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Chile

AstraZeneca

AstraZeneca UK Limited
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Cambridge Biomedical Campus
Cambridge, CB2 0AA
United Kingdom
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TO WHOM IT MAY CONCERN

Good Manufacturing Practice Certificate

It is hereby confirmed that the attached Certificate is a true copy of the original document.

Signed: ..... Dated 11/2/19.

Vicky Beattie
Regulatory Project Assistant
Regulatory Project Management Group
AstraZeneca UK Limited

Signature Attested by Phillip Jones
Solicitor and Notary
Windsor House, Victoria Street,
Windsor, Berks, SL4 IEN, England,
Tel: 01753 851591

12/2/19

283/19

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: Pays / Pais:	United Kingdom of Great Britain and Northern Ireland
This public document Le présent acte public / El presente documento público	
2. Has been signed by a été signé par ha sido firmado por	Phillip H Jones
3. Acting in the capacity of agissant en qualité de quien actúa en calidad de	Notary Public
4. Bears the seal / stamp of est revêtu du sceau / timbre de y está revestido del sello / timbre de	The Said Notary Public

Certified

Attesté / Certificado

5. at á / en	London	**6. the** le / el día	13 February 2019
7. by par / por	Her Majesty's Principal Secretary of State for Foreign and Commonwealth Affairs		
8. Number sous no / bajo el numero	APO-1309531		
9. Seal / stamp Sceau / timbre Sello / timbre	FOREIGN AND COMMONWEALTH OFFICE LONDON	**10. Signature** Signature Firma	L. Smethurst

This Apostille is not to be used in the UK and only confirms the authenticity of the signature, seal or stamp on the attached UK public document. It does not confirm the authenticity of the underlying document. Apostilles attached to documents that have been photocopied and certified in the UK confirm the signature of the UK official who conducted the certification only. It does not authenticate either the signature on the original document or the contents of the original document in any way.

If this document is to be used in a country not party to the Hague Convention of the 5th of October 1961, it should be presented to the consular section of the mission representing that country

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Agence nationale de sécurité du médicament et des produits de santé

French National Agency for Medicines and Health Products Safety

CERTIFICATE NUMBER: *17MPP017HFR01*

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

Part 1

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

The competent authority of France confirms the following:
The manufacturer: ***MINAKEM DUNKERQUE PRODUCTION***
Site address: ***224 avenue de la Dordogne, Zone d'entreprises du Nord Gracht, DUNKERQUE, 59640, France***

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 ***2017-03-09*** , it is considered that it complies with :

- 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 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/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.*

Vu pour la certification conforme à l'original

143/147 boulevard Anatole France - F-93285 Saint-Denis Cedex - Tél.: +33(0)1 55 87 30 00 - www.ansm.sante.fr

Part 2

Manufacture of active substance. Names of substances subject to inspection :
ESOMEPRAZOLE MAGNESIUM TRIHYDRATE(en) / ESOMEPRAZOLE MAGNESIQUE TRIHYDRATE(fr)
ESOMEPRAZOLE SODIUM(en) / ESOMEPRAZOL SODOWY(pl) / ÉSOMÉPRAZOLE SODIQUE(fr)
ESOMEPRAZOLE MAGNESIUM DIHYDRATE(en) / ESOMEPRAZOLE MAGNESIQUE DIHYDRATE(fr)
OMEPRAZOLE(en) / OMÉPRAZOLE(fr)
OMEPRAZOLE MAGNESIUM(en)
OMEPRAZOLE SODIUM(en) / OMÉPRAZOLE SODIQUE(fr)
BUDESONID(de) / BUDESONIDUM(cs) / BUDESONIDE(en) / BUDEZONIDU(pl) / BUDÉSONIDE(fr)
PRAZIQUANTEL(en) / PRAZIQUANTEL(fr)
POSACONAZOLE(en) / POSACONAZOLE(fr)
VERUBECESTAT(en)
LACOSAMIDE(fr) / LACOSAMIDE(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : ESOMEPRAZOLE MAGNESIUM TRIHYDRATE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : Micronisation 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : ESOMEPRAZOLE SODIUM

