc	BR-1067

		(SC)			
31.	Pegylated Interferon alfa 2b	50 mcg Powder for Injection (SC)	Peg Intron* Clearclick	Merck Sharp & Dohme (I.A.) Corporation	BR-1034
		80 mcg Powder for Injection (SC)	Peg Intron* Clearclick	Merck Sharp & Dohme (I.A.) Corporation	BR-1033
		100 mcg Powder for Injection (SC)	Peg Intron* Clearclick	Merck Sharp & Dohme (I.A.) Corporation	BR-1032
		120 mcg Powder for Injection (SC)	Peg Intron* Clearclick	Merck Sharp & Dohme (I.A.) Corporation	BR-1031
		150 mcg Powder for Injection (SC)	Peg Intron* Clearclick	Merck Sharp & Dohme (I.A.) Corporation	BR-1030
32.	Pertuzumab	30 mg/mL Concentrate for Solution for I.V. Infusion	Perteja	Roche Philippines, Inc.	BR-927
33.	Ranibizumab	10 mg/mL Solution for Injection (Intravitreal)	Lucentis	Novartis Healthcare Phils., (Inc.)	BR-1072
34.	Rituximab	10 mg/mL Concentrate for Solution for I.V. Infusion	Mabthera	Roche Phils Inc	BR-1069
35.	Somatropin	10 IU/(3.33 mg) Lyophilized Powder for Injection (IM/SC)	Saizen	Merck, Inc.	BR-894
		8 mg Lyophilized Powder for Injection (IM/SC)	Saizen	Merck, Inc.	BR-841
		1 mg/1.5 mL (8 mg/mL) Solution for Injection (SC)	Saizen	Merck, Inc.	BR-878
		6 mg/1.03 mL (5.83 mg/mL) Solution for Injection (SC)	Saizen	Merck, Inc.	BR-880
		20 mg/2.5 mL (8 mg/mL) Solution for Injection (SC)	Saizen	Merck, Inc.	BR-879
		5 mg/1.5 mL (15 IU) Solution for Injection (SC)	Scitropin A	Metro Drug, Inc.	BR-1059
		4 IU (1.33 mg) Lyophilized powder for Injection (IM/SC)	Saizen	Merck, Inc.	BR-843
36.	Tocilizumab	400 mg/20 mL (20	Actemra	Roche (Phils) Inc	BR-689

		mg/mL) Concentrate for Solution for IV Infusion			
37.	Urofollitropin	75 IU Lyophilized Powder for Injection (SC)	Bravelle	Metro Drug, Inc.	BR-786
38.	Trastuzumab	150 mg Lyophilized Powder for Concentrate Solution (IV Infusion)	Herceptin	Roche Phils Inc	BR-1068
39.	Ustekinumab	90 mg/mL Solution for Injection (SC)	Stelara	Johnson & Johnson Phils Inc	BR-983
		45 mg/0.5 mL Solution for Injection (SC)	Stelara	Johnson & Johnson Phils Inc	BR-753

B. Insulin Products

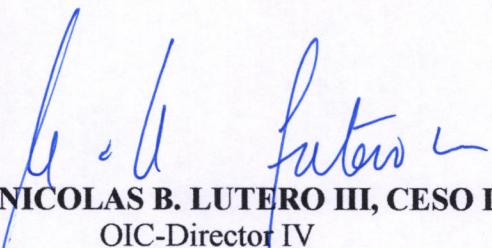
	Active Ingredient	Dosage Strength and Form	Brand Name	Marketing Authorization Holder	Registration Number
39.	Recombinant Human Insulin (70% Isophane/ 30% Soluble)	100 IU/mL Suspension for Injection (SC)	Humulin 70/30	Eli Lilly (Philippines), Inc.	BR-977
40.	Insulin Lispro (RDNA Origin)	100 Units/mL (3.5 mg/mL) Solution for Injection (IV/SC)	Humalog	Eli Lilly (Philippines), Inc.	BR-956
41.	Regular Insulin Human (Recombinant DNA)	100 IU/mL Solution for Injection (SC)	Humulin R	Eli Lilly (Philippines), Inc.	BR-980
42.	Isophane Insulin Human (Recombinant DNA)	100 IU/mL Suspension for Injection (SC)	Humulin N Kwikpen	Eli Lilly (Philippines), Inc.	BR-948
43.	Insulin Detemir	100 IU/mL Solution for Injection (SC)	Levemir Flexpen	Novo Nordisk Pharmaceuticals Philippines Inc.	BR-1011
44.	Insulin Aspart	100 IU/mL Solution for Subcutaneous Injection	Novo Rapid Flexpen	Novo Nordisk Pharmaceuticals Philippines Inc.	BR-1015
45.	Insulin Glulisine	3.49 mg/mL (equivalent to 100 units/mL) Solution for Subcutaneous/ Continuous SC Pump Infusion/ Intravenous	Apidra	Sanofi-Aventis Philippines Inc.	BR-1046

		Injection			
46.	Insulin Glargine	100 Units/mL Solution for Injection (SC)	Lantus	Sanofi-Aventis Philippines Inc.	BRP-015

For biotherapeutic/ biologic products considered as new and has never been introduced in the Philippine market, pertinent requirements for Biotechnological Products as provided under Association of Southeast Asian Nation (ASEAN) Common Technical Dossier (ACTD) for registration shall apply, with reference to other international standards such as the World Health organization (WHO) and International Conference on Harmonisation (ICH) guidelines. In this regard, submission of appropriate pre-clinical and clinical studies, as well as non-clinical studies is required to support product application.

Moreover, in the event that the sale and marketing of a currently listed RBP has been discontinued by the registered Marketing Authorization Holder (MAH), an alternative RBP shall be determined by FDA in its place.

For your information and guidance.



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