Caprelsa™
vandetanib

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

What is Caprelsa and what does it treat?

Caprelsa is a medicine that contains the active substance vandetanib. It 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.

Caprelsa 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. Caprelsa may also act directly on cancer cells to kill them or slow down their growth.

How is the dose of Caprelsa calculated?

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

Depending of the calculated BSA, the physician will prescribe to your child a **starting dose**, which can be changed (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 (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 report each dose taken on a daily tracker table (see below).

How is Caprelsa used?

The prescribed calculated dose should be taken:
- at about the same time
- with or without food.

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

If the 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 make the child drink it straight away.

To make sure there is no medicine left, refill the glass halfway with water and (have your child) drink it.

What are the side effects associated with Caprelsa? Which monitoring is requested?

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

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 heart will be necessary BEFORE and regularly DURING the treatment by vandetanib, especially:
- blood potassium, calcium, magnesium, and thyroid stimulating hormone (TSH)
- the electrical activity of the heart with a test called an electrocardiogram (ECG)

A good skin protection is requested (wearing clothes, sunscreen), especially if you are sensitive to sun.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines that you buy without a prescription and herbal medicines. These might interact with vandetanib and provoke lack of efficacy or increase side effects.

Report any side effect to your doctor. He/she may prescribe other medicines to help control the patient’s side effects. A suspension of treatment and dose reduction may also be necessary.

Tell your doctor straight away if you notice any of the following side effects – you 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 Caprelsa for medullary thyroid cancer. Your doctor may recommend you take Caprelsa at a lower dose or stop taking Caprelsa. Caprelsa has uncommonly been associated with life threatening changes in heart rhythm.

- Severe skin reactions affecting large areas of your 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 have an inflammation of the lungs called 'interstitial lung disease'. This is uncommon (affects less than 1 in 100 people) but 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). These usually go away when Caprelsa is stopped. 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:

- to remember when to take a new dose and which dose. It has to be completed by you after each dose intake.

- to report side effects and follow dose adjustments.

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 the patients and/or patient's caregivers.

Please find blank copies of the daily tracker after the examples of completed daily trackers.

Space reserved 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 Caprelsa : - 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	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg =  200 mg =  300 mg = 				

Space reserved 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 Caprelsa : - 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	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg =  200 mg =  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.

Space reserved 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 Caprelsa : - 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	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg =  200 mg =  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.	thurday - w 5 : skin reaction worsening. treatment suspended friday - w 6 : recovered from skin reaction.	new prescription. starting a reduced dose -> new daily tracker sheet.

Space reserved 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 Caprelsa : - 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	Comments for patient and/or patient's caregiver (side effects, other treatment, or important information)			
100 mg =  200 mg =  300 mg = 	increased dose after 8 w 200 mg daily			

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

Call for reporting
Healthcare professionals are encouraged to report all the adverse events suspected to be associated with the use of CAPRELSA to the Medicines Authority. Report Form can be downloaded from http://www.medicinesauthority.gov.mt/adrportal and sent to Post-licensing Directorate, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 Malta, or by e-mail to postlicensing.medicinesauthority@gov.mt

ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal

Alternatively any suspected adverse reactions can be reported to Sanofi Srl, Viale Luigi Bodio, 37/b - 20158 Milano, Italy at PharmacovigilanceMalta@sanofi.com

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