



EMA/42764/2021

## Dupixent

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
II/0038/G	This was an application for a group of variations.  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	14/01/2021	n/a		

<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).



	<p>the AS -replacement or addition of a site where batch control/testing takes place</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.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS</p> <p>B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method</p> <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.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>				
PSUSA/10645 /202003	Periodic Safety Update EU Single assessment - dupilumab	12/11/2020	11/01/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10645/202003.
IB/0040/G	This was an application for a group of variations.	05/01/2021	n/a		

	<p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> <p>B.II.f.1.e - Stability of FP - Change to an approved stability protocol</p> <p>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process</p>				
IB/0037/G	<p>This was an application for a group of variations.</p> <p>B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p>	22/12/2020		SmPC	
IB/0035/G	<p>This was an application for a group of variations.</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.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation</p> <p>B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol</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>	09/12/2020		SmPC	

II/0027	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	15/10/2020	25/11/2020	SmPC and PL	Please refer to Scientific Discussion 'EMA/H/C/004390/II/0027'.
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/10/2020	25/11/2020	PL	
II/0031/G	This was an application for a group of variations.  B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS  B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol  B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	01/10/2020	n/a		
II/0032	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/09/2020	25/11/2020	SmPC	
PSUSA/10645 /201909	Periodic Safety Update EU Single assessment - dupilumab	30/04/2020	25/06/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s) for PSUSA/10645/201909.

IAIN/0033	B.IV.1.b - Change of a measuring or administration device - Deletion of a device	12/06/2020	n/a		
II/0030	<p>Update of section 4.8 of the SmPC to include arthralgia as a new Adverse Drug Reaction (ADR) with a frequency not known. This is based on safety review of post-marketing data and PRAC recommendation adopted in the last PSUR assessment dated April 2020. The package leaflet is updated accordingly.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	14/05/2020	25/11/2020	SmPC and PL	Available data from the literature and reported post-marketing cases suggest evidence for a causal association between dupilumab exposure and 'Arthralgia', i.e. joint pain. Therefore, arthralgia is added as new ADR to section 4.8. of the SmPC with a frequency "unknown" based on post marketing data.
IB/0029/G	<p>This was an application for a group of variations.</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> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> <p>B.II.f.1.e - Stability of FP - Change to an approved stability protocol</p>	05/05/2020	n/a		
II/0024/G	<p>This was an application for a group of variations.</p> <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</p>	17/04/2020	25/06/2020	Annex II	

<p>intermediate used in the manufacture of the AS or manufacturer of a novel excipient</p> <p>B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method</p> <p>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol</p> <p>B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>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</p> <p>B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change</p>				
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	outside the approved specifications limits range				
IB/0028	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	04/03/2020	n/a		
IB/0025/G	This was an application for a group of variations.  B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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 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	08/01/2020	n/a		
IB/0023	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	20/12/2019	25/06/2020	SmPC	
IB/0022/G	This was an application for a group of variations.	21/11/2019	n/a		

	<p>B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation</p> <p>B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation</p> <p>B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation</p> <p>B.II.d.2.a - Change in test procedure for the finished product - 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>				
PSUSA/10645 /201903	Periodic Safety Update EU Single assessment - dupilumab	31/10/2019	n/a		PRAC Recommendation - maintenance
II/0017	<p>The application is for an extension of indication in patients with severe CRSwNP, who are</p> <p>As a consequence of this new indication on patients with CRSwNP, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are being updated to include pharmacological, efficacy and safety data. The Package Leaflet (PL) is updated accordingly. Additionally minor editorial QRD changes on excipients to the SmPC are introduced in section 6.6 in the 300mg and 200mg strength accordingly. Corresponding changes are implemented in the 200mg strength. Consequently the Annex IIIA is updated.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) -</p>	19/09/2019	24/10/2019	SmPC and PL	Please refer to the assessment report.



	Addition of a new therapeutic indication or modification of an approved one				
II/0018/G	<p>This was an application for a group of variations.</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> <p>B.II.b.2.c.3 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing for a biol/immunol product and any of the test methods is a biol/immunol/immunochemical method</p> <p>B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation</p> <p>B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation</p> <p>B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products</p> <p>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</p> <p>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</p> <p>B.II.e.5.a.1 - Change in pack size of the finished</p>	17/10/2019	25/06/2020	SmPC, Annex II and Labelling	

	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				
IB/0021	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	20/08/2019	n/a		
II/0012	<p>Extension of Indication for Dupixent to extend the atopic dermatitis indication to the paediatric adolescent population 12 years to 17 years. This is also submitted in accordance with the requirement of Article 46.</p> <p>As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.</p> <p>The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP).</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p>	27/06/2019	01/08/2019	SmPC and PL	Please refer to the variation assessment report.
IB/0019/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>	10/07/2019	n/a		

	<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> <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>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>				
IB/0015	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	16/05/2019	01/08/2019	SmPC and PL	
X/0004/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.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p>	28/02/2019	06/05/2019	SmPC, Labelling and PL	
PSUSA/10645 /201809	Periodic Safety Update EU Single assessment - dupilumab	11/04/2019	n/a		PRAC Recommendation - maintenance

IA/0016	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	29/03/2019	n/a		
II/0013/G	<p>This was an application for a group of variations.</p> <p>B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes</p> <p>B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method</p> <p>B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product or a new bioequivalence study</p> <p>B.II.d.2.a - Change in test procedure for the finished product - 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> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p>	28/03/2019	n/a		

	<p>product - Minor changes to an approved test procedure</p> <p>B.II.e.z - Change in container closure system of the Finished Product - Other variation</p> <p>B.II.e.z - Change in container closure system of the Finished Product - Other variation</p> <p>B.II.e.3.a - Change in test procedure for the immediate packaging of the finished product - Minor changes to an approved test procedure</p> <p>B.II.e.4.b - Change in shape or dimensions of the container or closure (immediate packaging) - The change in shape or dimensions concerns a fundamental part, which may have a significant impact on the delivery, use, safety or stability of the FP</p>				
II/0009/G	<p>This was an application for a group of variations.</p> <p>B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product</p> <p>B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method</p> <p>B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test</p>	17/01/2019	06/05/2019	Annex II	

	<p>method at the site is a biol/immunol method</p> <p>B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB</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.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.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.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>				
II/0006/G	<p>This was an application for a group of variations.</p> <p>B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product</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</p>	29/11/2018	06/05/2019	Annex II	

	<p>batch control/testing takes place</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.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method</p> <p>B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method</p> <p>B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method</p> <p>B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB</p>				
PSUSA/10645 /201803	Periodic Safety Update EU Single assessment - dupilumab	04/10/2018	n/a		PRAC Recommendation - maintenance
IA/0011	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	01/10/2018	n/a		

IB/0010	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	07/09/2018	17/12/2018	SmPC	
IA/0007	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	14/06/2018	n/a		
II/0003/G	This was an application for a group of variations.  B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol  B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS	25/05/2018	n/a		
II/0002	B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS	26/04/2018	n/a		
IB/0005	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	20/04/2018	n/a		



IB/0001	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	16/01/2018	17/12/2018	SmPC and PL	
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