CAPRELSA
(vandetanib)

VANDETANIB DOSING
AND MONITORING GUIDE FOR
PATIENTS AND PATIENTS'
CAREGIVERS (PAEDIATRIC USE)

vandetanib

What is vandetanib and what does it treat?

Vandetanib is available in film-coated tablets (100 mg and 300 mg). It is used to treat medullary thyroid cancer that is called Rearranged during Transfection (RET) mutant and which cannot be removed by surgery or has spread to other parts of the body.
Vandetanib works by slowing down the growth of new blood vessels in tumours (cancers). This cuts off the supply of food and oxygen to the tumour. Vandetanib may also act directly on cancer cells to kill them or slow down their growth.

How is the dose of vandetanib calculated?

The calculation of the dose of vandetanib is made by the treating physician, based on the body surface area (BSA), depending on the height and weight of the patient.

Depending of the calculated BSA, the physician will prescribe your child a **starting dose,** which the prescriber may change (dose adjustments):

- for an **increased dose,** if vandetanib is well tolerated after 8 weeks at starting dose
- for a reduced dose in case of undesirable side effects, after a suspension of treatment for at least a week.

The dose can also change if the BSA changes during the treatment.

The treatment schedule will correspond to one of the 3 following schemes:
"daily" schedule (same dose every day)
"every other day" schedule (same dose every other day)
"7 day" schedule (treatment every day but two different doses alternately)

Please note that the dosing scheme can change during treatment.
For example, you can follow a "daily" schedule for the starting dose period and switch to a "7 day" schedule after a dose adjustment.

You will have to record each dose taken on a daily tracker table (see below).

How is vandetanib used?

The prescribed calculated dose should be taken:

- at about the same time every day.
- with or without food.

The total daily dose in children must not exceed 300 mg.

If you/your child has trouble swallowing the tablet, you can mix it with water as follows:

- Take half a glass of still (non carbonated) water. Only use water, do not use any other liquids.
- Put the tablet into the water.
- Stir the tablet until it has dispersed into the water. This may take about 10 minutes.
- Then ensure you/your child drinks the solution straight away.
- To make sure there is no medicine left, half fill the glass with water again and ensure that you/your child drinks all of the water.

What are the side effects associated with vandetanib? What monitoring is advised?

Your doctor will inform you of the main risks of vandetanib. Please also read carefully the package leaflet for more information about vandetanib.

The most commonly reported side effects with vandetanib are diarrhoea, rash or other skin reaction, nausea (feeling sick), hypertension (high blood pressure) and headache.

Monitoring of blood and the heart will be necessary BEFORE and regularly DURING the treatment with vandetanib, especially:

- blood potassium, calcium, magnesium, and thyroid stimulating hormone (TSH)
- the electrical activity of the heart with a test called an electrocardiogram (ECG)

While taking vandetanib, protect yourself/your child when outside by always using sun cream and wearing clothes to avoid exposure to the sun, especially if you/your child is sensitive to the sun.

Tell your doctor or pharmacist if you/your child is taking, has recently taken or might take any other medicines, including medicines that you buy without a prescription and herbal medicines. This is because vandetanib can affect the way some medicines work and some medicines can have an effect on vandetanib. Further information on the effects of other medicines can be found in the Patient Information Leaflet (PIL) which comes in the package with the medicine.

Report any side effect to your doctor. He/she may prescribe other medicines to help control your/your child's side effects. Suspending treatment and/or reducing the dose of vandetanib may be required.

You can report side effects directly to HPRA Pharmacovigilance, website **www.hpra.ie**.

Side effects should also be reported to Esteve Pharmaceuticals Ltd
Tel: **+44 (0)330 1359 437** Email to: **medinfo.uk@esteve.com**

Tell your doctor straight away if you/your child notices any of the following side effects – you/your child may need urgent medical treatment:

- Fainting, dizziness or heart rhythm changes. These may be signs of a change in the electrical activity of the heart. They are seen in 8% of people taking vandetanib for medullary thyroid cancer. Your doctor may recommend you/your child take vandetanib at a lower dose or stop taking vandetanib. vandetanib has uncommonly been associated with life threatening changes in heart rhythm.

- Severe skin reactions affecting large areas of the body. The signs may include redness, pain, ulcers, blisters and shedding of the skin. The lips, nose, eyes and genitals may also be affected. These may be common (affecting less than 1 in 10 people) or uncommon (affects less than 1 in 100 people) depending on the type of skin reaction.

- Severe diarrhoea.

- Serious breathlessness, or sudden worsening breathlessness, possibly with a cough or a high temperature (fever). This may mean that you/your child have an inflammation of the lungs called 'interstitial lung disease'. Although this is uncommon, it can be life threatening.

