Vandetanib

Indication
First line treatment of histologically confirmed, unresectable, locally advanced or metastatic medullary thyroid cancer in patients with progressive and symptomatic disease.

ICD-10 codes
Codes with a pre-fix C73.

Regimen details

Day	Drug	Dose	Route
1-28*	Vandetanib	300mg OD	PO

*continuously

****start all patients on 200mg once daily increasing to 300mg once daily after two weeks if well tolerated, blood pressure controlled, ECG stable and blood tests unremarkable.**

Cycle frequency
28 days

Number of cycles
Continue until disease progression or unacceptable toxicity

Administration
Vandetanib is available as 100mg and 300mg tablets. Vandetanib should be taken at the same time each day, with or without food. If a dose is missed, it should be taken as soon as the patient remembers. If it is less than 12 hours before the next dose is due, patients should not take the missed dose.

If a patient is unable to swallow, the tablets may be dispersed in half a glass of non-carbonated water. The tablets should be dropped in the water and stirred until dispersed (approximately 10 minutes). The resultant liquid should be swallowed immediately and then the glass rinsed with a further half glass of water which should then also be swallowed. The liquid may also be administered via a nasogastric or gastrostomy tube.

Pre-medication
Nil

Emetogenicity
This regime has low emetic potential.

Additional supportive medication
Patients should be supplied with loperamide on commencing treatment. They should be advised to use loperamide immediately at the first sign of diarrhoea and continue for persistent diarrhoea until loose movements cease.

Patients should be advised to use a regular moisturiser from the start of vandetanib treatment to prevent and minimise problems with skin dryness.

No routine prophylactic anti-emetics required but all patients to be given an initial prescription of antiemetics (as per local policy) to use as required.

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U + E (including creatinine)	14 days
LFTs	14 days
Calcium	14 days
Magnesium	14 days
TSH	14 days
ECG	14 days
Blood pressure	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	7 days
U + E (including creatinine)*	7 days
LFTs	7 days
Calcium*	7 days
Magnesium*	7 days
TSH*	7 days
ECG*	7 days
Blood pressure	7 days

* should be carried out 3, 6 and 12 weeks after starting treatment and then 3 monthly for at least 1 year. This additional monitoring should also be carried out after a dose reduction due to QTc prolongation or after a ≥ 2 week break in treatment.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine clearance	≥ 30mL/min
AST/ALT	< 1.5 x ULN
Bilirubin	< 1.5 x ULN
Calcium	≥ 2.20
Magnesium	≥ 0.70
ECG QTc	≤ 480ms

Dose modifications

Dose level	Vandetanib dose
Full dose	300mg OD
1st dose reduction	200mg OD
2nd dose reduction	100mg OD
Further dose reductions	Not recommended

- **Haematological toxicity**

If neutrophils <1.0 x 10^9/L and/or platelets <100 x 10^9/L delay until recovery and recommence with a one level dose reduction. More than two dose reductions are not recommended.

- **Renal impairment**

CrCl (mL/min)	**Vandetanib dose**
≥50	300mg OD
30 - 49	200mg OD
<30	Not recommended due to limited data

- **Hepatic impairment**

Vandetanib is not recommended for use in patients with hepatic impairment (bilirubin > 1.5 x ULN) since there is limited data in patients with hepatic impairment and safety and efficacy have not been established.

- **Other toxicities**

Toxicity	**Definition**	**Dose adjustment**
Prolonged QTc	480-<500ms	If QTc increases markedly but remains below 500ms – seek cardiologist advice.
	≥ 500ms	Withhold vandetanib. Resume at reduced dose with additional monitoring once QTc returns to pre-treatment baseline.
Posterior reversible encephalopathy syndrome (PRES)	Suspect in patients presenting with seizures, confusion, visual disturbances or altered mental status.	Withhold vandetanib and obtain urgent MRI brain.
Hypertension	BP > 140/90	Withhold vandetanib and commence antihypertensives. Resume once blood pressure controlled to < 140/90.
Diarrhoea	Grade 1-2	Routine loperamide. Monitor QTc and serum electrolytes (see monitoring section above).
	Grade 3-4	Withhold vandetanib until diarrhoea resolves. Upon improvement resume vandetanib at reduced dose.
Skin reactions	Mild/Moderate (including photosensitivity reactions and palmar-plantar erythrodysaethesia syndrome)	Can be treated with symptomatic management, dose reduction or interruption.
	Severe skin reaction (including Stevens-Johnson Syndrome)	Withhold vandetanib and seek urgent medical review. May require glucocorticosteroids and permanent discontinuation of vandetanib.
ALT/AST elevations	Majority of elevations resolve with continuation of treatment	Continue vandetanib and monitor liver enzymes. If ongoing rise, withhold until ALT/AST normalised and then recommence.
Heart failure		Withhold and consider discontinuation of vandetanib.
Interstitial lung disease	Respiratory symptoms including; dyspnoea, cough, fever.	Withhold vandetanib and investigate. If interstitial lung disease is confirmed discontinue vandetanib.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Prolonged Q-T interval and arrhythmias
Posterior reversible encephalopathy syndrome (PRES)
Heart failure
Pneumonitis

- **Frequently occurring side effects**

Diarrhoea
Hypertension
Palmar-planter syndrome
Blurred vision
Nausea, vomiting
Fatigue
Skin rash, photosensitivity reactions

- **Other side effects**

Anorexia
Hypocalcaemia
Neutropenia
Insomnia
Renal impairment
Hair loss
Mucositis
Taste changes
Fluid retention
Heart failure
Headache
Dizziness
Altered transaminases
Deranged electrolytes

Significant drug interactions – for full details consult product literature/ reference texts

Medications which prolong the QT interval (e.g. anti-arrhythmics, ondansetron, domperidone, clarithromycin, erythromycin, venlafaxine) avoid or use with caution and close monitoring. Concomitant use of **ondansetron** is not recommended.

Metformin: vandetanib may increase metformin levels- close monitoring required, may require reduced metformin dose.

Digoxin: vandetanib may increase risk of bradycardia which may increase the risk of QTc prolongation with vandetanib. Close clinical and ECG monitoring required if concomitant use and reduced dose of digoxin may be required.

CYP3A4 inducers (including rifampicin, carbamazepine, phenobarbital, St Johns Wort): avoid concomitant use.

Additional comments

All prescribers must be familiar with the Physician Information and Management Guidelines. The prescriber must discuss the risks of vandetanib therapy with the patient and provide the patient with the Patient Alert Card with each prescription.

Women of childbearing potential must use effective contraception during therapy and for at least four months following the last dose.

References

- Summary of Product Characteristics Vandetanib (Genzyme) accessed 2 November 2016 via www.medicines.org.uk
- Wells et al Vandetanib in Patients With Locally Advanced or Metastatic Medullary Thyroid Cancer: A Randomized, Double-Blind Phase III Trial. (2012) J Clin Oncol 30 (2)134-41

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