FORM: Certificate of Compliance Havant finished products

Certificate of Compliance Manufacturer's Declaration

PFIZER MANUFACTURING BELGIUM NV
RIJKSWEG 12
PUURS (BELGIUM)
TEL: +32(0)3 890.92.11
FAX: +32(0)3 889.65.32

Product Name: Enbrel 25mg SFDPO 2x2 VL+SYR

Date generated: 03-2019

Strength/Potency:

Each pre-filled syringe contains 25mg of etanercept
Each pre-filled syringe contains 50mg of etanercept
Each vial contains 10mg of etanercept
Each vial contains 25mg of etanercept
Each pre-filled pen contains 25mg of etanercept
Each pre-filled pen contains 50mg of etanercept

Packed Batch Number: AK6678

Item Number Packed Batch: F000040247

Date of Manufacture: 08-2018

Expiration Date : 07-2022

Quantity: 638 packs

Manufacturing Site Packed Batch: Wyeth Pharmaceuticals, New Lane, Havant, Hampshire, PO9 2NG, United Kingdom

Bulk Batch Number: X63781

Diluent Batch Number(s): X84472

Certificate of Compliance
Manufacturer's Declaration

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I HEREBY CERTIFY THAT THE ABOVE INFORMATION IS AUTHENTIC AND ACCURATE. THE ABOVE PRODUCT INCLUDING THE ACTIVE SUBSTANCE HAS BEEN MANUFACTURED AND TESTED IN ACCORDANCE WITH MANUFACTURING INSTRUCTIONS, TESTING STANDARDS AND CGMP. IT CONFORMS WITH SPECIFICATIONS AND IS SUITABLE FOR RELEASE UNDER THE CONDITIONS AGREED WITH THE COMPETENT AUTHORITY, WITH RESPECT TO ITS MA IN THE STATED COUNTRY.

THIS IS ALSO TO CERTIFY THAT, WHERE APPLICABLE, ANY MATERIAL DERIVED FROM RUMINANTS (BOVINE, OVINE, CAPRINE) USED IN THE MANUFACTURE AND/OR FORMULATION OF THE BATCH OF PRODUCT SPECIFIED ABOVE FULFIL THE PRESCRIPTIONS DEFINED IN EMA/410/01 AND HAVE THEREFORE BEEN DEMONSTRATED TO BE IN ACCORDANCE WITH THE CURRENT CGMP "NOTE FOR GUIDANCE ON MINIMIZING THE RISK OF TRANSMITTING ANIMAL SPONGIFORM ENCEPHALOPATHY AGENTS VIA MEDICINAL PRODUCTS", THROUGH THE PH. EUR. CERTIFICATION PROCEDURE.

Destination country/countries of the batch: Austria

Final disposition of the batch: released

Name: Hilde Heinickx Signature: [signature] Date: 04/03/2019

ALL ACTIVITIES ARE PERFORMED BY QUALIFIED PEOPLE, UNDER THE SUPERVISION OF THE QUALIFIED PERSON.

Certificate of Analysis

PFIZER MANUFACTURING BELGIUM NV
RIJKSWEG 12
B-2870 PUURS (BELGIUM)
TEL: +32 (0)3 890.92.11
FAX: +32 (0)3 889.65.32

Puurs Batch Number: X63781

Date Generated: 11-2018

Product Name: ENBREL LYO 25MG/ML 2ML GVL HC (ETANERCEPT)

