# Tasmar

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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| PSUSA/2985/ 202403 | Periodic Safety Update EU Single assessment - tolcapone | 03/10/2024 | n/a | | PRAC Recommendation - maintenance |
| IB/0068 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 23/07/2024 | | Annex II and PL | |

[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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| T/0066 | Transfer of Marketing Authorisation | 28/10/2022 | 21/11/2022 | SmPC, Labelling and PL | |
| PSUSA/2985/ 202103 | Periodic Safety Update EU Single assessment - tolcapone | 28/10/2021 | n/a | | PRAC Recommendation - maintenance |
| IB/0064 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 24/09/2020 | 19/10/2021 | SmPC, Annex II, Labelling and PL | |
| IA/0063 | 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 | 25/05/2020 | n/a | | |
| IB/0062/G | This was an application for a group of variations.<br><br>B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate<br>B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition<br>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 | 17/05/2019 | n/a | | |
| II/0061 | Submission of an updated RMP version 7.0 in order to: | 14/02/2019 | n/a | | |

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| | - reflect currently available data from post-marketing experience and patient exposure data;<br>- align the RMP with the new GVP RMP template rev.2;<br>- remove the important identified risk 'dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)' and the potential risks 'drug interactions with significant clinical consequence including sudden sleep onset', 'melanoma' and 'intense urges';<br>- revise the targeted follow-up questionnaire for hepatic events and the Patient Diary.<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 | | | | |
| PSUSA/2985/ 201803 | Periodic Safety Update EU Single assessment - tolcapone | 04/10/2018 | n/a | | PRAC Recommendation - maintenance |
| IB/0060 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 08/08/2018 | 26/08/2019 | Labelling and PL | |
| IA/0058 | B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold | 15/06/2017 | n/a | | |
| IA/0057 | A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder | 16/05/2017 | n/a | | |

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| | or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient | | | | |
| IA/0056 | B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State | 22/09/2016 | n/a | | |
| IA/0055 | B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State | 12/08/2016 | n/a | | |
| N/0054 | Update of the package leaflet with revised contact details of the local representatives for Spain and France.<br><br>Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 06/07/2016 | 22/08/2016 | PL | |
| IA/0053 | B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s) | 06/11/2015 | 22/08/2016 | SmPC, Labelling and PL | |
| PSUSA/2985/ 201503 | Periodic Safety Update EU Single assessment - tolcapone | 08/10/2015 | n/a | | PRAC Recommendation - maintenance |
| IAIN/0052 | B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. | 14/08/2015 | 22/08/2016 | SmPC, Labelling and | |

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| | tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes | | | PL | |
| IA/0050 | 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 | 25/06/2015 | n/a | | |
| R/0047 | Renewal of the marketing authorisation. | 22/05/2014 | 18/07/2014 | SmPC, Annex II, Labelling and PL | Tolcapone is indicated in combination with levodopa/benserazide or levodopa/carbidopa for use in patients with levodopa-responsive idiopathic Parkinson's disease and motor fluctuations, who fail to respond to or are intolerant of other catechol-O-methyltransferase (COMT) inhibitors. Based on a safety data collected since the time of last renewal and the known efficacy of Tasmar the CHMP considered that the benefits of the product continue to outweigh the risks and therefore recommended the renewal of the marketing authorisation with unlimited validity. |
| N/0048 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 16/02/2014 | 05/03/2014 | PL | |
| IB/0046/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS<br>A.7 - Administrative change - Deletion of manufacturing sites | 27/08/2013 | n/a | | |

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| | 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<br>A.7 - Administrative change - Deletion of manufacturing sites<br>A.7 - Administrative change - Deletion of manufacturing sites | | | | |
| IG/0277 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 26/03/2013 | n/a | | |
| IB/0044 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 06/03/2013 | 05/03/2014 | SmPC and Annex II | Annex I (SmPC) and Annex II of the product information was brought in line with the latest QRD template. Annex II has been updated in line with revision 3 of QRD template version 8. |
| IB/0043 | C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH | 17/10/2012 | 29/10/2012 | SmPC and PL | Following CHMP conclusions from 19 July 2012 the product information (PI) has been updated in line with the recommendations in relation to impulse control disorders for products containing levodopa, dopamine agonists and/or COMT inhibitor and the risk of impulse control disorders.<br>Additionally, the address of the local representative in Greece has been updated. |
| IB/0042 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 06/02/2012 | 21/03/2012 | SmPC, Annex II, Labelling and PL | The scope of this variation is to bring the Annex II and Annex III of the current Product Information in line with the latest version of the QRD template (August 2011). Minor editorial changes have been introduced in Annex I. In addition, the Annex IIIB has been amended following the results of a User Testing, and the local representatives |

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| | | | | | section has been updated. |
| IB/0041 | 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 | 17/08/2011 | 17/08/2011 | SmPC, Labelling and PL | |
| IB/0040 | B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation | 28/04/2011 | n/a | | |
| R/0039 | Renewal of the marketing authorisation. | 23/07/2009 | 02/10/2009 | SmPC, Annex II, Labelling and PL | Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers that the benefit/risk profile of Tasmar continues to be favourable., but considers that its safety profile is to be closely monitored for the following reasons:<br>- Since the lifting of the suspension there has been a relatively limited exposure in Europe. The CHMP also noted that this is effectively the first renewal since the lifting of the suspension.<br>- Specific measures are still in place in relation to be monitoring of particular safety issues including hepatotoxicity and NMS, also remaining submision of yearly PSURs<br>Therefore, the CHMP concluded that the MAH should submit one additional renewal application in 5 years time.<br>Intense urges has been added to the section 4.4 of the SPC on the basis of the data submitted with the renewal dossier. |

