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Bezirksregierung Düsseldorf

CERTIFICATE NUMBER: ***DE_NW_03_GMP_2023_0012***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER [1,2]

Part 1

Issued following an inspection in accordance with :
Art. 15 of Directive 2001/20/EC
Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of Germany confirms the following:
The manufacturer: ***Bayer AG***
Site address: ***Kaiser-Wilhelm-Allee 1, Wiesdorf, Leverkusen, North Rhine-Westphalia, 51373***
OMS Organisation Id. / OMS Location Id.: ***ORG-100000011*** / ***LOC-100001505***

Has been inspected under the national inspection programme in connection with manufacturing authorisation no. ***DE_NW_03_MIA_2022_0037*** in accordance with Art. 13 of Directive 2001/20/EC.

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2023-01-18***, it is considered that it complies with:

- The principles and guidelines of Good Manufacturing Practice laid down in Directive (EU) 2017/1572 and Commission Delegated Regulation (EU) 2017/1569 [3]
- The principles of GMP for active substances [3] referred to in Article 47 of Directive 2001/83/EC.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2.The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

[1] *The certificate referred to in paragraph Art. 15 of Directive 2001/20/EC and Art. 111(5) of Directive 2001/83/EC, shall also be required for imports coming from third countries into a Member State.*

[2] *Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.*

[3] *These requirements fulfil the GMP recommendations of WHO.*

Part 2

Human Investigational Medicinal Products Human Medicinal Products

1 MANUFACTURING OPERATIONS	
1.4	**Other products or manufacturing activity**
	1.4.1 Manufacture of 1.4.1.3 Other: 1. Biotechnological API acc. to SECT. 4 (19) AMG: a) Recombinant, human, monoclonal antibodies & fragments of antibodies. Manufacturing in building 151 (Cell Culture Pilot Plant 151), 46 (Cell Culture Pilot Plant) & 226 (Biologics Pilot Plant- protein purification only). b) Conjugation products of human, monoclonal antibodies with pharmacologically effective, low-molecular-weight substances (e.g. with a linker & toxophore). Conjugation in building 151 (Cell Culture Pilot Plant), 226 (Biologics Pilot Plant) & 132. c) Gene therapy medicinal products as ATMP The manufacturing operation includes only the batch release of the finished product. 2. Chemical API: a) including micronization (building 132) b) including acc. to SECT. 13 (1) No. 3 AMG, where during synthesis in the Bergkamen site also microorganisms were used, finalized in Elberfeld Site(en)
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.2 Microbiological: non-sterility* *1.6.3 Chemical/Physical* *1.6.4 Biological*

2 IMPORTATION OF MEDICINAL PRODUCTS	
2.2	**Batch certification of imported medicinal products**
	2.2.1 Sterile products 2.2.1.1 Aseptically prepared
	2.2.3 Biological medicinal products 2.2.3.4 Gene therapy products

2.3	Other importation activities
	2.3.1 Site of physical importation
	2.3.4 Other: 2.3.3 Biological Active Substance Subject to permission in accordance with sect 13 (1) AMG: (1) anti-ILDR2 (BAY 1905254) (2) FXIa Reversal Agent (BAY 2521665) (3) COM902 (Anti-TIGIT Antibody) (4) Anti-a2AP (Bay 3018250) (5) IgG-ANP (Bay 2701250) (6) Anti-CCR8 (Bay 3375968) (7) anti-Sema 3A (Bay 3401016). Delivering companies: No. 1-7: Bayer Healthcare LLC, 800 Dwight Way, Berkeley, CA 94710 USA (until 18/03/2025).(en)

Clarifying remarks (for public users)

Manufacturing of active substances: The certificate is valid for following active substances: a) biological active substances Acarbose Monoclonal antibodies and their conjugates, fragments of antibodies; b) chemical active substances Ciprofloxacin Ciprofloxacin HCl Ciprofloxacin hydrated Copanlisib Dihydrochlorid DTPA (Diethylentriamine pentaacetic acid) Finerenone Fludarabine phosphate Iloprost Miglitol Molidustat Natrium Moxifloxacin HCl Nifedipine Nifurtimox Nimodipine Nisoldipine Nitrendipine Ramatroban Regorafenib Riociguat Rivaroxaban Sorafenib Tosylate Vardenafil Vericiguat The certificate include also quality control of active ingredients, human investigational medicinal products and following finished medicinal products: - Kallikrein (Padutin) - Aflibercept (Eylea) - Recombinant Factor VIII, rF VIII-PF/Kovaltry - Bifonazole - Damotocog alfa pegol (Recombinant Factor VIII, rF VIII-N)/Jivi - Larotrectinib sulphate (only analytical QC-testing) Quality Cont (text missing)

2023-02-09

Name and signature of the authorised person of the Competent Authority of

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Bezirksregierung Düsseldorf
Tel:***Confidential***
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