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**

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	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : ESOMEPRAZOLE MAGNESIUM DIHYDRATE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance : OMEPRAZOLE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : Micronisation 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : OMEPRAZOLE MAGNESIUM

3.1	**Manufacture of Active Substance by Chemical Synthesis**

	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : OMEPRAZOLE SODIUM

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : BUDESONIDE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : -
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : Micronisation 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)

3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : PRAZIQUANTEL

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance : POSACONAZOLE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance : VERUBECESTAT

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance : LACOSAMIDE

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3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Clarifying remarks (for public users)

Posaconazole manufacturing limited to the PAZ-D intermediate //// Verubecestat manufacturing limited to the MK-8931-J intermediate //// Lacosamide manufacturing limited to the SPM20200 intermediate

2017-05-03

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

Le chef du pôle inspection des matières premières
Direction de l'inspection

Guillaume RENAUD

Mr. Guillaume Renaud
French National Agency for Medicines and Health Products Safety
Tel: ***+33 1 55873911***
Fax: ***+33 1 55873912***

Vu pour la certification conforme à l'original

143/147 boulevard Anatole France F-93285 Saint Denis Cedex - Tél.: +33(0)1 55 87 30 00 -

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AstraZeneca

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Cambridge Biomedical Campus
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United Kingdom
T: +44 (0) 20 3749 5000

astrazeneca.com

TO WHOM IT MAY CONCERN

Good Manufacturing Practice Certificate

It is hereby confirmed that the attached Certificate is a true copy of the original document.

Signature Attested by Phillip Jones
Solicitor and Notary
Windsor House, Victoria Street,
Windsor, Berks, SL4 IEN, England,
Tel: 01753 851591

Signed: ..... Dated 31/1/19

Vicky Beattie
Regulatory Project Assistant
Regulatory Project Management Group
AstraZeneca UK Limited

1/2/19

185/19

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1.	**Country:** Pays / País:	United Kingdom of Great Britain and Northern Ireland
	This public document Le présent acte public / El presente documento público	
2.	**Has been signed by** a été signé par ha sido firmado por	Phillip H Jones
3.	**Acting in the capacity of** agissant en qualité de quien actúa en calidad de	Notary Public
4.	**Bears the seal / stamp of** est revêtu du sceau / timbre de y está revestido del sello / timbre de	The Said Notary Public

Certified

Attesté / Certificado

5.	**at** á / en: London	6.	**the** le / el día: 07 February 2019
7.	**by** par / por	Her Majesty's Principal Secretary of State for Foreign and Commonwealth Affairs	
8.	**Number** sous no / bajo el numero	APO-1297153	
9.	**Seal / stamp** Sceau / timbre Sello / timbre	FOREIGN AND COMMONWEALTH OFFICE LONDON	
10.	**Signature** Signature Firma	D. Brigden	

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French National Agency for Medicines and Health Products Safety

CERTIFICATE NUMBER: ***2019/HPF/FR/035***

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

The competent authority of France confirms the following:
The manufacturer: ***ASTRAZENECA DUNKERQUE PRODUCTION***
Site address: ***224 avenue de la Dordogne, DUNKERQUE, 59640, France***

Has been inspected under the national inspection programme in connection with manufacturing authorisation no. ***M 19/028*** in accordance with Art. 13 of Directive 2001/20/EC transposed in the following national legislation:
Art. L.5124-3 of Public Health Code

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-12-21*** , it is considered that it complies with :

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC [3]

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 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/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	
1 MANUFACTURING OPERATIONS	
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.9 Pressurised preparations
	1.2.2 Batch certification
1.5	**Packaging**
	1.5.1 Primary Packing 1.5.1.9 Pressurised preparations
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.2 Microbiological: non-sterility *1.6.3 Chemical/Physical*

Clarifying remarks (for public users)

This site is not authorised for blinding operations. Signatory: Mrs Dominique Debourges, deputy head of the pharmaceutical product inspection and counterfeiting fight department --- The ANSM does not issue paper copies of good manufacturing practice certificates.

2019-01-29

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

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French National Agency for Medicines and Health Products Safety
Tel: ***Confidential***
Fax: ***Confidential***