EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Translarna

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
PSUSA/10274 /202407	Periodic Safety Update EU Single assessment - ataluren	13/02/2025	13/02/2025		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10274/202407.
IAIN/0078/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release	28/10/2024	10/02/2025	SmPC, Annex II, Labelling	

[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 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.1 - Administrative change - Change in the name and/or address of the MAH			and PL	
PSUSA/10274 /202401	Periodic Safety Update EU Single assessment - ataluren	05/09/2024	05/09/2024		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10274/202401.
PSUSA/10274 /202307	Periodic Safety Update EU Single assessment - ataluren	07/03/2024	07/03/2024		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10274/202307.
II/0074	The CHMP is of the opinion that the requested update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology information in paediatric population, to update the summary of safety profile and to update pharmacokinetic information on paediatric population based on the final results from study PTC124-GD-048-DMD "A Phase 2, multiple-dose, open-label study evaluating the safety and PK of ataluren in patients with nmDMD aged ≥6 months to <2 years old" (as well as the subsequent updates to the Package Leaflet and the additional editorial changes to the PI are supported by the data submitted. However, in view of the CHMP opinion for the annual renewal EMEA/H/C/002720/R/071	22/02/2024		SmPC and PL	Not applicable Please refer to Scientific Discussion 'Translarna-H-C-002720-II-74'.

	adopted on 24 January 2024 to not recommend the renewal of the marketing authorisation of Translarna, as a favourable benefit-risk balance was not confirmed in the treatment of ambulant patients with nmDMD aged 2 years or older, no changes to the marketing authorisation can be recommended at this stage. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0075	B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	08/11/2023	n/a		
PSUSA/10274 /202301	Periodic Safety Update EU Single assessment - ataluren	31/08/2023	n/a		PRAC Recommendation - maintenance
PSUSA/10274 /202207	Periodic Safety Update EU Single assessment - ataluren	16/03/2023	n/a		PRAC Recommendation - maintenance
II/0068	Update of section 5.1 of the SmPC in order to update efficacy information upon the request by the CHMP following the outcome of P46/026 based on final results from study PTC124-GD-045-DMD (Study 045); this is an open-label, single-arm, phase 2 study designed to evaluate the ability of ataluren treatment to increase dystrophin protein levels in muscle cells of subjects with nonsense mutation Duchenne muscular dystrophy (nmDMD). C.I.3.b - Change(s) in the SPC, Labelling or PL	16/03/2023	09/02/2024	SmPC	Section 5.1 of the SmPC is updated to include a brief description of the exploratory PTC124-GD-045-DMD aiming to explore quantitative levels of dystrophin in muscle tissue before and after 40 weeks of treatment with ataluren in 20 subjects with nmDMD aged 2-7 years. The baseline median dystrophin level as measured by electrochemiluminescence assay was 0.42% of normal (range 0.00% to 41.85%). At the end of the study, the median dystrophin level was 0.33% of normal (range 0.04% to 48.55%). For immunohistochemistry assay, the median percentage of positive fibres at baseline was 73% (range 0.42% to

	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				99.6%). At the end of the study, the median percentage of positive fibres was 66% (range 0.51% to 99.77%). At the end of the study, the mean (median) worsening from baseline on the rNSAA was 0.1 (1.0) points in total score and the mean (median) change from baseline for the time to stand, to run or walk 10 meters, climb 4 stairs, and descend 4 stairs was -1.56 (-0.6), -0.41 (-0.35), -1.09 (-0.5), and -2.43 (-0.7) seconds, respectively. For more information, please refer to the Summary of Product Characteristics.
IA/0072/G	This was an application for a group of variations. B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	15/03/2023	n/a		
R/0067	Renewal of the marketing authorisation.	22/04/2022	20/06/2022		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 Translarna, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
PSUSA/10274 /202107	Periodic Safety Update EU Single assessment - ataluren	10/03/2022	n/a		PRAC Recommendation - maintenance

