Zykadia

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
IAIN/0048/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	06/12/2023		Annex II and PL	

[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).

	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 B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site				
IA/0047	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	27/06/2023	n/a		
PSUSA/10372 /202210	Periodic Safety Update EU Single assessment - ceritinib	08/06/2023	n/a		PRAC Recommendation - maintenance
IA/0046	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	18/05/2023	n/a		
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/0043	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	07/06/2022	n/a		
R/0042	Renewal of the marketing authorisation.	16/12/2021	16/02/2022	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Zykadia in the approved indication remains favourable and

					therefore recommended the renewal of the marketing authorisation with unlimited validity. The pharmacotherapeutic group and ATC code of ceritinib were updated in the SmPC as per the WHO ATC/DDD updated index for ceritinib.
N/0041	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/09/2021	16/02/2022	PL	
IB/0040/G	This was an application for a group of variations. B.I.c.2.z - Change in the specification parameters and/or limits of the immediate packaging of the AS - 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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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 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.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other	23/08/2021	n/a		

	variation B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold 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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - 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.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 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 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				
IB/0039/G	This was an application for a group of variations. B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.z - Change in control of the AS - 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	06/08/2021	n/a		
IAIN/0038	To replace a site responsible for batch release of the Zykadia 150 mg hard gelatin capsule (EU/1/15/999/001-003). 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	28/05/2021	16/02/2022	Annex II and PL	
IB/0037/G	This was an application for a group of variations. B.II.e.2.z - Change in the specification parameters	07/04/2021	16/02/2022	Annex II and PL	

	and/or limits of the immediate packaging of the finished product - Other variation B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary 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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
II/0034	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect the results of study CLDK378A2112 as recommended by the CHMP. The study assesses the steady-state PK of 450 mg or 600 mg ceritinib taken daily with a low-fat meal as compared with that of 750 mg ceritinib taken daily in the fasted state in patients with metastatic ALK-positive NSCLC. The Package Leaflet is updated accordingly. The RMP version 16 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1. Other editorial changes include the addition of the Sodium content in the SmPCs and PLs and the removal of the black triangle C.I.4 - Change(s) in the SPC, Labelling or PL due to	11/03/2021	16/02/2022	SmPC, Annex II, Labelling and PL	The final efficacy and safety analysis of study CLDK378A2112 (ASCEND-8), a phase I study investigating the systemic exposure, efficacy, and safety of ceritinib administered at 450 mg or 600 mg with a low-fat meal vs. 750 mg in the fasted state following oral daily dosing in subjects with metastatic ALK-positive NSCLC, was submitted. Diarrhoea, nausea, or vomiting occurred in 76.9% of 108 patients treated with Zykadia at the recommended dose of 450 mg taken with food in a dose optimisation study and were mainly grade 1 (52.8%) and grade 2 (22.2%) events. Two patients (1.9%) experienced one grade 3 event each (diarrhoea and vomiting respectively). Nine patients (8.3%) required study drug interruption due to diarrhoea, nausea or vomiting. One patient (0.9%) required dose adjustment due to vomiting. In the same study, the incidence and severity of gastrointestinal adverse drug

	new quality, preclinical, clinical or pharmacovigilance data				reactions were higher for patients treated with Zykadia 750 mg fasted (diarrhoea 80.0%, nausea 60.0%, vomiting 65.5%; 17.3% reported a grade 3 event) compared to 450 mg with food (diarrhoea 59.3%, nausea 42.6%, vomiting 38.0%; 1.9% reported a grade 3 event). In the 450 mg with food and 750 mg fasted arms of this dose optimisation study, no patients required discontinuation of Zykadia due to diarrhoea, nausea or vomiting. A total of 147 previously untreated patients with ALK positive locally advanced or metastatic NSCLC were randomised to receive Zykadia 450 mg once daily with food (N=73) or Zykadia 750 mg once daily under fasted conditions (N=74). The ORR was comparable in the treatment arms; 78.1% (95% CI: 66.9, 86.9) in the 450 mg fed arm, and 75.7% (95% CI: 64.3, 84.9) in the 750 mg fasted arm. For more information, please refer to the Summary of Product Characteristics.
IA/0036/G	This was an application for a group of variations. 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 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	11/12/2020	n/a		

