NINTEDANIB DOCETAXEL

INDICATION (ICD10) C34

1. Previously treated locally advanced, metastatic, or locally recurrent NSCLC. PS 0, 1, 2 (TA347).

REGIMEN

Cycles 1 to 6

Day 1 Premedication: Dexamethasone 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days
DOCETAXEL 75mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

Days 2 to 21 NINTEDANIB 200mg twice daily orally

Cycle 7 onwards (must have completed at least 4 cycles in combination with docetaxel)

NINTEDANIB 200mg twice daily orally continuously (use nintedanib regimen to prescribe)

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for at least 4 cycles, up to 6 cycles
If completed at least 4 cycles of docetaxel nintedanib combination, nintedanib may continue as monotherapy (prescribe nintedanib regimen), until disease progression.

ADMINISTRATION

Available as 100mg and 150mg capsules.
Swallow whole preferably with food
Nintedanib is contra-indicated in patients allergic to peanut or soya.

ANTI-EMETICS

Low risk all days

CONCURRENT MEDICATION REQUIRED

Docetaxel	Ensure premedication given before docetaxel. This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. Loperamide prn every docetaxel cycle
Nintedanib	Ensure patient has supply of loperamide

EXTRAVASATION AND TYPE OF LINE / FILTERS

Docetaxel – exfoliant

Filter not required
Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Docetaxel	Cutaneous reactions, peripheral neuropathy or fluid retention, hypersensitivity reactions
Nintedanib	Diarrhoea, raised LFTs, haemorrhage, thromboembolism

DOSE MODIFICATIONS

The docetaxel dose can be reduced, only once, as follows:
• from 75mg/m^2 to 60mg/m^2
• patients that require a second docetaxel reduction and have not completed a minimum of 4 cycles of combination therapy should be discontinued. Those that have completed 4 cycles may continue to receive nintedanib monotherapy.
In some cases treatment should be temporarily interrupted, to allow for the adverse event to recover to CTCAE grade ≤1 or baseline before re-starting at a reduced dose.

Haematological

Docetaxel
In patients who experienced either febrile neutropenia, neutrophil count <0.5x10^9/L for more than one week, severe or cumulative cutaneous reactions or severe peripheral neuropathy during docetaxel therapy, the dose of docetaxel should be reduced from 75 to 60mg/m². If the patient continues to experience these reactions at 60mg/m², the treatment should be discontinued.

Non haematological

Docetaxel
Discuss dose reductions if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Nintedanib
As initial measure for the management of adverse reactions treatment with nintedanib should be temporarily interrupted until the specific adverse reaction has resolved to levels that allow continuation of therapy (to grade 1 or baseline).
Nintedanib treatment may be resumed at a reduced dose. Dose adjustments in 100mg steps per day (ie a 50mg reduction per dosing) based on individual safety and tolerability are recommended.
In case of further persistence of the adverse reaction(s), ie if a patient does not tolerate 100mg twice daily, treatment with nintedanib should be permanently discontinued.

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

Hepatic impairment

Docetaxel

ALT and/or AST >1.5xULN and ALP >2.5xULN	SPC contains dose recommendations for 100mg/m^2 only therefore clinician discretion
Bilirubin >ULN and ALT and AST >3.5xULN with ALP >6xULN	should not be used unless strictly indicated.

Nintedanib

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

Renal impairment

Nintedanib

Cases of renal impairment/failure, in some cases with fatal outcome, have been reported with nintedanib use, patients should be monitored, with particular attention to those patients exhibiting risk factors for renal impairment / failure.

REFERENCES

1. Shepherd F et al. J Clin Oncol 2000; 18: 2095-2103.
2. Fossella F et al. J Clin Oncol 2000; 18: 2354-2362