EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Advocate

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued / amended on	Product Information affected[2]	Summary[3]
IB/0047	C.I.3.z - Change(s) in the SPC, Labelling or PL of veterinary medicinal products intended to implement the outcome of a procedure concerning PSUR: implementation of wording agreed by the competent authority that does not require additional assessment	08/10/2021		SPC and PL	The Agency accepted the variation to amend section 4.6 of the summary of product characteristics and the corresponding section 6 of the package leaflet of Advocate for dogs, following assessment of the surveillance of adverse events.
IA/0045	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	11/03/2021	n/a		n/a
II/0043	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	05/11/2020	31/03/2021	SPC and PL	The Agency accepted the variation to revise section 4.7 of the SPC as regards the use of the product during pregnancy and lactation. Additionally, the MAH proposes to replace the pictures included in section 4.9 of the SPC under 'Method of administration' and to delete the special precaution for use relating to oral uptake by dogs from the cats SPC.
IB/0044/G	This was an application for a group of variations.	10/07/2020	n/a		n/a

[1] Notifications are issued for type I variations (unless part of a group including a type II variation or higher procedure or a worksharing application). Opinions are issued for all other procedures.
[2] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).
[3] Since October 2019 summary information is no longer published for variations that do not impact upon the product information

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	B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition) 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				
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	17/04/2020	31/03/2021	SPC, Labelling and PL	The Agency accepted the variation to update the Summary of Product Characteristics (SPC) and the package leaflet to implement an agreed wording following assessment of a PSUR. The product information was also updated in accordance with the latest version of the QRD template.
II/0041/G	This was an application for a group of variations. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/06/2019	29/07/2019	SPC, Labelling and PL	The European Commission amended the decision granting the marketing authorisation to add new therapeutic indications: the prevention and treatment of Aelurostrongylus abstrusus in cats and the treatment of Thelazia callipaeda in cats and to amend the product information with regard to pharmacological properties of moxidectin in cats (persistent action, half-life, steady-state serum levels after multiple applications). Also, the applicant takes the opportunity to update the list of local representatives.
IG/0963/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure C.I.9.c - 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 PhV system	16/07/2018	n/a		The Agency accepted the group of variations to update the detailed description of pharmacovigilance system (DDPS).
II/0039/G	This was an application for a group of variations. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/01/2018	20/02/2018	SPC, Labelling and PL	The European Commission amended the decision granting the marketing authorisation to change the current indications for Advocate spot-on solution for cats and ferrets / Advocate spot-on solution for dogs to add the following therapeutic indications: · the treatment of the lungworm Eucoleus aerophilus (syn. Capillaria aerophila) in cats, · the treatment of Eucoleus (syn. Capillaria) boehmi in dogs, · the treatment of the eye worm Thelazia callipaeda in dogs. Furthermore, section 5.2 (Pharmacokinetic particulars) of the SPC for Advocate spot-on solution for dogs has been amended with regard to studies evaluating the pharmacokinetic behaviour of moxidectin after multiple

					applications (persistent action). Also, the applicant took the opportunity to update the list of local representatives and the Product Information in line with QRD template v 8.1.
IAIN/0038	C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative	18/05/2017	20/02/2018	PL	The Agency accepted the variation to update the list of local representatives in the package leaflet.
IAIN/0037	C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative	21/02/2017	06/06/2017	PL	The Agency accepted the variation to update the list of local representatives in the package leaflet.
IA/0036	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	10/02/2017	n/a		The Agency accepted the variation to change the name of the manufacturer of the active substance.
IB/0035	B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS	22/12/2016	n/a		The Agency accepted the variation to change the storage conditions of the active substance.
IA/0034	A.7 - Administrative change - Deletion of manufacturing sites	08/09/2016	n/a		The Agency accepted the variation to delete a site responsible for manufacture of the active substance.
IAIN/0033	C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative	05/09/2016	06/06/2017	PL	The Agency accepted the variation to update the list of local representatives in the package leaflet.
IAIN/0032	C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative	09/06/2016	06/06/2017	PL	The Agency accepted the variation to update the list of local representatives in the package leaflet.
IB/0031/G	This was an application for a group of variations. C.I.4.z - Change(s) in the SPC, Labelling or package leaflet further to a veterinary PSUR C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative	20/05/2016	06/06/2017	SPC and PL	The Agency accepted the group of variations to update sections 4.3 and 4.5 of the SPC and the corresponding sections 5 and 12 of the Package Leaflet to implement agreed wording changes previously requested by the CVMP following the assessment of a Periodic Safety Update Report and to update the list of local representatives in the package leaflet.
IG/0663/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) in the safety database and/or major contractual arrangements for the fulfilment of PhV obligations, and/or change of the site undergoing PhV activities C.I.9.c - 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 PhV system	25/02/2016	n/a		The Agency accepted the variation to update the Detailed Description of the Pharmacovigilance System (DDPS).
IAIN/0029	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	28/10/2015	n/a		The Agency accepted the variation to add a new secondary packaging site.
II/0026/G	This was an application for a group of variations.	09/07/2015	06/08/2015	SPC, Labelling	The European Commission amended the decision granting the marketing authorisation to add a new therapeutic