IA/0035	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	01/12/2020	n/a		
IA/0033/G	This was an application for a group of variations. 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 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 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 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 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	24/06/2020	n/a		

	new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				
PSUSA/10372 /201910	Periodic Safety Update EU Single assessment - ceritinib	14/05/2020	n/a		PRAC Recommendation - maintenance
IB/0031/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/importer 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/importer of the finished product, including quality control sites (excluding manufacturer for batch release) 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	13/01/2020	14/01/2021	SmPC, Annex II and PL	

	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 B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold 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) B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation				
PSUSA/10372 /201810	Periodic Safety Update EU Single assessment - ceritinib	16/05/2019	n/a		PRAC Recommendation - maintenance
X/0025	Annex I_2.(d) Change or addition of a new pharmaceutical form	31/01/2019	02/04/2019	SmPC, Labelling and PL	
II/0026	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/01/2019	11/03/2019	SmPC and PL	
II/0027	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/02/2019	n/a		

IA/0029/G	This was an application for a group of variations. 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 B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material	19/12/2018	n/a		
IB/0028	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	07/12/2018	n/a		
II/0016	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	31/05/2018	06/07/2018	SmPC and PL	The SmPC has been modified to include a recommendation that a dose reduction by approximately one-third is recommended in patients with severe hepatic impairment. Additionally, those patients should be carefully monitored for hepatotoxicity.

T/0024	Transfer of Marketing Authorisation	09/05/2018	07/06/2018	SmPC, Labelling and PL	
IB/0023/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits	29/05/2018	n/a		
IB/0022/G	This was an application for a group of variations. 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 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.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 B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	29/05/2018	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold 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.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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.1.z - Change in the specification parameters and/or limits of an AS, starting				

	material/intermediate/reagent - Other variation 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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.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.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 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				
PSUSA/10372 /201710	Periodic Safety Update EU Single assessment - ceritinib	17/05/2018	n/a		PRAC Recommendation - maintenance
II/0015	C.I.4 - Change(s) in the SPC, Labelling or PL due to	22/03/2018	23/04/2018	SmPC and PL	The recommended dose of Zykadia is 450 mg taken orally

	new quality, preclinical, clinical or pharmacovigilance data				once daily with food at the same time each day. It is important that Zykadia is taken with food to reach the appropriate exposure. Food can range from a light to a full meal. The maximum recommended dose with food is 450 mg taken orally once daily. If vomiting occurs during the course of treatment, the patient should not take an additional dose, but should continue with the next scheduled dose. In case severe or intolerable nausea, vomiting or diarrhoea despite optimal anti emetic or anti diarrhoeal therapy occur, withhold Zykadia until improved, then reinitiate Zykadia with dose reduced by 150 mg. Zykadia should be discontinued in patients unable to tolerate 150 mg daily taken with food. For patients who develop a concurrent medical condition and are unable to take Zykadia with food, Zykadia can be taken on an empty stomach as the alternate continued treatment regimen, in which no food should be eaten for at least two hours before and one hour after the dose. Patients should not alternate between fasted and fed dosing. Dose must be adjusted properly, i.e for patients treated with 450 mg or 300 mg with food, the dose should be increased to 750 mg or 450 mg taken on an empty stomach, respectively and for patients treated with 150 mg with food treatment should be discontinued. The maximum allowable dose under fasted condition is 750 mg. For more information please refer to the Summary of Product Characteristics.
PSUSA/10372 /201704	Periodic Safety Update EU Single assessment - ceritinib	30/11/2017	n/a		PRAC Recommendation - maintenance

IB/0019	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	20/11/2017	n/a		
IAIN/0020	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	10/11/2017	23/04/2018	SmPC, Labelling and PL	
IB/0018	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	09/11/2017	n/a		
II/0010	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/05/2017	26/07/2017	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion Zykadia EMEA/H/C/003819/II/0010.
II/0012	Extension of Indication to include new indication/population for Zykadia as first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC); as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect the information based primarily on the supporting study, CLDK378A2301 (ASCEND-4). The Package Leaflet is updated in accordance. The Risk Management Plan version 10.0 was agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	18/05/2017	23/06/2017	SmPC and PL	Please refer to the Scientific Discussion Zykadia EMEA/H/C/003819/II/0012.

