



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## Vyndaqel

Procedural steps taken and scientific information after the authorisation

| Application number | Scope   | Opinion/ Notification <sup>1</sup> issued on | Commission Decision Issued <sup>2</sup> / amended on | Product Information affected <sup>3</sup> | Summary                           |
|--------------------|---|--|--|---|-----------------------------------|
| IA/0069            | A.7 - Administrative change - Deletion of manufacturing sites | 11/02/2021                                   |  | Annex II and PL                           |                                   |
| PSUSA/2842/202005  | Periodic Safety Update EU Single assessment - tafamidis       | 14/01/2021                                   | n/a  |   | PRAC Recommendation - maintenance |

<sup>1</sup> 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.

<sup>2</sup> 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.

<sup>3</sup> SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).



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| IB/0068   | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation  | 11/01/2021 | n/a |             |  |
| IAIN/0066 | B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing  | 08/12/2020 | n/a |             |  |
| IA/0064   | B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size  | 20/11/2020 | n/a |             |  |
| IB/0063   | B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)  | 18/11/2020 | n/a |             |  |
| IB/0062   | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation  | 22/10/2020 |     | SmPC and PL |  |
| IA/0061/G | This was an application for a group of variations.<br><br>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure<br><br>B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer | 14/09/2020 | n/a |             |  |

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| IB/0057   | B.II.c.2.d - Change in test procedure for an excipient<br>- Other changes to a test procedure (including replacement or addition)  | 03/07/2020 | n/a |  |  |
| IB/0059   | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation  | 15/06/2020 | n/a |  |  |
| IA/0058/G | This was an application for a group of variations.<br><br>B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)<br><br>B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) | 29/05/2020 | n/a |  |  |
| S/0055    | 8th annual re-assessment   | 30/04/2020 | n/a |  | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Vyndaquel should be maintained. |
| IA/0056/G | This was an application for a group of variations.<br><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 originally approved batch size<br><br>B.II.b.2.a - Change to importer, batch release   | 27/03/2020 | n/a |  |  |

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|                   | <p>arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place</p> <p>B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place</p>  |            |            |                                  |                                   |
| X/0049/G          | <p>This was an application for a group of variations.</p> <p>Annex I_2.(c) Change or addition of a new strength/potency</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> <p>Annex I_1.(a) Replacement of a chemical AS by diff. salt/ester complex/derivative, with the same therapeutic moiety</p> | 12/12/2019 | 17/02/2020 | SmPC, Annex II, Labelling and PL |                                   |
| IB/0053/G         | <p>This was an application for a group of variations.</p> <p>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p>   | 20/12/2019 | n/a        |                                  |                                   |
| PSUSA/2842/201905 | Periodic Safety Update EU Single assessment - tafamidis   | 28/11/2019 | n/a        |                                  | PRAC Recommendation - maintenance |

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| N/0054      | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)   | 13/11/2019 | 17/02/2020 | PL                           |   |
| IB/0050/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.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms<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)                      | 31/07/2019 | 22/11/2019 | SmPC,<br>Labelling and<br>PL |   |
| S/0047      | 7th annual re-assessment   | 26/04/2019 | n/a        |                              | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Vyndaqel should be maintained. |
| IAIN/0048/G | This was an application for a group of variations.<br><br>B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place<br>B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing | 20/12/2018 | 22/11/2019 | Annex II and<br>PL           |   |

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| PSUSA/2842/<br>201805 | Periodic Safety Update EU Single assessment - tafamidis  | 29/11/2018 | n/a        |                                  | PRAC Recommendation - maintenance   |
| T/0045                | Transfer of Marketing Authorisation  | 11/07/2018 | 03/08/2018 | SmPC,<br>Labelling and<br>PL     |   |
| S/0044                | 6th annual re-assessment   | 31/05/2018 | n/a        |                                  | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Vyndaqel should be maintained. |
| II/0041/G             | This was an application for a group of variations.<br><br>B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier<br>B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS | 18/01/2018 | n/a        |                                  |   |
| PSUSA/2842/<br>201705 | Periodic Safety Update EU Single assessment - tafamidis  | 30/11/2017 | n/a        |                                  | PRAC Recommendation - maintenance   |
| II/0043               | Update of section 5.3 of the SmPC to include 'fertility and early embryonic development' in the list of non-clinical studies.<br><br>In addition, the MAH took the opportunity to  | 12/10/2017 | 03/08/2018 | SmPC, Annex II, Labelling and PL |   |

