



CHIEF PHARMACEUTICAL INSPECTOR

2024 -08- 0 1

ISF.405.89.2024.IP.1
WTC/0167_02_02/158

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

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

Chief Pharmaceutical Inspector

/the Competent Authority of Poland/

confirms the following:

the manufacturer

Nobilus Ent Tomasz Koźluk
ul. Swarzewska 45, 01-821 Warszawa, POLAND

site address

Nobilus Ent Tomasz Koźluk
ul. Metalowa 6a, 99-300 Kutno, POLAND

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation: Pharmaceutical Law of 6th of September 2001 (Journal of Laws from 2024, item 686) in connection with the entry in the Register no **50/WTC0167/API/15**.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on **09/05/2024**, it is considered that it complies with the Good Manufacturing Practice requirements laid down in Directive (EU) 2017/1572 and the principles of GMP for active substances 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.

Updates to restrictions or clarifying remarks can be identified through the EudraGMDP website (<http://eudragmdp.ema.europa.eu/>)

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.



Chief Pharmaceutical Inspector


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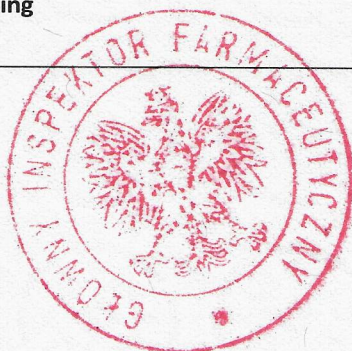
Part 2

3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES**Active Substance(s):**

- Metildigoxin, β -Methyldigoxin

3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Purification steps (column chromatography) 3.1.4 Other (crystallization)
3.5	General Finishing Steps
	3.5.1 Physical processing steps (drying, milling) 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) 3.5.4 Other (blending)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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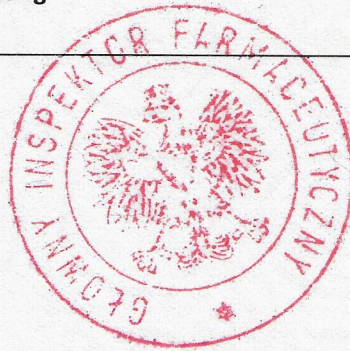
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Part 2

<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> Aluminium chloride 25% sol. 	
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3.1	<p>Manufacture of Active Substance by Chemical Synthesis</p>
	<p>3.1.2 Manufacture of crude active substance</p> <p>3.1.3 Purification steps (purification of the solution on the activated charcoal, filtration)</p>
3.5	<p>General Finishing Steps</p>
	<p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p>
3.6	<p>Quality Control Testing</p>
	<p>3.6.1 Physical / Chemical testing</p>

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Part 2

<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> • Deslanoside
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3.1	Manufacture of Active Substance by Chemical Synthesis
	<p>3.1.2 Manufacture of crude active substance (hydrolysis of Lanatoside C)</p> <p>3.1.3 Purification steps (crystallisation)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying, milling)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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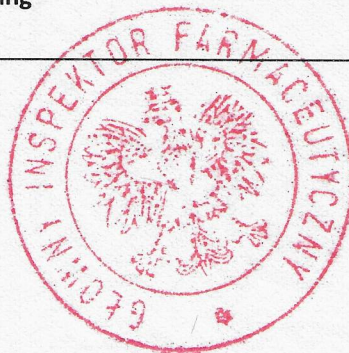


Part 2

<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> • Digoxin
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3.2	Extraction of Active Substance from Natural Sources
	<p>3.2.1 Extraction of substance from plant source</p> <p>3.2.5 Modification of extracted substance</p> <p>3.2.6 Purification of extracted substance</p> <p>3.2.7 Other (purification of the crude substance by separation on a sorbent bed, ultrafiltration and crystallisation)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying, micronization)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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Part 2

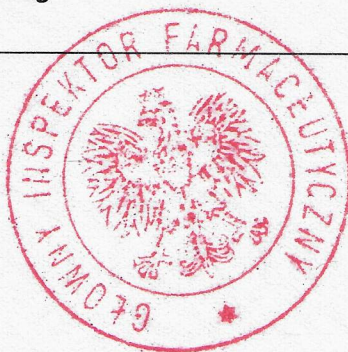
3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES

Active Substance(s):

