Boehringer Ingelheim

Boehringer Ingelheim Pharma GmbH & Co. KG, Birkendorfer Strasse 65, 88397 Biberach, Germany
Manufacturing Authorization No DE_BW_01_MIA_2022_0059 Certificate No DE_BW_01_GMP_2023_0154

Certificate of Conformance BI

Product Name:	ACTILYSE 50MG BY
Finished Product Article-No.:	59305184
SKU-No. - SKU-Version:	305184-018
Finished Product Lot-No.:	306360
Local Tradename:	ACTILYSE lyophilizate for infusion solution 50 mg/vial with solvent
Importing Country:	BELARUS
Marketing Authorization Number:	2285/97/03/05/08/09/13/17/18
Active Ingredients / Strength:	alteplase / 50 mg/vial
Dosage form:	lyophilisate + solvent for injection
Pack Size:	1 Each
Type of Primary Package:	Vial (colourless glass, type 1)
Order-No.:	90398909
Batch / Lot Quantity released:	2.009 ST
Date of Manufacture:	30.06.2023
Date of Expiry:	30.06.2026
Semi Finished Product Lyo Article-No.:	89478
Semi Finished Product Lyo Lot-No.:	305206
Manufacturing Specification No. Lyo:	79815_P330AL0105
Semi Finished Product Solvent Article-No.:	85115
Semi Finished Product Solvent Lot-No.:	303027-1
Manufacturing Specification No. Solvent:	79815_P330AL0202
Testing Specification:	refer to Certificate of Analysis

Digitally signed by Moraru Grigore
Date: 2024.07.04 09:07:04 EEST
Reason: MoldSign Signature
Location: Moldova

Boehringer Ingelheim

Boehringer Ingelheim Pharma GmbH & Co. KG, Birkendorfer Strasse 65, 88397 Biberach, Germany
Manufacturing Authorization No DE_BW_01_MIA_2022_0059 Certificate No DE_BW_01_GMP_2023_0154

Certificate of Conformance BI

Product Name:	ACTILYSE 50MG	BY
Finished Product Article-No.:	59305184	
SKU-No. - SKU-Version:	305184-018	
Finished Product Lot-No.:	306360	

The following countries are part of this presentation:

Importing Country	Marketing Authorization Number
BELARUS	2285/97/03/05/08/09/13/17/18
UZBEKISTAN (1)	DV/X02073/08/16
GEORGIA	036355
TURKMENISTAN	LS-A 008196
ARMENIA	N 20988
MONGOLIA	F20120423BP02977 NO.0021398

This Certificate of Conformance covers the approval of the Certificate of Analysis for the respective product batch.
I hereby certify that the above information is authentic and accurate. This batch of product has been manufactured, including packaging and quality control at the above mentioned site(s) in full compliance with the GMP requirements of the local Regulatory Authority, and with the specifications in the Marketing Authorisation of the importing country.
The batch processing, packaging and analysis records have been reviewed and found to be in compliance with GMP. Any deviations have been assessed prior to batch/ lot release.

The batch has been released by a Qualified Person.

Remarks: (1) cannot be delivered.

21. Dez. 2023 CPi

21. Dez. 2023 Dr. Morad Schorr

Date / Name / Signature (Qualified Person)

Signatures - 12233666-TPA-02-P-QC-P05

Boehringer Ingelheim

Object: Project 12233666-TPA-02-P-QC-P05

Productcode: TPA-02

Product: Actilyse lyophilisate 50 mg/vial

Drug product lot: 305206

Description	User	Full Name	Date / Time
Preparation of batch release relevant data	MUELANGE	Zeller, Angela	15-Nov-2023 15:04:06
Review data completeness of CoA Report	REHMP	Maichel, Petra	16-Nov-2023 08:07:15
Review of batch release documentation Quality Control	BRUECKJA	Brückmann, Dr., Jannik	16-Nov-2023 09:48:32
Review and approval of Certificate of Analysis (CoA)	KRECH	Krech, Dr., Ingo	23-Nov-2023 11:36:05

Certificate of Analysis

Boehringer Ingelheim
Pharma GmbH & Co. KG
Birkendorfer Straße 65
D-88397 Biberach an der Riß

Productcode: TPA-02 **Project Suffix:** TPA-02-P-QC-P05

Product: Actilyse lyophilisate 50 mg/vial

Spec.No.: TPA-02-P-Q-S04 (V10) **Drug product lot:** 305206

Grade: RELEASE **Description:** Release

Test-Spec.No.: 79815-p510al0201

1. Lyophilisate

Doc-No	*Test*	*Category*	*Acceptance Criteria*	*Result*	*Spec*
QA16195	Appearance	Appearance and description	White to pale yellow cake	white cake	pass
QA16197	Reconstitution time	General tests	Dissolves within 2 min	Dissolves within 2 min	pass
QA3232	Water content	General tests	<= 5 %	2 %	pass
QA3510	Uniformity of mass	General tests	Complies with Ph.Eur.	complies with Ph. Eur.	pass
QA3510	Uniformity of mass - min	General tests		2.47 g	---
QA3510	Uniformity of mass - max	General tests		2.49 g	---