- Seizures, headache, confusion or finding it difficult to concentrate. These may be signs of a condition called RPLS (Reversible Posterior Leukoencephalopathy Syndrome). RPLS is uncommon (affects less than 1 in 100 people).

How to use the daily tracker table

While prescribing the starting dose, your doctor will complete the “prescriber part” of the daily tracker and explain how to use it. The daily tracker is made to help you:

- remember when to take a new dose and which dose
- report side effects

The tracker should be completed by you/your child after each dose taken.

The daily tracker is adapted to all dose regimens. In the event that a dose change is made, a new daily tracker sheet should be provided by your doctor to you/your child and/or your caregivers.

Please find below blank copies of the daily tracker and examples of trackers that have been completed for your reference.

Space reserved for prescriber	Daily tracker for patient
Weight :_____ Height :_____ BSA: ____ m^2 Date of prescription :_____ □ starting dose □ increased dose □ reduced dose (see posology recommendations)	Name of patient : _____ Date of Birth : _____ If you forget to take vandetanib : - If it is 12 hours or more until your next dose: take the missed tablet as soon as you remember. Then take the next dose at the normal time. - If it is less than 12 hours until your next dose: skip the missed dose. Then take the next dose at the normal time. DO NOT TAKE a double dose (two doses at the same time) to make up for a forgotten tablet.

Day of week	Dose prescribed	Week 1-2 Start:	Week 3-4 Start:	Week 5-6 Start:	Week 7-8 Start:
Monday D1					
Tuesday D2					
Wednesday D3					
Thursday D4					
Friday D5					
Saturday D6					
Sunday D7					

Day of week	Dose prescribed	Week 1-2 Start:	Week 3-4 Start:	Week 5-6 Start:	Week 7-8 Start:
Monday D8					
Tuesday D9					
Wednesday D10					
Thursday D11					
Friday D12					
Saturday D13					
Sunday D14					

Doses available (tablets not actual size)	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg = 200 mg (2 x 100mg) = 300 mg = 				

EXAMPLE OF STARTING DOSE FOR A CHILD WITH BSA FROM 0.7 m² to <0.9 m² (" EVERY OTHER DAY" SCHEDULE : D1 ≠ D8)

Space reserved for prescriber	Daily tracker for patient
Weight : _____ Height : _____ BSA : 0,8 m² Date of prescription : 12/09/16 ☑ starting dose ☐ increased dose ☐ reduced dose (see posology recommendations)	Name of patient : _____ Date of Birth : _____ If you forget to take vandetanib : - If it is 12 hours or more until your next dose: take the missed tablet as soon as you remember. Then take the next dose at the normal time. - If it is less than 12 hours until your next dose: skip the missed dose. Then take the next dose at the normal time. DO NOT TAKE a double dose (two doses at the same time) to make up for a forgotten tablet.

Day of week	Dose prescribed	Week 1-2 Start: 12/09/16	Week 3-4 Start: 26/09/16	Week 5-6 Start: 10/10/16	Week 7-8 Start: 24/10/16
Monday D1	-	0	0	0	0
Tuesday D2	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg
Wednesday D3	-	0	0	0	0
Thursday D4	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg
Friday D5	-	0	0	0	0
Saturday D6	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg
Sunday D7	-	0	0	0	0

Day of week	Dose prescribed	Week 1-2 Start: 12/09/16	Week 3-4 Start: 26/09/16	Week 5-6 Start: 10/10/16	Week 7-8 Start: 24/10/16
Monday D8	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg
Tuesday D9	-	0	0	0	0
Wednesday D10	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg
Thursday D11	-	0	0	0	0
Friday D12	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg
Saturday D13	-	0	0	0	0
Sunday D14	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg

Doses available (tablets not actual size)	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg = 200 mg (2 x 100mg) = 300 mg = 		side effect : small skin reaction. called doctor, no interruption. recovered using stronger sun protection.		well tolerated after 8 week, new prescription with increased dose (100 mg daily) -> new daily tracker sheet.

EXAMPLE OF INCREASED DOSE FOR A CHILD WITH BSA FROM 0.9m² to <1.2m² (" 7 DAYS" SCHEDULE: D1 = D8)

Space reserved for prescriber	Daily tracker for patient
Weight : 35 kg Height : 125 cm BSA : 1,1 m² Date of prescription : 12/09/16 ☐ starting dose ☑ increased dose ☐ reduced dose (see posology recommendations)	Name of patient : _____ Date of Birth : _____ If you forget to take vandetanib : - If it is 12 hours or more until your next dose: take the missed tablet as soon as you remember. Then take the next dose at the normal time. - If it is less than 12 hours until your next dose: skip the missed dose. Then take the next dose at the normal time. DO NOT TAKE a double dose (two doses at the same time) to make up for a forgotten tablet.