IA/0066/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.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)	04/02/2022	n/a		
R/0061	Renewal of the marketing authorisation.	22/04/2021	17/06/2021		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 Translarna, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.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 Translarna, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IB/0063	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other	16/04/2021	n/a		

	variation				
IB/0064	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	15/04/2021	n/a		
N/0062	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/04/2021	17/06/2021	PL	
PSUSA/10274 /202007	Periodic Safety Update EU Single assessment - ataluren	11/03/2021	n/a		PRAC Recommendation - maintenance
R/0057	Renewal of the marketing authorisation.	28/05/2020	23/07/2020		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 Translarna, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0058	Update of section 4.1 of the SmPC to remove the statement 'efficacy has not been demonstrated in non-ambulatory patients' based on SmPC guideline and the 'Guide for Assessors of Centralised Applications' on the wording of the therapeutic indication'. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/06/2020	17/06/2021	SmPC	Update of section 4.1 of the SmPC to remove the sentence "efficacy has not been demonstrated in non-ambulatory patients" based on SmPC guideline and the 'Guide for Assessors of Centralised Applications' on the wording of the therapeutic indication'. The removal of this sentence from the indication does not lift the currently imposed restriction. The currently approved therapeutic indication remains the same as the benefit-risk balance of Translarna remains positive only in ambulatory nmDMD patients aged ≥2years as indicated in Section 4.1 of the SmPC

					"Translarna is indicated for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 2 years and older (see section 5.1)."
IA/0059	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)	22/06/2020	n/a		
II/0056/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission	12/03/2020	n/a		

	of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
PSUSA/10274 /201907	Periodic Safety Update EU Single assessment - ataluren	13/02/2020	n/a		PRAC Recommendation - maintenance
II/0053/G	This was an application for a group of variations. C.I.4: Update of section 5.3 of the SmPC in order to update the safety information based on final results Charles River 9001126 Three-month juvenile toxicology and toxicokinetic study planned in neonatal dogs listed as category 3 study in the RMP (MEA-005). C.I.13 Submission of the final report from study WIL-523008 listed as category 3 study in the RMP (MEA/003). This is a Seven-day tolerability and pharmacokinetic study in neonatal dogs. C.I.13 Submission of the final report from study WIL-523009 listed as category 3 study in the RMP (MEA/004). This is a One-month juvenile dose range-finding toxicology and toxicokinetic study planned in neonatal dogs age correlating with dosing in new-born paediatric patients to 2 years of age. C.I.13 Submission of the final report from study (Charles River 5700755 listed as category 3 study in the RMP (MEA/0024). This is a 28-day investigational toxicology and toxicokinetic study of ataluren in juvenile beagle dogs with an 8-week recovery period – Category 3.	24/10/2019	23/07/2020	SmPC	The reports of 4 juvenile toxicity studies with ataluren in dogs did not find any relevant safety issue and therefore, toxicology studies support chronic administration of ataluren in patients as young as neonates (see SmPC 5.3).

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
R/0051	Renewal of the marketing authorisation.	29/05/2019	25/07/2019	Annex II	The CHMP recommended the renewal of the conditional marketing authorisation for Translarna, concluding that the MAH demonstrated that the criteria for the renewal of the conditional marketing authorization continued to be met, including a positive benefit-risk balance of Translarna in the context of a conditional approval. As a result of the annual renewal assessment, the due date of the Final study report (PTC124-GD-041-DMD) of the specific obligation has changed from 2021 to September 2022.
II/0046	Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In addition the MAH took the opportunity to amend section 5.2 to propose correction of the	26/04/2019	06/06/2019	SmPC and PL	No dosage adjustment is required for patients with mild or moderate renal impairment. Treatment of patients with severe renal impairment (eGFR <30 ml/min) or end-stage renal disease is not recommended. An increase in ataluren exposure and in ataluren metabolite has been reported in patients with severe renal impairment

	biotransformation statement. The Package leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				(eGFR <30 ml/min). The toxicity of the metabolite is unknown. Higher ataluren exposure was associated with potential decrease in efficacy. Therefore, patients with severe renal impairment or end-stage renal disease should be treated with ataluren only if the anticipated clinical benefit outweighs the potential risk, and should be closely monitored for possible metabolite toxicity and decrease in efficacy. A lower ataluren dose should be considered. Treatment should not be initiated in previously untreated patients with eGFR <30 ml/min.
IA/0054/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	31/05/2019	n/a		
IAIN/0052/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.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 B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	09/04/2019	06/06/2019	Annex II and PL	

PSUSA/10274 /201807	Periodic Safety Update EU Single assessment - ataluren	14/02/2019	n/a		PRAC Recommendation - maintenance
II/0045	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/02/2019	06/06/2019	SmPC and PL	
II/0049	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	31/01/2019	n/a		
IA/0050/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size 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.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.2.a - Change in test procedure for AS or	13/12/2018	n/a		

	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.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
II/0037	Extension of Indication to include a new population (children from 2 to less than 5 years of age) for Translarna; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 7.1) is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	31/05/2018	23/07/2018	SmPC and PL	Please refer to the published Assessment Report Translarna H-2720-II-37.
R/0041	Renewal of the marketing authorisation.	31/05/2018	19/07/2018		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 Translarna, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. No changes to SmPC are proposed.