2. After Reconstitution

Doc-No	*Test*	*Category*	*Acceptance Criteria*	*Result*	*Spec*
QA16200	Clarity and degree of opalescence	Appearance and description	<= 3 NTU	1 NTU	pass
QA16199	Degree of coloration	Appearance and description	<= Reference solution Y7	<reference solution Y7	pass
QA3249	Particulate contamination - sub-visible particles	General tests	>= 10 µm <= 6000 particles/ vial	80 particles	pass
QA3249	Particulate contamination - sub-visible particles	General tests	>= 25 µm <= 600 particles/ vial	3 particles	pass
QA1190	pH	General tests	>= 6.8 and <= 7.8	7.3	pass
QA1220	Osmolality	General tests	>= 170 and <= 230 mOsmol/ kg	205 mOsmol/kg	pass
Q70013	High performance size exclusion chromatography	Purity	Monomer: >= 95 %	99 %	pass
Q70014	Single-chain	Purity	>= 60 and <= 100 %	81 %	pass
018-QA061989	Capillary gel electrophoresis reduced	Purity	Main peak: >= 72 %	77 %	pass
018-QA061989	Capillary gel electrophoresis reduced	Purity	Fragment region 1: <= 2 %	1 %	pass
018-QA061897	Type I/II	Heterogeneity	Type I: >= 42 and <= 59 %	47 %	pass
018-QA061897	Type I/II	Heterogeneity	Type II: >= 41 and <= 58 %	53 %	pass

Status: Approved Printed on: 23-Nov-2023 Printed by: Zeller, Angela (LabWare BP Produktion)

Certificate of Analysis

Boehringer Ingelheim
Pharma GmbH & Co. KG
Birkendorfer Straße 65
D-88397 Biberach an der Riß

Productcode: TPA-02 **Project Suffix:** TPA-02-P-QC-P05

Product: Actilyse lyophilisate 50 mg/vial

Spec.No.: TPA-02-P-Q-S04 (V10) **Drug product lot:** 305206

Grade: RELEASE **Description:** Release

Test-Spec.No.: 79815-p510al0201

2. After Reconstitution (cont.)

Doc-No	*Test*	*Category*	*Acceptance Criteria*	*Result*	*Spec*
018-QA061991	Imaged capillary isoelectric focusing	Heterogeneity	Region 1: >= 21 and <= 33 %	27 %	pass
018-QA061991	Imaged capillary isoelectric focusing	Heterogeneity	Region 2: >= 60 and <= 68 %	62 %	pass
018-QA061991	Imaged capillary isoelectric focusing	Heterogeneity	Region 3: >= 5 and <= 14 %	11 %	pass
QA18414	Sialic acid	Heterogeneity	>= 80 and <= 120 % of reference material	87 %	pass
QA52547	Clot lysis	Potency	>= 0.90 and <= 1.20 U/mg	1.00 U/mg	pass
QA52547	Clot lysis	Potency	>= 45.0 and <= 60.0 U/vial	50.1 U/vial	pass
QA52547	Clot lysis	Potency	>= 26.1 and <= 34.8 x 10E6 IU/vial	29.1 10^6 IU/vial	pass
018-QA062593	Arginine	Excipient	>= 32 and <= 38 mg/mL	34 mg/mL	pass
QA2031	Polysorbate 80	Excipient	>= 68 and <= 106 µg/mL	89 µg/mL	pass
QA1020	Protein concentration by UV-scan	Quantity	>= 0.95 and <= 1.05 mg/mL	1.00 mg/mL	pass
QA1020	Protein concentration by UV-scan	Quantity	>= 47.5 and <= 52.5 mg/vial	49.9 mg/vial	pass
QA1090	Bacterial endotoxins	Microbiological tests	< 1 EU/mL	<1 EU/mL	pass
AA021-93	Sterility	Microbiological tests	No growth	no growth	pass

RESULT: Meet Acceptance Criteria: PASS

Manufacturing Date: 05-Oct-2023

The expiration date of the package unit with lyophilisate + solvent for injection is documented on the Certificate of Conformance

Status: Approved Printed on: 23-Nov-2023 Printed by: Zeller, Angela (LabWare BP Produktion)

Certificate of Analysis

Boehringer Ingelheim
Pharma GmbH & Co. KG
Birkendorfer Straße 65
D-88397 Biberach an der Riß