Day of week	Dose prescribed	Week 1-2 Start: 12/09/16	Week 3-4 Start: 26/09/16	Week 5-6 Start: 10/10/16	Week 7-8 Start: 24/10/16
Monday D1	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	
Tuesday D2	200 mg	2 x 100 mg	2 x 100 mg	2 x 100 mg	
Wednesday D3	100 mg	1 x 100 mg	1 x 100 mg	1 x 100 mg	
Thursday D4	200 mg	2 x 100 mg	2 x 100 mg	2 x 100 mg	
Friday D5	100 mg	1 x 100 mg	1 x 100 mg	suspended	
Saturday D6	200 mg	2 x 100 mg	2 x 100 mg	suspended	
Sunday D7	100 mg	1 x 100 mg	1 x 100 mg	suspended	

Day of week	Dose prescribed	Week 1-2 Start: 12/09/16	Week 3-4 Start: 26/09/16	Week 5-6 Start: 10/10/16	Week 7-8 Start: 24/10/16
Monday D8	100 mg	1 x 100 mg	1 x 100 mg	suspended	
Tuesday D9	200 mg	2 x 100 mg	2 x 100 mg	suspended	
Wednesday D10	100 mg	1 x 100 mg	1 x 100 mg	suspended	
Thursday D11	200 mg	2 x 100 mg	2 x 100 mg	suspended	
Friday D12	100 mg	1 x 100 mg	1 x 100 mg	suspended	
Saturday D13	200 mg	2 x 100 mg	2 x 100 mg	Restart with reduced dose	
Sunday D14	100 mg	1 x 100 mg	1 x 100 mg		

Doses available (tablets not actual size)	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg = 200 mg (2 x 100mg) = 300 mg = 	increased dose after 8 w 100 mg daily tired (weakness) friday - w1 : diarrhoea (1 episode), called doctor -> no change	tonsillitis : amoxicillin thursday - w 4 : small skin reaction, called doctor -> survey and no sun exposition.	thursday - w 5 : skin reaction worsening. treatment suspended friday - w 6 : recovered from skin reaction.	new prescription. starting a reduced dose.-> new daily tracker sheet.

EXAMPLE OF INCREASED DOSE FOR A CHILD WITH BSA > 1.6 m² (“ DAILY” SCHEDULE: D1 = DX)

Space reserved for prescriber	Daily tracker for patient
Weight : _____ Height : _____ BSA : 1,68 m² Date of prescription : 12/09/16 ☐ starting dose ☑ increased dose ☐ reduced dose (see posology recommendations)	Name of patient : _____ Date of Birth : _____ If you forget to take vandetanib : - If it is 12 hours or more until your next dose: take the missed tablet as soon as you remember. Then take the next dose at the normal time. - If it is less than 12 hours until your next dose: skip the missed dose. Then take the next dose at the normal time. DO NOT TAKE a double dose (two doses at the same time) to make up for a forgotten tablet.

Day of week	Dose prescribed	Week 1-2 Start: 12/09/16	Week 3-4 Start: 26/09/16	Week 5-6 Start: 10/10/16	Week 7-8 Start: 24/10/16
Monday D1	300 mg	1 x 300 mg	1 x 300 mg		
Tuesday D2	300 mg	1 x 300 mg	1 x 300 mg		
Wednesday D3	300 mg	1 x 300 mg	1 x 300 mg		
Thursday D4	300 mg	1 x 300 mg	1 x 300 mg		
Friday D5	300 mg	1 x 300 mg	1 x 300 mg		
Saturday D6	300 mg	1 x 300 mg	1 x 300 mg		
Sunday D7	300 mg	1 x 300 mg	etc.		

Day of week	Dose prescribed	Week 1-2 Start: 12/09/16	Week 3-4 Start: 26/09/16	Week 5-6 Start: 10/10/16	Week 7-8 Start: 24/10/16
Monday D8	300 mg	1 x 300 mg			
Tuesday D9	300 mg	1 x 300 mg			
Wednesday D10	300 mg	1 x 300 mg			
Thursday D11	300 mg	1 x 300 mg			
Friday D12	300 mg	1 x 300 mg			
Saturday D13	300 mg	1 x 300 mg			
Sunday D14	300 mg	1 x 300 mg			

Doses available (tablets not actual size)	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg = 200 mg (2 x 100mg) =  300 mg = 	increased dose after 8 w 200 mg daily			

Blank copies
Package leaflet has to be provided with dosing guide.

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