Material Number: H000017356

Date of Manufacture: 08-2018

Expiration Date:07-2022

Specification Name: P4010001003QC

TEST	RESULT	UNIT	LIMITS
APPEARANCE (LYOPHILIZED PRODUCT)	MEETS TEST		WHITE CAKE
COLOR (RECONSTITUTED PRODUCT)	MEETS TEST		<= B6 - COLORLESS TO SLIGHTLY YELLOW OR PALE BROWN LIQUID
CLARITY (RECONSTITUTED PRODUCT)	MEETS TEST		<= REF II - CLEAR TO SLIGHTLY OPALESCENT LIQUID
RECONSTITUTION TIME: MEAN VALUE	45	SEC	<= 120 SECONDS
RECONSTITUTION TIME: HIGH VALUE	85	SEC	<= 250 SECONDS
PH	7.5		7.1 - 7.7
OSMOLALITY	264	MOSM/KG	260 - 320 MOSM/KG AT RELEASE, 232 - 348 MOSM/KG DURING SHELF LIFE
RESIDUAL MOISTURE: MEAN OF 10 VIALS	0.2	%	<= 2.0 % AT RELEASE, <= 3.0 % DURING SHELF LIFE
RESIDUAL MOISTURE INDIVIDUAL VALUES	0.2	%	<= 3.0 % AT RELEASE, <= 4.0 % DURING SHELF LIFE
CONTENT UNIFORMITY	MEETS TEST		MEETS USP REQUIREMENTS
SE-HPLC: PEAK B	1.5	%	<= 6.0 % AT RELEASE, <= 8.0 % DURING SHELF LIFE
SE-HPLC: PEAK A + PEAK A'	98.5	%	>= 94.0 % AT RELEASE, >= 92.0 % DURING SHELF LIFE
SIZE-EXCLUSION CHROMATOGRAPHY	MEETS TEST		PROFILE COMPARABLE TO REFERENCE MATERIAL
PARTICLES >= 10 MCM	14	PART/CONT	<= 6000 PARTICLES
PARTICLES >= 25 MCM	1	PART/CONT	<= 600 PARTICLES
APOPTOSIS BIOASSAY (GRANGE CASTLE)	2.1	X10^6 UNITS/MG	1.0 - 2.9 X 10^6 UNITS/MG
SDS-PAGE (COOMASSIE) MONOMER	97	%	>= 88 %
SDS-PAGE (COOMASSIE) HMWC	1	%	<= 6 %
SDS-PAGE (COOMASSIE) LMWC	2	%	<= 8 %
SDS-PAGE SILVER STAIN	POSITIVE		COMPARABLE TO REFERENCE MATERIAL
HIC PEAK 1	1	%	<= 5 %
HIC PEAK 2	86	%	>= 70 %
HIC PEAK 3	14	%	<= 28 %
ENDOTOXIN	< 0	EU/MG	<= 2 EU/MG AT RELEASE ONLY
STERILITY TEST: DRUG PRODUCT	MEETS TEST		NO GROWTH AFTER 14 DAYS
STERILITY TEST: BULK	MEETS TEST		NO GROWTH AFTER 14 DAYS

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Puurs Batch Number: X63781

Date Generated: 11-2018

Product Name: ENBREL LYO 25MG/ML 2ML GVL HC (ETANERCEPT)

Material Number: H000017356

Date of Manufacture: 08-2018

Expiration Date:07-2022

Specification Name: P4010001003QC

TEST	RESULT	UNIT	LIMITS
PROTEIN CONTENT (UV SPECTROSCOPY)	23.0	MG/VIAL	22.5 - 27.5 MG/VIAL

BATCH: N/A

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THIS BATCH OF PRODUCT HAS BEEN FABRICATED/MANUFACTURED, IN FULL COMPLIANCE WITH THE GMP REQUIREMENTS OF THE APPROVED MARKETS

THE BATCH PROCESSING AND ANALYSIS WERE REVIEWED AND FOUND TO BE IN COMPLIANCE WITH GMP.

QUALITY CONTROL - QC

ALL ACTIVITIES ARE PERFORMED BY QUALIFIED PEOPLE, UNDER THE SUPERVISION OF THE QUALIFIED PERSON.

Electronic Signature: Johan Baeten Lot Release Local Timestamp: 26-NOV-2018 15:43:27 Server Timestamp: 26-NOV-2018 15:43:21

Certificate of Analysis

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RIJKSWEG 12
B-2870 PUURS (BELGIUM)
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Puurs Batch Number: X84472

Date Generated: 11-2018

Product Name: WFI 1ML DS ENBREL DILUENT

Material Number: H000010725

Date of Manufacture: 08-2018

Expiration Date:07-2022

Specification Name: P4070001001EU

TEST	RESULT	UNIT	LIMITS
ACIDITY OR ALKALINITY	MEETS TEST		MEETS PH EUR REQUIREMENTS
CONDUCTIVITY	4	MCS/CM	NMT 25 MCS/CM
OXIDISABLE SUBSTANCES	MEETS TEST		MEETS PH EUR REQUIREMENTS
CHLORIDES	MEETS TEST		NMT 0.5 PPM
NITRATES	MEETS TEST		NMT 0.2 PPM
SULFATES	MEETS TEST		MEETS PH EUR REQUIREMENTS
AMMONIUM	MEETS TEST		NMT 0.6 PPM
CALCIUM AND MAGNESIUM	MEETS TEST		MEETS PH EUR REQUIREMENTS
RESIDUE ON EVAPORATION	0.000	%	NMT 0.004 %
PARTICLES NLT 10MCM	65	PART/CONT	NMT 6000 PART/CONT
PARTICLES NLT 25MCM	1	PART/CONT	NMT 600 PART/CONT
STERILITY	MEETS TEST		MEETS PH EUR REQUIREMENTS
BACTERIAL ENDOTOXINS	< 0.03	EU/ML	LT 0.25 EU/ML
EXTRACTABLE VOLUME	1.063	ML	1.045 - 1.155 ML
APPEARANCE	MEETS TEST		CLEAR, COLORLESS SOLUTION, ESSENTIALLY FREE FROM PARTICLES

BATCH: N/A

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THE BATCH PROCESSING AND ANALYSIS WERE REVIEWED AND FOUND TO BE IN COMPLIANCE WITH GMP.

QUALITY CONTROL - QC

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Electronic Signature: Eline Patteet Lot Release Local Timestamp: 06-NOV-2018 11:31:13 Server Timestamp: 06-NOV-2018 11:31:07