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|         | <p>implement minor revisions to sections 2 and 4.6 of the SmPC, to correct a typographical error in Annex IIE and to align the PI with the latest QRD template version 10.0.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> |            |     |  |  |
| IB/0040 | 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  | 05/05/2017 | n/a |  |  |
| IA/0039 | B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure  | 30/03/2017 | n/a |  |  |
| S/0036  | 5th Annual Re-assessment  | 23/03/2017 | n/a |  | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that Marketing Authorisation of Vyndaqel is maintained. |
| IA/0038 | A.7 - Administrative change - Deletion of manufacturing sites   | 01/03/2017 | n/a |  |  |
| IA/0037 | B.II.a.3.b.1 - Changes in the composition (excipients) of the finished product - Other excipients - Any minor adjustment of the quantitative composition of the finished product with respect to excipients   | 31/01/2017 | n/a |  |  |

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| PSUSA/2842/201605 | Periodic Safety Update EU Single assessment - tafamidis  | 01/12/2016 | n/a        |                                  | PRAC Recommendation - maintenance  |
| N/0035            | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)   | 07/09/2016 | 03/08/2018 | PL                               |  |
| R/0032            | Renewal of the marketing authorisation.  | 26/05/2016 | 22/07/2016 | 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 Vyndaqel in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. |
| IA/0033           | B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place | 18/05/2016 | n/a        |                                  |  |
| S/0031            | 4th Annual Re-assessment   | 25/02/2016 | n/a        |                                  | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that Marketing Authorisation of Vyndaqel should be maintained.      |
| IA/0030           | B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS   | 10/12/2015 | n/a        |                                  |  |
| PSUSA/2842/201505 | Periodic Safety Update EU Single assessment - tafamidis  | 03/12/2015 | n/a        |                                  | PRAC Recommendation - maintenance  |
| IA/0029/G         | This was an application for a group of variations.   | 30/10/2015 | n/a        |                                  |  |



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|           | <p>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</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p>  |            |            |                        |  |
| II/0027/G | <p>This was an application for a group of variations.</p> <p>B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings</p> <p>B.II.a.2.a - Change in the shape or dimensions of the pharmaceutical form - Immediate release tablets, capsules, suppositories and pessaries</p> <p>B.II.a.3.a.1 - Changes in the composition (excipients) of the finished product - Changes in components of the flavouring or colouring system - Addition , deletion or replacement</p> <p>B.II.a.3.b.5 - Changes in the composition (excipients) of the finished product - Other excipients - Change that is supported by a bioequivalence study</p> <p>B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site</p> <p>B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products</p> | 17/09/2015 | 22/07/2016 | SmPC, Labelling and PL |  |

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|  | <p>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process</p> <p>B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold</p> <p>B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits</p> <p>B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits</p> <p>B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test</p> <p>B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits</p> <p>B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation</p> <p>B.II.d.2.f - Change in test procedure for the finished product - To reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number</p> <p>B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding</p> |  |  |  |  |
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|        | <p>test method</p> <p>B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)</p> <p>B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product</p> <p>B.II.h.z - Adventitious Agents Safety - Other variation</p> <p>B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer</p> |            |            |    |  |
| N/0026 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)  | 24/06/2015 | 22/07/2016 | PL |  |

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| IB/0025/G | <p>This was an application for a group of variations.</p> <p>B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits</p> <p>B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits</p> <p>B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits</p> | 26/05/2015 | n/a        |                              |   |
| S/0022    | Annual re-assessment.   | 26/02/2015 | n/a        |                              | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that Marketing Authorisation of Vyndaquel should be maintained.  |
| II/0021   | <p>Update of section 5.1 of the SmPC in order to include information from a recently completed thorough QT study.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>  | 26/02/2015 | 13/05/2015 | SmPC                         | <p>The following addition to section 5.1 of the SmPC has been approved in this variation:</p> <p>"A supra-therapeutic, single, 400 mg oral dose of tafamidis solution in mostly healthy male volunteers demonstrated no significant QTc interval prolongation effect, but a trend towards a shortening of QT interval of unknown clinical relevance."</p> |
| IB/0024   | 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   | 15/01/2015 | 13/05/2015 | SmPC,<br>Labelling and<br>PL |   |

