Exubera

Procedural steps taken and scientific information after the authorisation

MAJOR CHANGES[1]

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
II/0015	Update of section 4.4 of the Summary of Product Characteristics to include information on observed lung cancer cases.	30/05/2008	09/07/2008	SPC	In clinical trials of Exubera, there have been 6 newly diagnosed cases of primary lung malignancies among Exubera-treated patients, and 1 newly diagnosed case among comparator treated patients. There has also been 1 post-marketing report of a primary lung malignancy in an Exubera-treated patient. All patients who were diagnosed with lung cancer had a prior history of cigarette smoking. There were too few cases to determine whether the emergence of these events is related to Exubera. The CHMP requested the MAH to update section 4.4 of the Summary of Product Characteristics to include the information above.
II/0014	Update of Summary of Product Characteristics and Package Leaflet	13/12/2007	25/01/2008	SPC, PL	Update of sections 4.4 and 6.6 of the Summary of Product Characteristics (SPC) and of the Package Leaflet to include a stricter wording regarding exposure of the inhaler to extremely moist conditions which usually decrease the emitted dose of insulin.
II/0012	Quality changes	19/07/2007	24/07/2007		
II/0011	Update of the section 4.4 of the Summary of Product Characteristics (SPC) to include a warning regarding pulmonary function in line with the Core Data Sheet (CDS). In addition information on improvement in blister design was added in the Package Leaflet (PL) following the submission of a follow-up measure. The Marketing Authorisation Holder (MAH) also took the opportunity to update the annexes in line with the current QRD template version (version 7.2) and to update the list of local representatives in the Package Leaflet.	19/07/2007	29/08/2007	SPC, Annex II, Labelling, PL	Across the clinical development program for Exubera, subjects with a baseline FEV1 < 70% predicted were excluded from participation within the studies. The rationale for this exclusion criteria was based on the MAH's initial goal of fully characterising the effect of Exubera therapy on the lung of patients with relatively normal lung function prior to studying Exubera in patients with lung processes such as asthma or COPD. This guidance has therefore been incorporated into the CDS. In line with the CDS the following warning has been included in Section 4.4 of the SPC under the sub heading "Decline in pulmonary function". All patients initiated on EXUBERA should have a baseline lung function examination (e.g. spirometry to measure FEV1). The efficacy and safety of inhaled human insulin in patients with baseline FEV1 < 70% predicted have not been established and the use of inhaled human insulin in this population is not recommended. A follow-up lung function measurement is recommended

[1] Major changes e.g. Type II variations, Annex II applications, Renewals and Annual Reassessments
[2] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet)

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					after the first 6 months of therapy. If at 6 months a decline of < 15% FEV1 is observed, spirometry should be repeated at one year and then annually. If at 6 months a decline of 15-20% or > 500ml from baseline lung function is observed, spirometry should be repeated after 3 months. Information on improvement in blister design was added in the Package Leaflet (section 6) following the submission of a follow-up measure. The information is also reflected in the instruction for Use Leaflet. The Marketing Authorisation Holder (MAH) also took the opportunity to update the annexes in line with the current QRD template version (version 7.2) and to update the list of local representatives in the Package Leaflet.
II/0006	Quality changes	24/01/2007	29/01/2007		
II/0005	Quality changes	14/12/2006	19/12/2006		
T/0001	Transfer of Marketing Authorisation Holder	03/03/2006	21/03/2006	SPC, Labelling, PL	

MINOR CHANGES[3]

No	Scope	Product Information affected[2]	Date[4]
IA/0010	04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	Annex II	17/04/2007
IA/0009	06_a_Change in ATC code: Medicinal products for human use	SPC, Labelling, PL	08/03/2007
IA/0008	07_a_Replacement/add. of manufacturing site: Secondary packaging site		18/12/2006
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	Labelling, PL	13/02/2007
IA/0002	41_a_01_Change in pack size - change in no. of units within range of appr. pack size	SPC, Labelling, PL	12/04/2006

[3] Minor changes e.g. Type I variations and Notifications
[4] Date of entry into force of the change