# Eurartesim

Procedural steps taken and scientific information after the authorisation

| Application number | Scope | Opinion/ Notification[1] issued on | Commission Decision Issued[2] / amended on | Product Information affected[3] | Summary |
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| IB/0042 | C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation | 22/11/2024 | | SmPC and PL | |
| IA/0043 | B.II.b.4.a - Change in the batch size (including batch | 24/10/2024 | n/a | | |

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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| | size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size | | | | |
| PSUSA/1069/ 202210 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 22/06/2023 | 25/08/2023 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1069/202210. |
| IB/0038/G | This was an application for a group of variations.<br><br>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes<br>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes | 22/07/2021 | 08/07/2022 | SmPC, Labelling and PL | Addition of the new pack-size of 270 film-coated 320mg/40mg (EU/1/11/716/006) and 300 film-coated 320mg/40mg (EU/1/11/716/007). |
| PSUSA/1069/ 201910 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 25/06/2020 | 28/08/2020 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1069/201910. |
| II/0036 | Update of sections 4.2 and 5.1 of the SmpC with reference to the posology in patients weighing ≥ 100 kg. Update of sections 4.4, and 4.6 of the SmPC with recommendations during pregnancy. Annex II has been updated to reflect the closure of the Eurartesim Pregnancy Registry (as endorsed by CHMP in procedure II/32).<br>The package leaflet is amended accordingly and<br>The list of local representatives has also been updated in the Package leaflet. | 12/12/2019 | 20/01/2020 | SmPC, Annex II and PL | Data from the European Safety Registry showed that 25 patients weighing ≥ 100 kg (range 100 -121 kg) were treated with 4 tablets 320/40 mg PQP/artenimol for 3 days. Twenty-two of these patients were shown to be parasitic free at the last microscopic analysis of the blood sample; three patients did not complete parasitological blood analysis. All patients were clinically cured.<br>Recommendation There are no data on which to base a dose recommendation in patients weighing >100 kg is now introduced in the product information.<br>Based on animal data, Eurartesim is suspected to cause |

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| | C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | | | | serious birth defects when administered during the first trimester of pregnancy (see sections 4.4 and 5.3). Reproductive studies with artemisinin derivatives have demonstrated teratogenic potential with an increased risk during early gestation. Piperaquine was not teratogenic in the rat or rabbit. Therefore, Eurartesim should not be used during the 1st trimester of pregnancy in situations where other suitable and effective anti-malarials are available. A large amount of data (more than 3000 exposed outcomes) from the use of artenimol/piperaquine during the 2nd and 3rd trimester indicate no fetotoxicity. In perinatal and postnatal studies in rats, piperaquine was associated with delivery complications. However, there was no delay in neonatal development following exposure in utero or via milk. Consequently, if Eurartesim is more suitable for a pregnant woman than other artemisinin-based combination therapies with a higher range of experience (or sulfadoxine–pyrimethamine), Eurartesim may be used in the 2nd and 3rd trimester. |
| SW/0034 | Post Authorisation Safety Study results - EMEA/H/C/PSR/S/0018 | 31/01/2019 | 20/06/2019 | Annex II | Following submission and assessment of the final study report, no new safety signals were identified and there are no outstanding issues. Therefore, the PRAC considers that the obligation is fulfilled. In view of available data regarding the PASS final study report, the PRAC considered that changes to the conditions of the marketing authorisation were warranted. |
| N/0035 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 06/03/2019 | n/a | | |
| PSUSA/1069/ 201804 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 13/12/2018 | 20/02/2019 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for |

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| | | | | | PSUSA/1069/201804. |
| II/0032 | C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required | 14/02/2019 | n/a | | |
| IAIN/0031 | A.1 - Administrative change - Change in the name and/or address of the MAH | 26/07/2018 | 20/02/2019 | SmPC, Labelling and PL | |
| N/0030 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 19/06/2018 | 20/02/2019 | PL | |
| PSUSA/1069/201704 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 30/11/2017 | n/a | | PRAC Recommendation - maintenance |
| T/0029 | Transfer of Marketing Authorisation | 29/08/2017 | 14/09/2017 | SmPC, Labelling and PL | |
| IAIN/0027 | A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release | 12/06/2017 | 14/09/2017 | Annex II and PL | |
| IA/0026 | B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 15/05/2017 | n/a | | |
| N/0025 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 04/04/2017 | 14/09/2017 | SmPC, Labelling and | |

