Procedural steps taken and scientific information after the authorisation
Changes made after 01/02/2004

Trazec

For procedures finalised before 01/02/2004, please refer to module 8A

MAJOR CHANGES[1]

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
II/0016	Update of Summary of Product Characteristics and Package Leaflet This variation refers to an update of section 4.8 of the Summary of Product Characteristics concerning gastro-intestinal events associated with nateglinide following a request from the CHMP to reflect the findings from a six month observational safety study in patients treated with nateglinide or gliclazide in combination with metformin. The Package Leaflet has been updated accordingly.	01/06/2006	13/07/2006	SPC, PL	Study DJN608AGB05 was a 6-months multi center, prospective, observational non interventional and non blinded study in subjects treated with either nateglinide or gliclazide in combination with metformin. A statistically significant difference in the frequency of gastrointestinal disorders was reported between the total nateglinide and total gliclazide groups (5.6 vs. 0.4%! ; p<0.001). This was the only System Organ Class (SOC) for which a significant difference was observed between treatment groups. The SPC has been updated to reflect these findings and therefore abdominal pain, diarrhoea, dyspepsia, nausea and vomiting have been included as an adverse reaction in section 4.8 of the SPC. Section 4 of the Package Leaflet has been updated accordingly.
R/0015	Renewal of the marketing authorisation	23/02/2006	24/04/2006	SPC, Annex II, Labelling, PL	
II/0014	Update of Summary of Product Characteristics, Labelling and Package Leaflet The Marketing Authorisation Holder (MAH) applied for this variation to update section 5.1 of the Summary of product Characteristics (SPC) to reflect information from a study comparing the efficacy of nateglinide plus metformin versus a sulphonylurea plus metformin, as requested	27/07/2005	05/09/2005	SPC, Labelling, PL	The efficacy of nateglinide in combination with metformin has been compared to the combination of gliclazide plus metformin in a 6-month randomised, double-blind trial in 262 patients using a superiority design. The decrease from baseline in HbA_{1C} was –0.41% in the nateglinide plus metformin group and -0.57% in the gliclazide plus metformin group (difference 0.17%, 95% CI -0.03, 0.36). Both treatments were well-tolerated. Section 5.1 of the SPC has been updated to reflect this information.

[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)

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
	by the CHMP. In addition, the MAH applied for a combined labelling text, combining the different pack-sizes of the same strength in accordance to the QRD template. The MAH also applied to include minor linguistic changes in different language versions of the Package Leaflet.				
II/0011	Update of Summary of Product Characteristics and Package Leaflet Update of the SPC and PL following the assessment of the 5th Periodic Safety Update Report.	03/06/2004	02/08/2004	SPC, Annex II, PL	As a response to the CHMP conclusions of the 5th Periodic Safety Update Report covering the period 1 January 2003 to 30 June 2003, the Marketing Authorisation Holder applied in this type II variation to add a warning to section 4.4 of the Summary of Product Characteristics (SPC) for the risk of hypoglycaemia in patients with severe renal impairment. A recommendation has also been added to section 4.2 of the SPC for a starting dose at 60 mg three times daily in patients who are close to their therapeutic target, assessed by HbA1c levels. Consequential changes have been made to the Package Leaflet.

MINOR CHANGES[3]

No	Scope	Product Information affected[2]	Date[4]
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	PL	23/07/2007
IA/0013	05_Change in the name and/or address of a manufacturer of the finished product		11/11/2004
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	PL	28/05/2004
IB/0010	13_b_Change in test proc. for active substance - other changes (replacement/addition)		28/04/2004
IB/0009	10_Minor change in the manufacturing process of the active substance		01/04/2004

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