Productcode:	TPA-02	**Project Suffix:**	TPA-02-P-QC-P05
Product:	Actilyse lyophilisate 50 mg/vial		
Spec.No.:	TPA-02-P-Q-S04 (V10)	**Drug product lot:**	305206

Local trade names:
Actilyse 50 mg
Actilyse 50 mg prasek in vehikel za raztopino za injiciranje ali infundiranje
Actilyse 50 mg por és oldószer oldatos injekcióhoz vagy infúzióhoz
Actilyse 50 mg powder and solvent for solution for injection
Actilyse Pulver und Lösungsmittel zur Herstellung einer Injektion- oder Infusionslösung
Actilyse lyophilisate for solution for infusion 50mg
Actilyse® lyophylized powder for solution for infusion 50 mg
Actilyse
ACTILYSE
ACTILYSE 50 MG
Actilyse 50 mg milteliai ir tirpiklis injekciniam ar infuziniam tirpalui
ACTILYSE 50 MG POLVERE E SOLVENTE PER SOLUZIONE INIETTABILE E PER INFUSIONE
Actilyse 50 mg poudre et solvant pour solution injectable et perfusion
Actilyse 50 mg powder and solvent for solution for injection and infusion
Actilyse 50 mg prašak i otapalo za otopinu za injekciju i infuziju
ACTILYSE 50 MG PRAŠEK IN VEHIKEL ZA RAZTOPINO ZA INJICIRANJE ALI INFUNDIRANJE
ACTILYSE 50 MG, pulbere şi solvent pentru soluţie injectabilă/perfuzabilă ACTILYSE, 50 MG
Actilyse 50mg
ACTILYSE 50mg
ACTILYSE INJECTION
ACTILYSE lyophilisate + solvent for injection 50 mg
ACTILYSE lyophilisate for solution for infusion 50mg
ACTILYSE lyophilizate for infusion solution 50 mg/vial with solvent
Actilyse Pó e solvente para solução injectável e perfusão
ACTILYSE POLVO Y DISOLVENTE PARA SOLUCION INYECTABLE Y PARA PERFUSION
ACTILYSE POR ÉS OLDÓSZER OLDATOS INJEKCIÓHOZ VAGY INFÚZIÓHOZ
ACTILYSE poudre et solvant pour solution injectable et perfusion
Actilyse pulver og væske til injeksjons-/infusjonsvæske, oppløsning 50 mg
ACTILYSE PULVER UND LÖSUNGSMITTEL ZUR HERSTELLUNG EINER INJEKTIONS- BZW. INF.LSG
ACTILYSE PULVER UND LÖSUNGSMITTEL ZUR HERSTELLUNG EINER INJEKTIONS- ODER INFUSIO
ACTILYSE VIALS
ACTILYSE® lyophylizate for solution for infusion 50 mg
AKTILIZE
ALTEPLASA

Dosage form:
Lyophilisate + solvent for injection

Remarks: ---

Status: Approved Printed on: 23-Nov-2023 Printed by: Zeller, Angela (LabWare BP Produktion)

Signatures - 13400656-SWFI-01-P-QC-P03

Boehringer Ingelheim

Object: Project 13400656-SWFI-01-P-QC-P03

Productcode: SWFI-01

Product: Solvent for Actilyse 50 mL

Drug product lot: 303027

Description	User	Full Name	Date / Time
Preparation of batch release relevant data	HOFMANSI	Dieme, Simone	29-Aug-2023 06:50:14
Review data completeness of CoA Report	SCHAEHIL	Schäfer, Hildegard	29-Aug-2023 07:52:00
Review of batch release documentation Quality Control	BRUECKJA	Brückmann, Dr., Jannik	29-Aug-2023 09:57:29
Review and approval of Certificate of Analysis (CoA)	KRECH	Krech, Dr., Ingo	02-Nov-2023 09:07:37

Certificate of Analysis

Boehringer Ingelheim
Pharma GmbH & Co. KG
Birkendorfer Straße 65
D-88397 Biberach an der Riß