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative			and PL	indication for Advocate spot-on solution for dogs, i.e. treatment of cutaneous dirofilariosis (adult stages of Dirofilaria repens) and to update the list of local representatives in the package leaflet.
IB/0028	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	09/07/2015	n/a		The Agency accepted the variation to make a change in the test procedure for the finished product
IA/0027/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	04/06/2015	n/a		The Agency accepted the variation to replace a certificate of suitability for the active substance and to tighten the specification limits of magnesium used in the manufacturing process of the active substance.
IAIN/0025	C.II.6.a - Changes to the labelling or the PL which are not connected with the SPC - Administrative information concerning the holder's representative	06/03/2014	05/03/2015	PL	The Agency accepted the variation to update the list of local representatives in the package leaflet.
II/0022	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	18/07/2013	18/10/2013	SPC, Labelling and PL	The European Commission amended the decision granting the marketing authorisation to add new therapeutic indications.
IA/0024	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	30/08/2013	n/a		The Agency accepted the variation to update the Ph. Eur. certificate of suitability from manufacturer of moxidectin for veterinary use and to change in the name of the manufacturer.
IB/0023	B.III.1.a.3 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	24/05/2013	n/a		The Agency accepted the variation on addition of a manufacturer of the active substance
R/0021	Renewal of the marketing authorisation.	08/11/2012	14/01/2013	SPC, Annex II, Labelling and PL	The European Commission amended the decision granting the marketing authorisation for Advocate.
WS/0006 (V)/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a	13/04/2012	13/04/2012		The Agency accepted the group of variations on the changes in the chemical synthesis of Imidacloprid.

	test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IA/0020/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test	07/12/2011	n/a		The Agency accepted the group of variations on the amendment in-process tests during the manufacture of the active substance.

	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits				
IA/0018	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)	08/07/2011	08/07/2011		The Agency accepted the variation on deletion of specification parameter from the specification of propylene carbonate.
IB/0017/G	This was an application for a group of variations. 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 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	12/11/2010	14/06/2011	SPC, Labelling and PL	The Agency accepted the group of variations on adding pack sizes (1, 2, 9 and 12 pipettes) outside and within the range of currently approved pack sizes.
IA/0016/G	This was an application for a group of variations. B.III.2.a.1 - Change of specification('s) of a former non Pharmacopoeial substance to comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS B.III.1.a.1 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer	13/10/2010	13/10/2010		The Agency accepted the group of variations on compliance with the relevant monograph of the European Pharmacopoeia and with the new certificate of suitability for the active substance moxidectin.
II/0014	II - New Indication (same therapeutic area)	14/07/2010	26/08/2010	SPC, Labelling and PL	The European Commission amended the decision granting the marketing authorisation on adding new indications related to lungworm infections in dogs as well as revised recommendations regarding the treatment of canine demodicosis. Additionally within the scope of this application some minor corrections were implemented: update of the list of local representatives in the package leaflets; addition of "…or damage….." to section 4.5 of the SPC (and section 12 of the package leaflet); pipette label texts modified; blister foil texts for the "Small Cats" product (0.4 ml) corrected to include "and Ferrets" (approved in the previous variation application).
IB/0015/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	24/03/2010	24/03/2010		The Agency accepted the group of variations on filling volumes and in-process tests during the manufacture of the finished product.
II/0012	II - New Indication (same therapeutic area)	16/04/2009	25/05/2009	SPC, Annex II, Labelling and	The European Commission amended the decision granting the marketing authorisation on adding a new target species: ferrets. The indication for ferrets is for the

