# Fampyra

## 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 |
|---|---|---|---|---|---|
| R/0050 | Renewal of the marketing authorisation. | 24/02/2022 | 25/04/2022 | 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 Fampyra in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. |

[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).

**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
**Send us a question** Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

| | | | | | |
|---|---|---|---|---|---|
| II/0049 | Following a PSUR 10 assessment, update to the section 4.8 of SmPC to include new symptoms of trigeminal neuralgia. The package leaflet to be updated accordingly. The Marketing authorisation holder (MAH) introduced further editorial updates including bringing SmPC template to version 10.2 and updating contact details of the local representatives.<br><br>C.I.3.b - 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 - Change(s) with new additional data submitted by the MAH | 28/10/2021 | 25/04/2022 | SmPC and PL | Section 4.8 of the SmPC updated to include de novo symptoms of trigeminal neuralgia. For more information, please refer to the Summary of Product Characteristics. |
| PSUSA/1352/ 202001 | Periodic Safety Update EU Single assessment - fampridine | 03/09/2020 | n/a | | PRAC Recommendation - maintenance |
| N/0048 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 09/07/2020 | 20/11/2020 | PL | |
| II/0046 | Update of sections 4.2, 4.3, 4.4, 4.8, 4.9 and 5.2 of the SmPC in order to remove the contraindication for patients with mild renal impairment, add a warning for patients with mild renal impairment, update the frequency of seizure to uncommon, add vertigo with frequency common, add dizziness in section 4.9 to reflect safety information based on from final results of study 218MS401 (LIBERATE) listed as category 3 study in the RMP; Study 218MS401 was a Phase IV prospective, noninterventional, multicentre, | 09/07/2020 | 20/11/2020 | SmPC and PL | The SmPC has been updated as follows:<br>Section 4.3: removal of contraindication mild renal impairment.<br>Section 4.4: addition of warning that Fampyra should be used with caution in patients with mild renal impairment.<br>Section 4.8: addition of vertigo, frequency common based on LIBERATE study results.<br>Section 4.9: addition of dizziness as overdose symptom based on LIBERATE study results.<br>Section 5.2: deletion of statement that clinical studies of |

| | | | | | |
|---|---|---|---|---|---|
| | observational study in MS patients who began Fampyra treatment in the postmarketing setting. The Package Leaflet is updated accordingly. An updated RMP version 13.1 has also been submitted to align with the RMP Rev. 2 template and to remove all safety concerns; some continue to be monitored in PSUSA safety specifications.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | | | | Fampyra did not include sufficient number of patients older than 65 years old.<br>The Package Leaflet is updated accordingly.<br>The RMP was updated to remove of all safety concerns, some continue to be monitored in PSUSA safety specifications. |
| IB/0045 | B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms | 03/12/2019 | n/a | | |
| IA/0044 | A.7 - Administrative change - Deletion of manufacturing sites | 20/11/2019 | 20/11/2020 | Annex II and PL | |
| T/0043 | Transfer of Marketing Authorisation | 03/07/2018 | 02/08/2018 | SmPC, Labelling and PL | |
| 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 | 25/06/2018 | 02/08/2018 | SmPC and PL | |
| IB/0040 | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 07/02/2018 | n/a | | |

| | | | | | |
|---|---|---|---|---|---|
| IAIN/0041 | B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site | 01/02/2018 | n/a | | |
| PSUSA/1352/ 201701 | Periodic Safety Update EU Single assessment - fampridine | 01/09/2017 | n/a | | PRAC Recommendation - maintenance |
| IB/0039 | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 29/08/2017 | n/a | | |
| II/0036/G | This was an application for a group of variations.<br><br>This is a grouped variation proposing updates to the SmPC sections 4.2, 4.8, 5.1, Annex II and Package Leaflet based on the clinical study ENHANCE and to the SmPC section 4.6 based on the data from the FOLLOW pregnancy registry. The RMP (version 11) has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0. Finally, the CHMP recommends the granting of a marketing authorisation no longer subject to specific obligations.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data<br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance | 23/03/2017 | 22/05/2017 | SmPC, Annex II, Labelling and PL | In this group of variations the MAH submitted data from the Enhance study (218MS305) conducted in 636 subjects with multiple sclerosis and walking disability. Duration of double-blind treatment was 24 weeks with a 2 week post–treatment follow-up. The primary endpoint was improvement in walking ability, measured as the proportion of patients achieving a mean improvement of ≥ 8 points from baseline MSWS-12 score over 24 weeks. In this study there was a statistically significant treatment difference, with a greater proportion of Fampyra treated patients demonstrating an improvement in walking ability, compared to placebo-controlled patients (relative risk of 1.38 (95% CI: [1.06, 1.70]). Improvements generally appeared within 2 to 4 weeks of initiation of treatment, and disappeared within 2 weeks of treatment cessation. Based on the results of the study it was agreed that specific obligation has been fulfilled, and therefore it is deleted from the Annex II.<br>Furthermore, the MAH submitted results of the pregnancy registry FOLLOW which was terminated early due to lack of |

| | | | | | |
|---|---|---|---|---|---|
| | data<br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | | | | subject exposure to prolonged-release fampridine during pregnancy. The limited data available indicated no adverse effect of fampridine on the pregnancy outcomes. |
| R/0037 | Renewal of the marketing authorisation. | 23/03/2017 | 18/05/2017 | | |
| PSUSA/1352/ 201601 | Periodic Safety Update EU Single assessment - fampridine | 02/09/2016 | n/a | | PRAC Recommendation - maintenance |
| N/0035 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 21/07/2016 | 18/05/2017 | PL | |
| IB/0034 | B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) | 20/06/2016 | n/a | | |
| R/0029 | Renewal of the marketing authorisation. | 01/04/2016 | 26/05/2016 | | The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Fampyra, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. |
| IAIN/0033/G | This was an application for a group of variations.<br><br>A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release | 25/05/2016 | 18/05/2017 | Annex II and PL | |

