ILARIS

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
II/0085	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	31/10/2024		SmPC, Annex II, Labelling and PL	The SmPC sections has been updated to reflect the new presentation, 150 mg/ml solution for injection in pre-filled pen (pre-filled syringe (PFS) assembled into an autoinjector). A statement related to the Patient Card was also included. The Labelling and PL have been updated accordingly.

[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).

IAIN/0084/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	15/03/2024	n/a		
IAIN/0083/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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 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 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 -	25/08/2023	29/08/2024	Annex II and PL	

	Not including batch control/testing				
IB/0082/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation 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 B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	31/07/2023	n/a		
IB/0081/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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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	21/06/2023	n/a		

	manufacturer of a novel excipient				
IG/1521	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	23/06/2022	n/a		
IB/0079	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/04/2022	n/a		
PSUSA/526/202106	Periodic Safety Update EU Single assessment - canakinumab	10/02/2022	n/a		PRAC Recommendation - maintenance
II/0078	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	13/01/2022	n/a		
N/0076	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/09/2021	07/06/2022	PL	
IB/0073/G	This was an application for a group of variations. B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	02/07/2021	n/a		

	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
IA/0074	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/05/2021	07/06/2022	SmPC and PL	
II/0072/G	This was an application for a group of variations. B.II.h.1.b.2 - Update to the Adventitious Agents Safety Evaluation information - Replacement of obsolete studies related to manufacturing steps and adventitious agents already reported in the dossier - without modifications of risk assessment 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	14/01/2021	n/a		
IB/0071	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	25/11/2020	n/a		
IA/0070/G	This was an application for a group of variations. 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 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	09/09/2020	n/a		

II/0069/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	04/09/2020	n/a		
II/0068/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.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 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	19/03/2020	n/a		
II/0067	Update of section 4.4, 4.8, 5.1 and 5.2 of the of the SmPC and relevant sections of the PL with the results of study CACZ885GDE01T (a multi-centre, phase II, randomized, placebo-controlled trial of Ilaris for the	30/01/2020	23/07/2021	SmPC and PL	Study GDE01T was a phase II, randomized, placebo-controlled investigator-initiated clinical study of canakinumab for the treatment of AOSD in patients ≥18 to ≤75 years of age. The primary objective of this study was

	Treatment of adult-onset Still's Disease) and an updated pooled analyses of Systemic Juvenile Idiopathic Arthritis (SJIA) studies CACZ885A2203 (safety only), CACZ885G2305, CACZ885G2301, CACZ885G2301E1, CACZ885G2306 and CACZ885G1301. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				to evaluate the efficacy of canakinumab in patients with AOSD and active joint involvement in terms of the proportion of patients with a clinically relevant reduction in disease activity following 12 weeks of treatment. Also, the SJIA pooled dataset which supported the extension of the SJIA indication to include AOSD, submitted in Dec-2015, was updated with two recently completed studies. It can be concluded that the benefit-risk balance of canakinumab in the indication of Still´s disease is not altered even though this small investigator initiated study provides only limited but supportive assumptions. The results of the updated SJIA pooled dataset are comparable to the initially submitted dataset. Therefore, the updated pooled dataset is supportive and can confirm a comparable efficacy of canakinumab in SJIA patients across age groups. The overall safety profile of canakinumab in AOSD patients, as observed in the investigator-initiated trial GDE01T, was consistent with that observed in the updated SJIA pooled dataset and with that known for canakinumab in other indications.
IA/0066/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of	28/10/2019	n/a		

	manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites				
IB/0065	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	08/07/2019	n/a		
R/0062	Renewal of the marketing authorisation.	28/03/2019	06/06/2019	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 ILARIS in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IG/1100	A.7 - Administrative change - Deletion of manufacturing sites	24/05/2019	n/a		
IG/1099	A.7 - Administrative change - Deletion of manufacturing sites	24/05/2019	n/a		
PSUSA/526/201806	Periodic Safety Update EU Single assessment - canakinumab	17/01/2019	n/a		PRAC Recommendation - maintenance
II/0060	Update of section 5.1 of the SmPC based on the final clinical study report (CSR) from Study ACZ885G2306 (β-SPECIFIC 4 Patients: Study of Paediatric efficacy	13/09/2018	06/06/2019	SmPC	Study G2306 was an open-label study to assess maintenance of treatment response with Ilaris dose reduction (2 mg/kg every 4 weeks) or dose interval