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| T/0038 | Transfer of Marketing Authorisation | 22/01/2009 | 13/02/2009 | SmPC, Labelling and PL | |
| N/0037 | Update of the list of local representatives in section 6 of the Package Leaflet.<br><br>Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 10/04/2008 | n/a | PL | |
| IA/0036 | IA_08_b_02_Change in BR/QC testing - repl./add. manuf. responsible for BR - incl. BC/testing | 06/03/2008 | n/a | Annex II and PL | |
| IB/0032 | IB_07_c_Replacement/add. of manufacturing site: All other manufacturing operations ex. batch release | 04/03/2008 | n/a | | |
| IA/0035 | IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms | 27/02/2008 | n/a | | |
| IA/0034 | IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site | 27/02/2008 | n/a | | |
| IA/0029 | IA_05_Change in the name and/or address of a manufacturer of the finished product | 12/02/2008 | n/a | | |
| N/0028 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 14/03/2007 | n/a | PL | |
| II/0027 | This application refers to an update of Sections 4.4 (Special warnings and Special Precautions for Use) of the Summary of Product Characteristics (SPC) further to CHMP recommendation following | 28/06/2006 | 04/08/2006 | SmPC | Further to the assessment of the12th PSUR for Tasmar, the CHMP requested that the Marketing Authorisation Holder (MAH) updated the Summary of Product Characteristics (SPC) to refer to the possibility of late onset hepatitis. The |

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| | assessment of the 12th PSUR. In addition, section 4.8 of the SPC has been revised in accordance to the SPC guideline.<br><br>Update of Summary of Product Characteristics | | | | CHMP request follows the publication of a case of late onset hepatitis (approximately 18 months after the start of tolcapone treatment).<br><br>The MAH therefore applied for an update of Section 4.4 (Special warnings and Special Precautions for Use) to reflect the CHMP recommendation. Additionally, section 4.8 (Undesirable Effects) has also been updated to bring it in line with the latest SPC guideline on presentation of the information on adverse drug reactions. |
| IB/0026 | IB_42_a_01_Change in shelf-life of finished product - as packaged for sale | 22/12/2005 | n/a | SmPC | |
| IA/0025 | IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing | 20/12/2005 | n/a | Annex II and PL | |
| IA/0024 | IA_05_Change in the name and/or address of a manufacturer of the finished product | 20/12/2005 | n/a | | |
| IA/0023 | IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size | 19/07/2005 | 19/07/2005 | SmPC, Labelling and PL | |
| II/0021 | Change(s) to the manufacturing process for the active substance<br>Change(s) to the test method(s) and/or specifications for the active substance | 16/03/2005 | 23/03/2005 | | |
| N/0022 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 14/03/2005 | n/a | PL | |

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| IB/0017 | IB_33_Minor change in the manufacture of the finished product | 28/02/2005 | n/a | | |
| IB/0019 | IB_10_Minor change in the manufacturing process of the active substance | 08/02/2005 | n/a | | |
| IB/0018 | IB_10_Minor change in the manufacturing process of the active substance | 08/02/2005 | n/a | | |
| IA/0020 | IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site<br>IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms | 13/01/2005 | n/a | | |
| IA/0016 | IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.) | 13/01/2005 | n/a | | |
| T/0014 | Transfer of Marketing Authorisation | 25/11/2004 | 22/12/2004 | SmPC, Annex II, Labelling and PL | |
| IA/0015 | IA_09_Deletion of manufacturing site | 03/11/2004 | n/a | | |
| IA/0013 | IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing | 15/09/2004 | n/a | Annex II and PL | |
| IA/0012 | IA_39_Change/addition of imprints, bossing or other markings | 15/09/2004 | n/a | SmPC and PL | |
| Z/0011 | On 16 February 2004, the Marketing Authorisation Holder submitted documentation to support the review of the suspension of the Tasmar Marketing | 22/04/2004 | 31/08/2004 | SmPC, Annex II, Labelling and PL | |

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| | Authorisation, addressing the issues raised by CPMP during its October 2003 plenary meeting. This submission complements the supplementary information provided by the MAH on 15 July 2003, as part of the review of the suspension of the Marketing Authorisation. | | | | |
| Z/0010 | | 22/10/2003 | 14/01/2004 | | |
| Z/0009 | | 19/09/2002 | 07/01/2003 | | |
| Z/0008 | | 19/09/2001 | 17/12/2001 | | |
| Z/0007 | | 19/10/2000 | 29/01/2001 | | |
| Z/0006 | | 21/10/1999 | 20/01/2000 | | |
| Z/0005 | | 12/11/1998 | 11/12/1998 | | |
| II/0004 | New safety warning | 21/10/1998 | n/a | SmPC and PL | |
| I/0003 | 01_Change following modification(s) of the manufacturing authorisation(s) | 24/04/1998 | n/a | Annex II and PL | |
| I/0001 | 12_Minor change of manufacturing process of the active substance | 25/11/1997 | n/a | | |
| I/0002 | 20_Extension of shelf-life as foreseen at time of authorisation | 28/10/1997 | n/a | SmPC | |