COMPARATIVE TABLE
SHOWING SUBSTANTIAL MODIFICATIONS TO THE DOCUMENT PREVIOUSLY SUBMITTED
Concerned document: Investigator's Brochure Nintedanib
N° and date of the previous version: version 14 dated on 19 JANUARY 2015
N° and date of the new version: version 15 dated on 06 JUNE 2016

INITIAL TEXT	MODIFIED or ADDED TEXT	JUSTIFICATION OF THE CHANGE
Section 6.4 - MARKETING EXPERIENCE	**Section 6.4 - MARKETING EXPERIENCE** *During the late-breaking period of this IB-update, data concerning "pancreatitis" in patients taking nintedanib for the treatment of IPF and oncological indications were reviewed. Following this review, it has been recommended to include 'pancreatitis' as adverse reaction in the Reference Safety Information for nintedanib. This update does not affect the benefit risk-ratio of nintedanib.*	**Impact on the safety of the clinical trial participants and / or clinical trial protocol:** NO **Impact on the Reference Safety Information;** YES **New toxicological or pharmacological data or new interpretation of toxicological or pharmacological data which is of interest for the investigator.** NO
Section 8.2 LISTED ADVERSE EVENTS Table 8.2: 1 Listed AEs SOC Gastrointestinal disorders **Uncommon** (≥ 1/1,000 < 1/100) - Perforation SOC Hepatobiliary disorders **Very common (≥ 1/10)**	**Section 8.2 LISTED ADVERSE EVENTS** Table 8.2: 1 Listed AEs SOC Gastrointestinal disorders **Uncommon** (≥ 1/1,000 < 1/100) - Perforation - *Pancreatitis* [3] [3] *Events of pancreatitis have been reported in patients taking nintedanib for the treatment ofiPF and NSCLC. The majority of these events were reported for*	**Impact on the safety of the clinical trial participants and / or clinical trial protocol:** YES/NO **Impact on the Reference Safety Information;** YES **New toxicological or pharmacological data or new**

Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood alkaline phosphatase increased Gamma-Glutamyl **Common (≥ 1/100 < 1/10)** Hyperbilirubinaemia	*patients in the IPF indication.* SOC Hepatobiliary disorders **Very common (≥ 1/10)** Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood alkaline phosphatase increased ~~Gamma-Glutamyl~~ **Common (≥ 1/100 < 1/10)** Hyperbilirubinaemia *Gamma-Glutamyl Transferase increased*	**interpretation of toxicological or pharmacological data which is of interest for the investigator.** NO

Legend

- *In italic* = new information added in IB version 15 compared to IB version 14
- ~~Crossed~~ = information deleted from IB version 14