	and safety with first-line use of canakinumab: An open-label canakinumab (ACZ885) dose reduction or dose interval prolongation efficacy and safety study in patients with Systemic Juvenile Idiopathic Arthritis (SJIA)). The submission of the final CSR addresses the post-authorisation measure MEA 036.3 (PAES) and the requirements of article 46 of the paediatric regulation. In addition, the MAH took the opportunity to implement some minor editorial changes in the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				prolongation (4 mg/kg every 8 weeks) in SJIA patients who were receiving Ilaris 4 mg/kg every 4 weeks. Seventy five patients aged 2 to 22 years who maintained inactive disease status for at least 6 consecutive months (clinical remission) with canakinumab monotherapy, including patients who were able to maintain inactive disease status with discontinuation of concomitant corticosteroid and/or methotrexate use for at least 4 weeks, were randomised to receive Ilaris 2 mg/kg every 4 weeks (N=38) or Ilaris 4 mg/kg every 8 weeks (N=37). After 24 weeks, 71% (27/38) of patients who received the reduced dose (2 mg/kg every 4 weeks) and 84% (31/37) of patients who received the prolonged dosing interval (4 mg/kg every 8 weeks) were able to maintain inactive disease status for 6 months. Of the patients in clinical remission who continued with further dose reduction (1 mg/kg every 4 weeks) or dose interval prolongation (4 mg/kg every 12 weeks), 93% (26/28) and 91% (30/33) of patients, respectively, were able to maintain inactive disease status for 6 months. Patients who maintained inactive disease status for 6 additional months at this lowest dose regimen were allowed to discontinue Ilaris. Overall, 33% (25/75) of patients randomised to dose reduction or dose interval prolongation arms were able to discontinue treatment with Ilaris and maintain inactive disease status for 6 months. The rate of adverse events in both treatment arms was similar to the rate seen in patients treated with Ilaris 4 mg/kg every 4 weeks. For further information, see please refer to Scientific Discussion ‘Ilaris-H-C-1109-II-60’

T/0058	Transfer of Marketing Authorisation	16/05/2018	30/07/2018	SmPC, Labelling and PL	
IG/0950	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)	18/06/2018	n/a		
IB/0057	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	16/04/2018	30/07/2018	SmPC	
IB/0056	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	03/04/2018	n/a		
IB/0055/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.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	14/03/2018	n/a		

II/0053/G	This was an application for a group of variations. 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.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 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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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 test procedure (including replacement or addition) for the AS or a starting material/intermediate	18/01/2018	n/a		

PSUSA/526/201706	Periodic Safety Update EU Single assessment - canakinumab	11/01/2018	n/a		PRAC Recommendation - maintenance
IB/0054/G	This was an application for a group of variations. B.II.h.z - Adventitious Agents Safety - Other variation B.II.h.z - Adventitious Agents Safety - Other variation	04/01/2018	n/a		
IB/0052/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.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	01/12/2017	n/a		
IAIN/0050/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a	01/08/2017	n/a		

	manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IA/0049	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	14/07/2017	n/a		
S/0047	7th Annual Re-assessment	26/01/2017	22/03/2017	SmPC, Annex II and PL	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 ILARIS should be varied. In view of the data submitted as part of the Annual Re-Assessment, sections 4.8 and 5.1 of the SmPC were updated with the results of study CACZ885D2401. This 6-year observational registry study was conducted to provide data on the long-term safety and effectiveness of Ilaris treatment in paediatric and adult CAPS patients in routine clinical practice. A total of 243 CAPS patients (85 paediatric patients aged ≥ 2 to ≤ 17 years and 158 adult patients aged ≥ 18 years) were treated with Ilaris in routine clinical practice (mean of 3.8 years of Ilaris exposure). The safety profile of Ilaris observed following long-term treatment in this setting was consistent with what has been observed in interventional studies in CAPS patients. Disease activity was rated as absent or mild/moderate in more than 90% of patients at all post-baseline time points in the study, and median serological markers of inflammation (CRP and SAA) were

					normal (< 10 mg/litre) at all post-baseline time points. Although approximately 22% of patients receiving Ilaris required dose adjustment, only a small percentage of patients (1.2%) discontinued Ilaris due to lack of therapeutic effect. Further, the SmPC, Annex II and Package Leaflet were updated to reflect the conversion of the MA from a MA under exceptional circumstances to a full MA and the consequential removal of Ilaris from the list of medicinal products that are subject to additional monitoring.
X/0045/G	This was an application for a group of variations. Extension of the marketing authorisation concerning a new pharmaceutical form: solution for injection (150 mg/ml). Extension of indication based on the results of the pivotal phase 3 study CACZ885N2301 to include the treatment of adults, adolescents and children of 2 years of age and older with one of the following Periodic Fever Syndromes: - Tumour Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS); - Hyperimmunoglobulin D Syndrome (HIDS) / Mevalonate Kinase Deficiency (MKD); - Familial Mediterranean Fever (FMF) in combination with colchicine, if appropriate. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated and the Annex II and the Package Leaflet is proposed to be updated accordingly. In addition, the annexes have been aligned with the latest QRD template v.10. A	15/12/2016	23/02/2017	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion Ilaris EMEA/H/C/001109/X/0045/G.