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| IA/0023   | B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure   | 19/12/2014 | n/a        |      |  |
| PSUV/0018 | Periodic Safety Update   | 04/12/2014 | n/a        |      | PRAC Recommendation - maintenance  |
| IA/0020   | B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place   | 26/09/2014 | n/a        |      |  |
| II/0013   | Update of section 4.5 of the SmPC to include new data from completed in vitro studies concerning drug interactions.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 25/09/2014 | 13/05/2015 | SmPC | In vitro studies with tafamidis suggest that it is unlikely tafamidis will cause drug interactions at clinically relevant concentrations with substrates of UDP glucuronosyltransferase (UGT), P-gp transporters, or organic-transporting polypeptide transporters (OATP1B1 and 1B3).<br><br>However, in vitro tafamidis inhibits the efflux transporter BCRP (breast cancer resistant protein) with IC50=1.16 µM and may cause drug-drug interactions at clinically relevant concentrations with substrates of this transporter (e.g. methotrexate, rosuvastatin, imatinib). Likewise, tafamidis inhibits the uptake transporters OAT1 and OAT3 (organic anion transporters) with IC50=2.9 µM and IC50=2.36 µM, respectively, and may cause drug-drug interactions at clinically relevant concentrations with substrates of these transporters (e.g. non-steroidal anti-inflammatory drugs, bumetanide, furosemide, lamivudine, methotrexate, oseltamivir, tenofovir, ganciclovir, adefovir, cidofovir, zidovudine, zalcitabine). |

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| IAIN/0019 | A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release  | 01/09/2014 | 13/05/2015 | Annex II and PL        |   |
| PSUV/0015 | Periodic Safety Update  | 13/06/2014 | n/a        |                        | PRAC Recommendation - maintenance   |
| IB/0017   | B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale   | 22/05/2014 | 13/05/2015 | SmPC                   |   |
| S/0012    | 2nd Annual Re-assessment  | 22/05/2014 | n/a        |                        | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that the Marketing Authorisation of Vyndaqel should be maintained.   |
| IB/0016   | B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method  | 02/05/2014 | n/a        |                        |   |
| II/0014   | Update of section 4.9 of the SmPC based on the recently completed Study B3461040 using higher doses of tafamadis and inclusion of new adverse reactions (hordeolum, photosensitivity and presyncope).<br>Furthermore, the MAH took the opportunity to implement editorial changes with this variation.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 20/03/2014 | 06/05/2014 | SmPC, Labelling and PL | Following completion of a clinical pharmacology study (B3461040) the Product Information was updated to include new information on overdose.<br>Section 4.9 of the SmPC<br>No cases of acute overdose have been reported. In clinical trials of healthy volunteers, the highest dose of tafamidis given was 120480 mg in a single dose and 60 mg once daily for two weeks. Four treatment-related adverse events were reported at these doses levels in healthy volunteers: headache (mild), somnolence (mild), myalgia (moderate), and insomnia (mild). The reported treatment-related |

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|           |   |            |            |                        | adverse events were mild to moderate and included: headache, somnolence, myalgia, insomnia, hordeolum, photosensitivity reaction, and presyncope.   |
| IB/0011/G | <p>This was an application for a group of variations.</p> <p>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</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> | 15/01/2014 | n/a        |                        |   |
| IB/0010   | B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product  | 20/08/2013 | 06/05/2014 | SmPC, Labelling and PL |   |
| S/0006    | 1st Annual Re-assessment  | 25/07/2013 | n/a        |                        | The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that Marketing Authorisation of Vyndaqel should be maintained. |
| IA/0009   | B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place   | 25/04/2013 | n/a        |                        |   |

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| II/0007   | <p>Update of section 4.8 of the SmPC in order to upgrade the adverse drug reaction frequencies of "vaginal infection" and "upper abdominal pain" from "common" to "very common". The Package Leaflet was updated accordingly.</p> <p>In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.</p> <p>Furthermore, the PI was brought in line with the latest QRD template version 8.3.</p> <p>C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data</p> | 25/04/2013 | 06/05/2014 | SmPC, Annex II, Labelling and PL | The CHMP considered that the frequencies of adverse drug reactions using data from the placebo-controlled study for tafamidis were more relevant than using the pooled safety data including uncontrolled studies. Based on this consideration, the frequencies of vaginal infection and upper abdominal pain were re-classified from common ( $\geq 1/100$ to $< 1/10$ ) to very common ( $\geq 1/10$ ). |
| IG/0235/G | <p>This was an application for a group of variations.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p> <p>C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV</p>  | 06/12/2012 | n/a        |                                  | C.I.z - To replace the Detailed Description of the Pharmacovigilance System (DDPS) with the Pharmacovigilance System Master File (PSMF).  |
| IA/0004/G | <p>This was an application for a group of variations.</p> <p>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place</p> <p>B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion</p>  | 03/10/2012 | n/a        |                                  |   |



|           |   |            |            |                        |  |
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|           | <p>of a non-significant in-process test</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p>  |            |            |                        |  |
| T/0001    | Transfer of Marketing Authorisation   | 23/05/2012 | 28/06/2012 | SmPC, Labelling and PL | Transfer of Marketing Authorisation from Pfizer Specialty UK Ltd. to Pfizer Ltd. |
| IG/0169/G | <p>This was an application for a group of variations.</p> <p>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</p> <p>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</p> | 08/06/2012 | n/a        |                        |  |