| | | | | | |
|---|---|---|---|---|---|
| | B.II.f.1.e - Stability of FP - Change to an approved stability protocol | | | | |
| N/0030 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 17/03/2016 | 26/05/2016 | PL | |
| IAIN/0028 | C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority | 04/12/2015 | n/a | | |
| II/0024/G | This was an application for a group of variations.<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<br>B.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation | 26/11/2015 | n/a | | |
| IG/0615 | 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 | 11/09/2015 | n/a | | |
| PSUSA/1352/ 201501 | Periodic Safety Update EU Single assessment - fampridine | 10/09/2015 | n/a | | PRAC Recommendation - maintenance |
| IAIN/0025 | A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer | 30/07/2015 | 26/05/2016 | Annex II, Labelling and | |

| | | | | | |
|---|---|---|---|---|---|
| | responsible for batch release | | | PL | |
| R/0021 | Renewal of the marketing authorisation. | 26/03/2015 | 03/07/2015 | | The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Fampyra, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. |
| IA/0022 | A.7 - Administrative change - Deletion of manufacturing sites | 22/04/2015 | n/a | | |
| PSUSA/1352/ 201407 | Periodic Safety Update EU Single assessment - fampridine | 12/02/2015 | n/a | | PRAC Recommendation - maintenance |
| N/0020 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 24/10/2014 | 03/07/2015 | PL | |
| PSUV/0017 | Periodic Safety Update | 11/09/2014 | n/a | | PRAC Recommendation - maintenance |
| II/0016 | Update of section 4.8 of the SmPC to add a new ADR term, exacerbation of trigeminal neuralgia (TN). The patient leaflet is updated accordingly. Furthermore, minor editorial changes are introduced throughout the PI.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 24/07/2014 | 03/07/2015 | SmPC and PL | In this variation the company added a new side effect, worsening of nerve pain in the face (trigeminal neuralgia), with the incidence rate of 'uncommon'. |

| | | | | | |
|---|---|---|---|---|---|
| IB/0015 | B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation | 04/07/2014 | n/a | | |
| IAIN/0018/G | This was an application for a group of variations.<br><br>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site<br>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site<br>A.7 - Administrative change - Deletion of manufacturing sites | 27/06/2014 | n/a | | |
| R/0014 | Renewal of the marketing authorisation. | 20/03/2014 | 22/05/2014 | SmPC, Annex II and PL | The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Fampyra, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. |
| PSUV/0013 | Periodic Safety Update | 06/02/2014 | n/a | | PRAC Recommendation - maintenance |
| R/0011 | Renewal of the marketing authorisation. | 25/04/2013 | 01/07/2013 | Annex II | The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Fampyra, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. |
| II/0010 | Update of sections 4.4 and 4.8 of the SmPC in order to add information regarding hypersensitivity reactions (including anaphylaxis) and the respective warnings and precautions relevant to the prescriber. The Package Leaflet was proposed to be updated in accordance.<br>In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.<br>Furthermore, the PI was brought in line with the latest QRD template version 9.0.<br><br>C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data | 30/05/2013 | 22/05/2014 | SmPC and PL | The CHMP considered the cases of hypersensitivity reported in the post-marketing setting, including the cases of anaphylaxis, and was of the view that a causal relationship between fampridine administration and hypersensitivity (allergic reaction) cannot be excluded. Overall, the CHMP concluded that hypersensitivity should be added to section 4.8 of the SmPC and the respective warnings and precautions relevant to the prescriber should be introduced in section 4.4. The following text was introduced to the Package Leaflet:<br>"If you experience one or more of the following hypersensitivity symptoms: swollen face, mouth, lips, throat or tongue, reddening or itching of the skin, chest tightness and breathing problems stop taking Fampyra and see your doctor immediately". |
| N/0008 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 24/09/2012 | 01/07/2013 | Labelling | |
| IA/0009 | B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms | 07/09/2012 | n/a | | |
| R/0006 | Renewal of the marketing authorisation. | 15/03/2012 | 22/05/2012 | SmPC, Annex II, Labelling | The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the |

| | | | | | |
|---|---|---|---|---|---|
| | | | | and PL | opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Fampyra, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. |
| IAIN/0007/G | This was an application for a group of variations.<br><br>C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV<br>C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV<br>C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD<br>C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system | 05/03/2012 | n/a | | |
| IAIN/0005/G | This was an application for a group of variations.<br><br>B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site<br>B.II.b.1.b - Replacement or addition of a | 16/12/2011 | n/a | | |

| | | | | | |
|---|---|---|---|---|---|
| | manufacturing site for the FP - Primary packaging site<br>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site<br>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site | | | | |
| N/0003 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 16/12/2011 | 02/03/2012 | PL | |
| IAIN/0004 | A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release | 29/11/2011 | 02/03/2012 | Annex II and PL | |
| IB/0001/G | This was an application for a group of variations.<br><br>B.II.e.1.b.2 - Change in immediate packaging of the finished product - Type of container - Sterile medicinal products and biological/immunological medicinal products<br>B.II.e.1.b.2 - Change in immediate packaging of the finished product - Type of container - Sterile medicinal products and biological/immunological medicinal products | 27/09/2011 | 27/09/2011 | SmPC, Labelling and PL | |
| IA/0002 | A.7 - Administrative change - Deletion of manufacturing sites | 08/09/2011 | n/a | | |