	revised RMP version 11.2 was agreed during the procedure. Annex I_2.(c) Change or addition of a new strength/potency C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/526/201606	Periodic Safety Update EU Single assessment - canakinumab	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0048	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	09/11/2016	n/a		
II/0043	Extension of Indication to amend the Systemic Juvenile Idiopathic Arthritis (SJIA) indication to include treatment of active Still's disease including Adult-Onset Still's Disease (AOSD) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. Further, the information in section 4.6 of the SmPC has been updated with regard to the administration of live vaccines in newborns exposed in-utero to canakinumab. In addition, the MAH took the opportunity to bring the annexes in line with the latest QRD template and to make a minor correction	23/06/2016	01/08/2016	SmPC, Annex II, Labelling and PL	Please refer to the scientific discussion 'Ilaris EMEA/H/C/01109/II/0043'.

	in the Annex A. An updated RMP version 10.2 was agreed during the procedure. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/526/201512	Periodic Safety Update EU Single assessment - canakinumab	07/07/2016	n/a		PRAC Recommendation - maintenance
PSUSA/526/201506	Periodic Safety Update EU Single assessment - canakinumab	14/01/2016	n/a		PRAC Recommendation - maintenance
S/0042	6th Annual Re-assessment	17/12/2015	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 Ilaris should be maintained.
II/0040/G	This was an application for a group of variations. C.I.4 Update of sections 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on the results of the CACZ885D2307 clinical study. C.I.4 Update of sections 4.5 of the SmPC in order to update the safety information based on the results of the CACZ885A2106 study.	12/11/2015	01/08/2016	SmPC and PL	

	The Package Leaflet has been updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/526/201412	Periodic Safety Update EU Single assessment - canakinumab	09/07/2015	n/a		PRAC Recommendation - maintenance
IB/0038	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	10/03/2015	n/a		
PSUV/0034	Periodic Safety Update	09/01/2015	n/a		PRAC Recommendation - maintenance
S/0035	5th Annual Re-assessment	18/12/2014	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 Marketing Authorisation of Ilaris should be maintained.
IA/0037	A.7 - Administrative change - Deletion of manufacturing sites	08/12/2014	n/a		
IAIN/0036	A.1 - Administrative change - Change in the name and/or address of the MAH	10/10/2014	23/09/2015	SmPC, Labelling and PL	

II/0033/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.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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	25/09/2014	n/a		
PSUV/0032	Periodic Safety Update	24/07/2014	18/09/2014	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0032.
R/0031	Renewal of the marketing authorisation.	25/04/2014	19/06/2014	SmPC, Labelling and PL	
PSUV/0028	Periodic Safety Update	09/01/2014	n/a		PRAC Recommendation - maintenance
S/0029	4th Annual Re-assessment	18/12/2013	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of the medicinal product, concluded that the benefit/risk balance for the product remains favourable.

IA/0030	A.7 - Administrative change - Deletion of manufacturing sites	30/10/2013	n/a		
II/0026	Extension of Indication to include new indication/population for Ilaris for the treatment of active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. Ilaris can be given as monotherapy or in combination with methotrexate. As a consequence sections 4.1, 4.2, 4.4, 4.7, 4.8, 5.1 and 5.2 of the SmPC have been updated. Annex II and sections 1, 2, 3 and 4 of the Package Leaflet were updated accordingly. Furthermore, the PI is being brought in line with the latest QRD template version 9.0. In addition, the MAH took the opportunity to include the contact details of the Croatian local representative and to update the contact details of the Maltese local representative in the Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	25/07/2013	26/08/2013	SmPC, Annex II and PL	Please refer to the Scientific Discussion Ilaris/H/C/001109/II/26 for further information.
II/0010	Update of sections 4.1, 4.2, 4.4, 4.7, 4.8, 5.1 and 5.2 of the SmPC: extension of indication for symptomatic treatment of adult patients with frequent gouty arthritis attacks (at least 3 attacks in the previous 12 months) in whom non-steroidal anti-	17/01/2013	18/02/2013	SmPC, Annex II and PL	Please refer to the Scientific Discussion Ilaris/H/C/001109/II/10 for further information.

