Dose Modification Schedule & Management of adverse reactions to Nintedanib (Vargatef®)

Table 1 : Recommended dose adjustments for Nintedanib (Vargatef®) in case of diarrhoea, vomiting and other non-haematological or haematological adverse reactions.

CTCAE* Adverse reaction	**Dose adjustment**
Diarrhoea ≥ grade 2 for more than 7 consecutive days despite anti-diarrhoeal treatment ***OR*** Diarrhoea ≥ grade 3 despite anti-diarrhoeal treatment	After treatment interruption and recovery to grade 1 or baseline, dose reduction from 200 mg twice daily to 150 mg twice daily and - if a 2nd dose reduction is considered necessary - from 150 mg twice daily to 100 mg twice daily.
Vomiting ≥ grade 2 ***AND/OR*** Nausea ≥ grade 3 despite anti-emetic treatment	
Other non-haematological or haematological adverse reaction of ≥ grade 3	

* CTCAE: Common Terminology Criteria for Adverse Events

Table 2: Recommended dose adjustments for Nintedanib (Vargatef®) in case of AST and/or ALT and bilirubin elevations

AST / ALT and bilirubin elevations	**Dose adjustment**
Elevation of AST and/or ALT values to > 2.5 x ULN in conjunction with total bilirubin elevation to ≥ 1.5 x ULN ***OR*** Elevation of AST and/or ALT values to > 5x ULN	After treatment interruption and recovery of transaminase-values to ≤ 2.5 x ULN in conjunction with bilirubin to normal, dose reduction from 200 mg twice daily to 150 mg twice daily and - if a 2nd dose reduction is considered necessary - from 150 mg twice daily to 100 mg twice daily.
Elevation of AST and/or ALT values to > 3 x ULN in conjunction with an increase of total bilirubin to ≥ 2 x ULN and ALKP < 2 x ULN	Unless there is an alternative cause established, Nintedanib should be permanently discontinued

Written by S Wade/C Waters
Approved by Lung NOG
Version 1 (12/09/2016)
N.B. Version numbers re-started from 1 when adverse reaction information separated from proforma