IAIN/0044	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	11/06/2018	n/a		
IB/0043	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	21/05/2018	19/07/2018	SmPC and PL	
IB/0042	B.II.a.3.z - Changes in the composition (excipients) of the finished product - Other variation	12/04/2018	n/a		
II/0039	Update of sections 4.2, 4.4, and 5.2 of the SmPC to amend posology recommendations, delete a warning and include pharmacokinetic information about patients with hepatic impairment, respectively, based on final results from study PTC124-GD-033-HV (Study 033) listed as a category 3 study in the RMP (MEA009); the Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to implement some editorial changes C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/02/2018	23/03/2018	SmPC, Labelling and PL	Based on a pharmacokinetic assessment conducted in groups with either mild, moderate or severe hepatic impairment versus a control group of healthy subjects, no dose adjustment is required for patients with any degree of hepatic impairment. No apparent differences of the total ataluren exposure in the control, mild, and severe hepatic impairment groups were observed. An approximately 40% decrease of mean total ataluren exposure in the moderate hepatic impairment group versus the control group was noted probably due to the small sample size and variability
PSUSA/10274 /201707	Periodic Safety Update EU Single assessment - ataluren	08/02/2018	n/a		PRAC Recommendation - maintenance

IAIN/0038/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	12/10/2017	n/a		
II/0036	UUpdate of section 4.5 of the SmPC in order to include information regarding the effects of ataluren on the pharmacokinetics of sensitive probe substrate of organic anion transporter 3 (OAT3)) following results from study PTC124-GD-037-HV (MEA015). In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/09/2017	23/03/2018	SmPC, Labelling and PL	Caution should also be exercised when ataluren is co-administered with OAT3 substrates (eg, ciprofloxacin), especially those OAT3 substrates with a narrow therapeutic window. In a clinical study, the extent of exposure for ciprofloxacin was 32% higher in the presence of ataluren.
PSUSA/10274 /201701	Periodic Safety Update EU Single assessment - ataluren	01/09/2017	n/a		PRAC Recommendation - maintenance
R/0032	Renewal of the marketing authorisation.	21/04/2017	16/06/2017		
IB/0033	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	24/05/2017	n/a		

IAIN/0035/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH 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	23/05/2017	23/03/2018	SmPC, Annex II, Labelling and PL	
II/0031	Update of section 4.5 of the SmPC in order to introduce a new warning on interaction with adefovir based on results from study "Safety and PK study of co-administration of ataluren and a sensitive probe substrate of organic anion transporter 1 (OAT1)" (MEA014). The MAH took the occasion to correct minor typographical errors in the product information and to bring the PI in line with the QRD version 9.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/03/2017	16/06/2017	SmPC, Annex II and PL	In a clinical study, the extent of exposure for adefovir was 60% higher in the presence of ataluren. Caution should be exercised when ataluren is co-administered with adefovir.
PSUSA/10274 /201607	Periodic Safety Update EU Single assessment - ataluren	09/02/2017	n/a		PRAC Recommendation - maintenance
II/0027	Update of section 4.8 of the SmPC to add that the safety profile of ataluren in non-ambulatory patients was similar to the safety profile in ambulatory patients to reflect the results of a 48-week open label extension study in patients with nonsense mutation Duchenne Muscular Dystrophy (nmDMD).	26/01/2017	16/06/2017	SmPC	In a 48-week open-label extension study in patients with nmDMD patients who were ambulant or non-ambulant demonstrated a similar safety profile. Long term safety data is not available.

	The RMP is updated accordingly (version 6.3). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
R/0022	Renewal of the marketing authorisation.	23/11/2016	09/01/2017	Annex II	The CHMP, having reviewed the totality of the clinical data available including the final results of the study 020, is of the opinion that these continued to support the positive benefit-risk balance of Translarna in the context of a conditional approval. As a result of the annual renewal assessment, the specific obligation is revised as follows: In order to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with nmDMD aged 5 years or older, the MAH should conduct and submit the results of a two-phase multicentre, randomised study, including a double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension, according to an agreed protocol; (Final study report to be submitted: September 2021). Please refer to the assessment report for further details.
II/0016/G	This was an application for a group of variations. Update of section 4.4 to remove precautions for use relating to the co-administration of ataluren with substrates of UGT1A9 and section 4.5 of the SmPC to remove statements relating to the potential effect of co-administration of ataluren with substrates of UGT1A9 and to add results from studies PTC124-GD-026-HV and PTC124-GD-027-HV (MEA 011 and MEA	15/12/2016	16/06/2017	SmPC and PL	n/a