Productcode: SWFI-01 **Project Suffix:** SWFI-01-P-QC-P03

Product: Solvent for Actilyse 50 mL

Spec.No.: SWFI-01-P-Q-S03 (V3) **Drug product lot:** 303027

Grade: PH_EUR **Description:** Ph. Eur. current Edition

Test-Spec.No.: 79251_p510al0101

Drug Product

Doc-No	*Test*	*Category*	*Acceptance Criteria*	*Result*	*Spec*
018-QA15940	Description	Appearance and description	Clear, colourless liquid	Clear, colourless liquid	pass
018-QA15941	Particulate Contamination - sub-visible particles	Appearance and description	>= 10 µm: <= 6,000 particles /container	201 particle/ container	pass
018-QA15941	Particulate Contamination - sub-visible particles	Appearance and description	>= 25 µm: <= 600 particles/ container	14 particle/ container	pass
018-QA15938	Extractable Volume	General tests	>= 100 and <= 110 % (for the single value)	101 %	pass
018-QA15934	Conductivity	General tests	<= 5 µS/cm	1 µS/cm	pass
018-QA15934	Temperature for Conductivity	General tests	>= 24 and <= 26 °C	25 °C	pass
018-QA15930	Acidity or alkalinity	General tests	Complies with Ph.Eur.	complies with Ph. Eur.	pass
018-QA15936	Oxidisable substances	General tests	Not detectable	not detectable	pass
018-QA15931	Ammonium	General tests	<= 0.2 ppm	<0.2 ppm	pass
018-QA15933	Calcium and Magnesium	General tests	Not detectable	not detectable	pass
018-QA15932	Chloride	General tests	<= 0.5 ppm	<0.5 ppm	pass
018-QA15935	Nitrate	General tests	<= 0.2 ppm	<0.2 ppm	pass
018-QA15929	Sulphate	General tests	Not detectable	not detectable	pass
018-QA15939	Residue on evaporation	General tests	<= 0.003 %	0.001 %	pass
018-GB12147	Sterility	Microbiological tests	Sterile	sterile	pass
018-QA16421	Bacterial endotoxins	Microbiological tests	< 0.25 EU/mL	<0.06 EU/mL	pass

RESULT: Meet Acceptance Criteria: PASS

Manufacturing Date: 30-Jun-2023

The expiration date of the package unit with lyophilisate + solvent for injection is documented on the Certificate of conformance

Status: Approved Printed on: 02-Nov-2023 Printed by: Schäfer, Hildegard (LabWare BP Produktion)

Certificate of Analysis

Boehringer Ingelheim
Pharma GmbH & Co. KG
Birkendorfer Straße 65
D-88397 Biberach an der Riß

Productcode:	SWFI-01	**Project Suffix:**	SWFI-01-P-QC-P03
Product:	Solvent for Actilyse 50 mL		
Spec.No.:	SWFI-01-P-Q-S03 (V3)	**Drug product lot:**	303027

Local trade names:
Actilyse 50 mg
Actilyse 50 mg prasek in vehikel za raztopino za injiciranje ali infundiranje
Actilyse 50 mg por és oldószer oldatos injekcióhoz vagy infúzióhoz
Actilyse 50 mg powder und solvent for solution for injection
Actilyse Pulver und Lösungsmittel zur Herstellung einer Injektion- oder Infusionslösung
Actilyse
ACTILYSE
ACTILYSE 50 MG
Actilyse 50 mg milteliai ir tirpiklis injekciniam ar infuziniam tirpalui
ACTILYSE 50 MG POLVERE E SOLVENTE PER SOLUZIONE INIETTABILE E PER INFUSIONE
Actilyse 50 mg poudre et solvant pour solution injectable et perfusion
Actilyse 50 mg powder and solvent for solution for injection and infusion
Actilyse 50 mg prašak i otapalo za otopinu za injekciju i infuziju
ACTILYSE 50 MG PRAŠEK IN VEHIKEL ZA RAZTOPINO ZA INJICIRANJE ALI INFUNDIRANJE
ACTILYSE 50 MG, pulbere şi solvent pentru soluţie injectabilă/perfuzabilă ACTILYSE, 50 MG
Actilyse 50mg
ACTILYSE 50mg
ACTILYSE INJECTION
ACTILYSE lyophilisate + solvent for injection 50 mg
ACTILYSE lyophilisate for solution for infusion 50mg
ACTILYSE lyophilizate for infusion solution 50 mg/vial with solvent
Actilyse Pó e solvente para solução injectável e perfusão
ACTILYSE POLVO Y DISOLVENTE PARA SOLUCION INYECTABLE Y PARA PERFUSION
ACTILYSE POR ÉS OLDÓSZER OLDATOS INJEKCIÓHOZ VAGY INFÚZIÓHOZ
ACTILYSE poudre et solvant pour solution injectable et perfusion
Actilyse pulver og væske til injeksjons-/infusjonsvæske, oppløsning 50 mg
ACTILYSE PULVER UND LÖSUNGSMITTEL ZUR HERSTELLUNG EINER INJEKTIONS- BZW. INF.LSG
ACTILYSE PULVER UND LÖSUNGSMITTEL ZUR HERSTELLUNG EINER INJEKTIONS- ODER INFUSIO
ACTILYSE VIALS
ACTILYSE® lyophylizate for solution for infusion 50 mg
AKTILIZE
ALTEPLASA

Dosage form:
Lyophilisate + solvent for injection

Remarks: ---

Status: Approved Printed on: 02-Nov-2023 Printed by: Schäfer, Hildegard (LabWare BP Produktion)