

Site ID:

Pat ID:

Date:

Completed by:

Requirements for the „Dosing at home“:

- The patient does not have an increased TLS-risk before the start of the Venetoclax Ramp-Up (C1D20).
- If the patient has an increased TLS-risk at randomization:
The CRF-pages RC1 and RC2 must be sent to the GCLLSG
- The patient was approved for the „Dosing at home“ by the GCLLSG.
- The Dosing at home is only applicable for the escalation to **100mg, 200mg or 400mg Venetoclax**.

Before the dose escalation:

- The concomitant medication should be checked for **potential cross reactions** with Venetoclax (please pay attention with CYP3A- inhibitors und -inductors (e.g. Clarithromycin, Fluconazol, Ketoconazol) as well as P-gp-, BCRP- or OATP1B1/B3 inhibitors).

Instructions for the patient:

- Necessity of **oral hydration** (minimum 2000 ml within 24 hours) **during the complete Venetoclax ramp-up phase**.
- Remind the patient that he must come to the clinic after the intake of Venetoclax at home.
- Consumption of **Sevilla-oranges, Grapefruit und starfruit** during the treatment with Venetoclax is forbidden.
- Venetoclax should be taken **during breakfast**.
 - o Important! The intake of Ibrutinib for patients in the GIVe arm should occur before breakfast
 - o The administration of the antibody should take place after the intake of Venetoclax (and Ibrutinib if applicable)

≤24 h before the dose escalation:

- No side effects grade CTC°III/IV (unless directly attributable to the underlying CLL)
- Lab assessments
These lab results **must** be evaluated by the physician to decide about the intake of venetoclax at home the next morning.

The following values are documented on the CRF (DE-page):

Hemoglobin, Leucocytes, Thrombocytes, Lymphocytes, Neutrophils, Creatinine, GOT/GPT, Bilirubin, Uric Acid, LDH, Sodium, Potassium, Calcium, Phosphate

Further lab testing should be done according to local standards, e.g. blood count.

On the day of dose escalation:

Intake of Venetoclax with approx. 250ml of water during breakfast at home.

Document the time of Venetoclax intake: _____:_____

- 100mg (take 1 tablet of 100mg out of the blister card)
- 200mg (take 2 tablets of 100mg out of the blister card)
- 400mg (take 4 tablets of 100mg out of the bottle)

Lab assessments within 2 hours after the intake of Venetoclax at home (as soon as the patient arrived in the clinic).

This lab assessment is considered as baseline value for the assessment of TLS.

The following values are documented on the CRF (DE-page):

Hemoglobin, Leucocytes, Thrombocytes, Lymphocytes, Neutrophils, Creatinine, GOT/GPT, Bilirubin, Uric Acid, LDH, Sodium, Potassium, Calcium, Phosphate

Further lab testing should be done according to local standards, e.g. blood count.

Lab assessments **6-8 h after Venetoclax dose escalation**

- The results of the lab assessment must be evaluated and compared to the baseline assessments by the physician on the **same day**.
- Deregulated electrolytes must be corrected immediately.
- The study protocol must be adhered to (Chapter „Laboratory changes and further actions“ and „Definition of tumor lysis syndrome (TLS)“).

The following values are documented on the CRF (LBC-page):

Potassium, Phosphate, Uric Acid, Creatinine, LDH, Calcium
(Documentation only if there is a change of more than 25% from baseline)

Further lab testing should be done according to local standards, e.g. blood count.

The day after dose escalation:

Lab assessments **≥24 h after Venetoclax dose escalation**

The results of the lab assessment must be evaluated by the physician **before intake on the next venetoclax tablet**.

- Deregulated electrolytes must be corrected immediately.
- The study protocol must be adhered to (Chapter „Laboratory changes and further actions“ and „Definition of tumor lysis syndrome (TLS)“).

The following values are documented on the CRF (LBC-page):

Potassium, Phosphate, Uric Acid, Creatinine, LDH, Calcium
(Documentation only if there is a change of more than 25% from baseline)

Further lab testing should be done according to local standards, e.g. blood count.

Intake of Venetoclax (see above) with approx. 250ml of water.