	012). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC. Moreover, the updated RMP version 4.2.2 has been agreed. 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				
IB/0030/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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products 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 B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	14/12/2016	n/a		

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size 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 B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
II/0020	Update of sections 4.4, 4.8, 5.1 and 5.3 of the SmPC in order to reflect the results from the submitted study TC124-GD-020-DMD object of the specific obligation (SOB 001) for the conditional marketing authorisation. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information.	23/11/2016	09/01/2017	SmPC and PL	The efficacy and safety of Translarna were assessed in 2 randomised, double-blind, placebo controlled, trials in nmDMD. The primary efficacy endpoint in both trials was change in 6 Minute Walk Distance (6MWD) at Week 48. Other endpoints included in both trials were time to persistent 10% worsening in 6MWD, change in time to run/walk 10 meters at Week 48, change in time to climb 4 stairs at Week 48, and change in time to descend 4 stairs at Week 48. Study 2 evaluated 230 male patients, ages 7 to 14 years.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Ataluren-treated patients experienced clinical benefit as measured by numerically favorable differences versus placebo across the primary and secondary efficacy endpoints. As the primary endpoint (change in 6MWD from baseline to Week 48) did not reach statistical significance ($p \leq 0.05$), all other p values should be considered nominal. Separation between ataluren and placebo was maintained from Week 16 through the end of the study. The most common adverse reactions in the 2 placebo-controlled studies were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence, all occurring in ≥5% of all ataluren-treated patients. Lipid levels shifted from normal at baseline to high (above the upper limit of normal) at Week 48 in slightly higher percentages of patients receiving ataluren compared to those receiving placebo (total cholesterol 15.1% vs. 6.1%, triglycerides 21.1% vs. 13.4%, respectively). In both studies, 1/232 (0.43%) patients treated with ataluren discontinued due to an adverse reaction of constipation and 1/172 (0.58%) placebo patients discontinued treatment due to an adverse reaction of disease progression (loss of ambulation). Adverse reactions were generally mild or moderate in severity, and no treatment-related serious adverse events were reported among ataluren-treated patients in these 2 studies.
II/0026	Update of sections 4.4 and 4.5 of the SmPC to remove the interaction with inhibitors of breast cancer resistant protein (BCRP) based on the results of a drug-drug interaction study of the co-administration of ataluren and inhibitors of BCRP. The package leaflet and the RMP (version 6.2) are	10/11/2016	09/01/2017	SmPC and PL	n/a

	updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0028/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	07/10/2016	n/a		
PSUSA/10274 /201601	Periodic Safety Update EU Single assessment - ataluren	02/09/2016	n/a		PRAC Recommendation - maintenance
IB/0025	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	23/06/2016	n/a		
II/0019	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/05/2016	n/a		
IA/0024/G	This was an application for a group of variations. B.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation B.I.b.2.a - Change in test procedure for AS or	16/05/2016	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure				
PSUSA/10274 /201507	Periodic Safety Update EU Single assessment - ataluren	11/02/2016	n/a		PRAC Recommendation - maintenance
IAIN/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	08/02/2016	n/a		
IB/0018	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	17/12/2015	n/a		
IA/0017	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	02/12/2015	n/a		
IB/0013/G	This was an application for a group of variations. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	01/12/2015	n/a		
IB/0015	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/11/2015	11/11/2016	SmPC	

PSUSA/10274 /201501	Periodic Safety Update EU Single assessment - ataluren	10/09/2015	n/a		PRAC Recommendation - maintenance
R/0007	Renewal of the marketing authorisation.	21/05/2015	28/07/2015		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 Translarna, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IAIN/0011	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	16/07/2015	n/a		
II/0005/G	This was an application for a group of variations. Submission of non-clinical study 100011749 (Study of Ataluren (PTC124) and M4 metabolite in the β3 binding assay) and non-clinical study 100012124 (Study of ataluren (PTC124) and M4 (PTC-0256858-04) functional activity in a beta-3 adrenergic cellular assay) in fulfilment of MEA006; the RMP is updated accordingly (version 3.0). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	25/06/2015	n/a		

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IB/0008/G	This was an application for a group of variations. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/06/2015	n/a		
IAIN/0010	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	21/05/2015	n/a		
IB/0006/G	This was an application for a group of variations. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	05/05/2015	n/a		
IAIN/0003	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/01/2015	28/07/2015	SmPC	

IA/0004	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	22/01/2015	n/a		
IAIN/0002	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	28/11/2014	n/a		
T/0001	Transfer of Marketing Authorisation	22/09/2014	10/10/2014	SmPC, Labelling and PL	