- α -Escin

3.2	Extraction of Active Substance from Natural Sources
	<p>3.2.1 Extraction of substance from plant source</p> <p>3.2.6 Purification of extracted substance from plant source (crystallisation)</p> <p>3.2.7 Other (inversion of β- Escin to α-Escin, demineralization)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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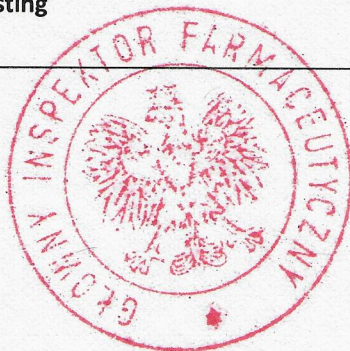
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<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> • β-Escin Amorphous

3.2	<p>Extraction of Active Substance from Natural Sources</p> <p>3.2.1 Extraction of substance from plant source</p> <p>3.2.6 Purification of extracted substance from plant source (crystallisation)</p> <p>3.2.7 Other (dissolving in methanol, filtration)</p>
3.5	<p>General Finishing Steps</p> <p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	<p>Quality Control Testing</p> <p>3.6.1 Physical / Chemical testing</p>

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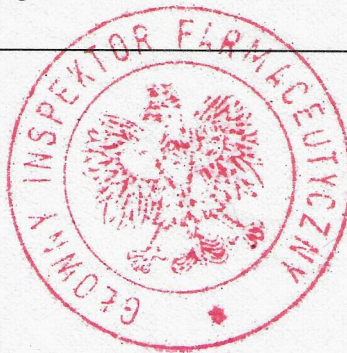
3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES

Active Substance(s):

- **β-Escin Crystalline**

3.2	Extraction of Active Substance from Natural Sources
	<p>3.2.1 Extraction of substance from plant source</p> <p>3.2.6 Purification of extracted substance from plant source (crystallisation)</p> <p>3.2.7 Other (purification of the solution on activated charcoal)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> • Esculin
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3.2	Extraction of Active Substance from Natural Sources
	<p>3.2.1 Extraction of substance from plant source</p> <p>3.2.6 Purification of the extract from plant source (including crystallisation)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying, milling)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES

Active Substance(s):

- Flutamide

3.1	Manufacture of Active Substance by Chemical Synthesis
	<p>3.1.2 Manufacture of crude active substance</p> <p>3.1.3 Purification steps (crystallisation)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying, milling)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES

Active Substance(s):

- Timonacic

3.1	Manufacture of Active Substance by Chemical Synthesis
	<p>3.1.2 Manufacture of crude active substance</p> <p>3.1.3 Salt formation / Purification steps (salt formation, purifying)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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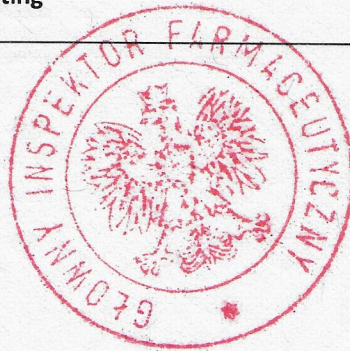
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Part 2

<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> Mesna
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3.1	Manufacture of Active Substance by Chemical Synthesis
	<p>3.1.2 Manufacture of crude active substance</p> <p>3.1.3 Purification steps (salt formation, crude Mesnum synthesis, purifying)</p>
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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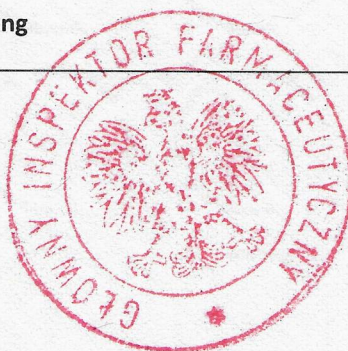
Part 2

3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES**Active Substance(s):**

- Aescin Sodium Salt

3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.4 Other (dissolving in methanol, filtration)
3.5	General Finishing Steps
	<p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

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<p>3 MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES</p> <p>Active Substance(s):</p> <ul style="list-style-type: none"> • Escin Sodium Polysulphate 	
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3.1	<p>Manufacture of Active Substance by Chemical Synthesis</p>
	<p>3.1.2 Manufacture of crude active substance</p> <p>3.1.3 Purification steps (purification, ultrafiltration)</p>
3.5	<p>General Finishing Steps</p>
	<p>3.5.1 Physical processing steps (drying)</p> <p>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)</p> <p>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)</p> <p>3.5.4 Other (blending)</p>
3.6	<p>Quality Control Testing</p>
	<p>3.6.1 Physical / Chemical testing</p>

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