	inflammatory drugs (NSAIDs) and colchicine are contraindicated, are not tolerated, or do not provide an adequate response, and in whom repeated courses of corticosteroids are not appropriate. Sections 1, 2, 3 ad 4 of the Package Leaflet are updated accordingly. The requested variation proposed amendments to the Summary of Product Characteristics, Annex II, Labelling and Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
S/0024	3rd Annual Re-assessment	15/11/2012	14/01/2013	Annex II	The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of the medicinal product, concluded that the benefit/risk balance for the product remains favourable.
IG/0248	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/12/2012	n/a		
II/0021	Update of sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC: extension of indication for the treatment of cryopyrin-associated periodic syndrome (CAPS) in patients aged 2 to <4 years of age and to increase the maximum dose to 600 mg or 8 mg/kg every 8 weeks. Sections 1, 2, 3 and 4 of the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to include minor editorial changes in the SmPC and in the	13/12/2012	24/01/2013	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion Ilaris/H/C/001109/II/21 for further information.

	Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template version 8. The requested variation proposed amendments to the Summary of Product Characteristics, Annex II, Labelling and Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0025/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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	08/11/2012	n/a		
II/0022/G	This was an application for a group of variations. This was an application for a group of variations on changes to the drug substance control. 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.b.1.b - Change in the specification parameters and/or limits of an AS, starting	20/09/2012	20/09/2012		

	material/intermediate/reagent - Tightening of specification limits 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.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.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.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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions 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				

	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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS				
IG/0209/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 in the	17/08/2012	n/a		

	contact details of the QPPV 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				
IB/0020	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	24/07/2012	n/a		
IG/0148/G	This was an application for a group of variations. 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 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	22/02/2012	n/a		
S/0012	2nd Annual Re-assessment	17/11/2011	13/01/2012	Annex II	The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of the medicinal product, concluded that the benefit/risk balance for the product remains favourable.
IB/0015	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	06/01/2012	n/a		

IA/0017/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites	15/12/2011	n/a		
IA/0016/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	15/12/2011	n/a		
X/0009	New presentation. Annex I_2.(d) Change or addition of a new pharmaceutical form	21/07/2011	16/09/2011	SmPC, Labelling and PL	
IG/0088/G	This was an application for a group of variations.	11/07/2011	n/a		

	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 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				
IB/0011	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	06/04/2011	n/a	SmPC	
II/0006	Changes to the drug substance manufacturing facility. 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	17/02/2011	09/03/2011		Changes to the drug substance manufacturing facility in order to reduce change over times.
S/0007	Annual Re-assessment	16/12/2010	28/02/2011	SmPC, Annex II and PL	The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of the medicinal product, concluded that the benefit/risk balance for the product remains favourable. The CHMP agreed that the Marketing Authorisation should remain under exceptional

					circumstances.
IG/0032/G	This was an application for a group of variations. To update the Detailed Description of the Pharmacovigilance System (DDPS) to version 9.0, to include: - a change in the deputy of the Qualified Person for Pharmacovigilance (QPPV); - a change in the major contractual arrangements. - administrative changes not impacting the operation of the pharmacovigilance system. Annex II.B has also been updated with the latest wording as per October 2010 CHMP procedural announcement. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV 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 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	21/12/2010	n/a	Annex II	
IB/0008	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	05/10/2010	n/a		

	re-test period/storage period supported by real time data				
IB/0005	To change the value of histidine concentration in Ilaris finished product from 20mM to 15mM. B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	09/07/2010	n/a		
IB/0004	To change the value of histidine concentration in the final canakinumab bulk active substance. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	09/07/2010	n/a		
IB/0003	To extend the shelf life of the finished product B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	17/05/2010	n/a	SmPC	
IB/0002	To extend the shelf life of the active substance 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	12/05/2010	n/a		
II/0001	Update of the Detailed Description of the Pharmacovigilance system (DDPS).	18/02/2010	26/03/2010	Annex II	With this variation the MAH submitted a new version of the DDPS (core version 8.0 and product specific version 5.0) in

	Changes to QPPV Update of DDPS (Pharmacovigilance)				accordance with the current Pharmacovigilance guideline. After assessing the documentation the CHMP concluded that the submitted DDPS contained all required elements. Consequently, Annex II has been updated with the new version numb er of the agreed DDPS.