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| PSUSA/1069/ 201604 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 01/12/2016 | n/a | | PRAC Recommendation - maintenance |
| R/0023 | Renewal of the marketing authorisation. | 21/07/2016 | 09/09/2016 | SmPC, Annex II, Labelling and PL | Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Eurartesim in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.<br>In order to address the issue of non-adherence to food restrictions, the outer carton has been updated to include a warning "take at least 3 hours before or after food". In addition, the SmPC/PL existing text on the recommendation regarding the food restrictions during the treatment period was emboldened with the addition of a frame emphasising the message. |
| II/0020 | Update to the RMP (version 15) with regards the delay to: start of resistance monitoring, collection of off-label use data, submission of reports of additional pharmacovigilance activities.<br>The MAH also took this opportunity to reformat the RMP to the new template.<br><br>C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required | 01/04/2016 | n/a | | |

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| IAIN/0022/G | This was an application for a group of variations.<br><br>A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient<br>A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release | 15/02/2016 | 21/06/2016 | Annex II and PL | |
| PSUSA/1069/ 201504 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 06/11/2015 | n/a | | PRAC Recommendation - maintenance |
| IA/0021 | A.7 - Administrative change - Deletion of manufacturing sites | 28/10/2015 | n/a | | |
| IB/0018/G | This was an application for a group of variations.<br><br>C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation<br>C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation<br>C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation<br>C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 27/07/2015 | n/a | | |

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| II/0015 | C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 25/06/2015 | 21/06/2016 | SmPC | |
| PSUSA/1069/ 201410 | Periodic Safety Update EU Single assessment - artenimol / piperaquine tetraphosphate | 07/05/2015 | n/a | | PRAC Recommendation - maintenance |
| IB/0017 | B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data | 11/03/2015 | n/a | | |
| PSUV/0014 | Periodic Safety Update | 04/12/2014 | n/a | | PRAC Recommendation - maintenance |
| N/0013 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 28/07/2014 | 10/03/2015 | PL | |
| PSUV/0011 | Periodic Safety Update | 13/06/2014 | n/a | | PRAC Recommendation - maintenance |
| IB/0010 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 28/03/2014 | 10/03/2015 | SmPC, Annex II, Labelling and PL | |
| IAIN/0012 | C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location | 14/03/2014 | n/a | | |
| II/0009 | To add a new manufacturer for piperaquine phosphate.<br><br>B.I.a.1.b - Change in the manufacturer of AS or of a | 20/02/2014 | n/a | | |

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| | starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF | | | | |
| II/0008 | To add a new manufacturer for dihydroartemisinin.<br><br>B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF | 20/02/2014 | n/a | | |
| II/0007/G | This was an application for a group of variations.<br><br>To add a new supplier of a starting material.<br>To add limits for residual solvents in the specification of a starting material.<br>To change the content of an impurity in the specification of a starting material.<br><br>B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions<br>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method<br>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its | 18/12/2013 | n/a | | |

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| | corresponding test method<br>B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP | | | | |
| IB/0006 | B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions | 13/08/2013 | n/a | | |
| IA/0005 | B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold | 01/08/2013 | n/a | | |
| IA/0003/G | This was an application for a group of variations.<br><br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS<br>B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the currently approved batch size<br>B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits | 08/07/2013 | n/a | | |
| IA/0004/G | This was an application for a group of variations. | 04/07/2013 | n/a | | |

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| | B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold<br>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure | | | | |
| II/0001/G | This was an application for a group of variations.<br><br>Change to the specifications of the finished product.<br>Change to the shelf life of the finished product.<br><br>B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range<br>B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) | 16/02/2012 | 26/03/2012 | SmPC | |
| N/0002 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 12/12/2011 | 26/03/2012 | PL | |