				PL	treatment and prevention of flea infestation (Ctenocephalides felis) and the prevention of heartworm disease (L3 and L4 larvae of Dirofilaria immitis). Only the smallest sized pipette (0.4 ml) of the 10% imidacloprid and 1% moxidectin strength is to be used for ferrets.
IA/0013	1A-25-b-2 Change to comply with Eu. Ph. or with the national pharmacopoeia of a Member State	12/12/2008	12/12/2008		The Agency accepted the variation on the update of the relevant monograph of the European Pharmacopoeia for the excipient.
T/0011	Transfer of Marketing Authorisation	01/08/2008	02/09/2008	SPC, Annex II, Labelling and PL	The European Commission transferred the marketing authorisation from "Bayer HealthCare AG" to "Bayer Animal Health GmbH".
R/0010	Renewal of the marketing authorisation.	12/12/2007	07/02/2008		The European Commission renewed the marketing authorisation for Advocate.
II/0009	II - New Indication (same therapeutic area)	11/07/2007	13/08/2007	SPC, Labelling and PL	The European Commission amended the decision granting the marketing authorisation on addition of two new indications (for the dog products) for the treatment of biting lice (Trichodectes canis) and the treatment of Angiostrongylus vasorum. At the same time the wording of the macrocyclic lactone warnings in the SPCs and package leaflets, for both the cat and dog products, was modified. Thirdly, a hypersensitivity warning was included in the SPCs and package leaflets, for both the cat and dog products : "The product may, in rare cases, cause local hypersensitivity reactions." (This amendment was requested by the CVMP following a PSUR). Lastly, the product information was updated, for example the format was updated into that of the current QRD template and the contact details of the local representatives were updated.
IB/0008	1B-42-a-2 Change in shelf life of finished product-after first opening	08/12/2006	08/12/2006	SPC, Labelling and PL	The Agency accepted the variation on additional pack sizes (for all six pipette sizes) of 21 and 42 pipettes per pack.
IA/0007	1A-04 Change in name and/or address of a manufacturer of the active substance	12/06/2006	12/06/2006		The Agency accepted the variation on the change of manufacturer's name of one of the active substances.
IA/0006	1A-32.b Change in the batch size of the finished product-Downscaling down to 10-fold	01/09/2005	n/a		The Agency accepted the variation on a change in the batch size of the finished product.
II/0005	II - New Indication (same therapeutic area)	10/11/2004	05/01/2005	SPC, Labelling and PL	The European Commission amended the decision granting the marketing authorisation on addition of an indication for the treatment of ear mite infestation in both cats and dogs, sarcoptic mange and demodicosis in dogs. The opportunity was taken to update the list of local representatives listed in the package insert, and also to update the operator warnings.
T/0004	Transfer of Marketing Authorisation	18/02/2004	13/04/2004	SPC, Annex II, Labelling and	The European Commission transferred the marketing authorisation from "Bayer AG" to "Bayer HealthCare AG".

				PL	
IB/0003	1B-42-a-1 Change in shelf life of finished product-as packaged for sale	18/02/2004	13/04/2004	SPC	The Agency accepted the variation on extension of the shelf-life of the product to 3 years.
I/0002	30_Change in pack size for a medicinal product	29/04/2003	04/06/2003	SPC and Labelling	The European Commission issued a decision for a type I variation (No. 30) for additional pack sizes (for all six pipette sizes) of 4 pipettes per pack. Amendments have been included in the relevant sections of the Commission Decision and EPAR.
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/04/2003	04/06/2003	Labelling	The Commission issued a decision after the marketing authorisation holder had notified them of a change in the (intermediate) labelling (introduction of text onto the blister foil) not connected to the SPC. Amendments have been included in the relevant sections of the Commission Decision and EPAR.