PSUSA/10372 /201610	Periodic Safety Update EU Single assessment - ceritinib	09/06/2017	n/a		PRAC Recommendation - maintenance
R/0009	Renewal of the marketing authorisation.	26/01/2017	22/03/2017		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Zykadia, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
II/0006/G	This was an application for a group of variations. Update of section 4.5 of the SmPC based on the final results of the clinical pharmacology study LDK378A2113 and results of a sub-group evaluating the impact of gastric PH-elevating agents on the steady-state PK, efficacy, and safety of ceritinib in ALK-positive NSCLC patients. The provision of the final CSR for study CLDK378A2113 addresses the post-authorisation measure (PAM) MEA 003. In addition, an updated RMP version 8.0 was agreed during the procedure. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	23/02/2017	23/06/2017	SmPC	Ceritinib demonstrates pH-dependent solubility and becomes poorly soluble as pH increases in vitro. Acid reducing agents (e.g., proton pump inhibitors, H2-receptor antagonists, antacids) can alter the solubility of ceritinib and reduce its bioavailability. Co administration of a single 750 mg ceritinib dose with a proton pump inhibitor (esomeprazole) 40 mg daily for 6 days in healthy, fasting subjects decreased ceritinib AUC by 76% and Cmax by 79%. A dedicated study to evaluate the effect of gastric acid reducing agents on the bioavailability of ceritinib under steady state has not been conducted. Caution is advised with concomitant use of proton pump inhibitors, as exposure of ceritinib may be reduced. There is no data with concomitant use of H2 blockers or antacids. However, the risk for a clinically relevant decrease in bioavailability of ceritinib is possibly lower with concomitant use of H2 blockers if they are administered 10 hours before or 2 hours after the ceritinib dose, and with antacids if they are administered 2 hours before or 2 hours after the ceritinib

					dose.
IB/0014	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	31/01/2017	n/a		
PSUSA/10372 /201604	Periodic Safety Update EU Single assessment - ceritinib	01/12/2016	n/a		PRAC Recommendation - maintenance
IB/0011	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	30/11/2016	n/a		
II/0008	To update section 5.1 (Pharmacodynamic properties) of the Summary of Product Characteristics as a result of the completion of a study related to a specific obligation of the marketing authorisation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/09/2016	22/03/2017	SmPC and Annex II	With this variation the MAH fulfilled one Specific Obligation linked to the MA for Zykadia "In order to further confirm the efficacy of ceritinib in the treatment of patients previously treated with crizotinib, the MAH should submit the final results of the phase II single-arm efficacy study A2201", by providing the final study report for study A2201. The final analysis confirmed the previous conclusion in terms of efficacy of ceritinib: results in patients with prior ALK inhibitor treatment have a meaningful clinical value since there is an unmet medical need. Although more mature data has been provided, the absence of controlled studies dot not allow a better understanding of the benefit on progression-free survival (PFS), the real effect on patient reported outcomes (PROs) and on overall survival (OS). No new safety concerns have been identified in this final analysis. The higher frequency of some adverse events (AEs) and serious adverse events (SAEs) (regardless of

					study drug relationship) is likely to be related to the longer period of study. Section 5.1 "Pharmacodynamic properties" of the SmPC was updated based on the conclusions from Study A2201. All the potential concerns are already described into the SmPC, with adequate warnings in section 4.4. In addition, reference to SOB 005 was deleted from the Annex II for Zykadia, as this condition has been fulfilled.
PSUSA/10372 /201510	Periodic Safety Update EU Single assessment - ceritinib	13/05/2016	n/a		PRAC Recommendation - maintenance
R/0004	Renewal of the marketing authorisation.	28/01/2016	22/03/2016		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Zykadia, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IB/0003	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/10/2015	n/a		
II/0001	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to include posology recommendations and to update the safety information after the MAH's assessment of the association between the use of ceritinib and acute pancreatitis. The Package Leaflet is updated accordingly. In addition, the updated RMP version 2.5 has been submitted.	23/07/2015	25/08/2015	SmPC and PL	Elevations of lipase and/or amylase have occurred in patients treated with ceritinib in clinical studies. Patients should be monitored for lipase and amylase elevations prior to the start of Zykadia treatment and periodically thereafter as clinically indicated. Cases of pancreatitis have been reported in patients treated with ceritinib. In case of lipase or amylase elevation grade ≥3, withhold

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Zykadia until lipase or amylase returns to grade ≤1, then reinitiate with dose reduced by one decrement.
IB/0002	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	11/06/2015	25/08/2015	SmPC, Labelling and PL	