

## Ocrelizumab Dose Preparation and Infusion Guidelines for Pharmacist/ Study Personnel

Please administer dual infusion at cycle 1 and single infusions from cycle 2 onwards.

### Schedule of Study Medication:

<b>Ocrelizumab</b>	<u>Cycle 1:</u> Two separate i.v. infusions of ocrelizumab 300 mg administered on day 1 cycle 1 and day 15 cycle 1  <u>Subsequent Cycles:</u> One i.v. infusion of ocrelizumab 600 mg
--------------------	---

### I. Drug Kits (General Remarks):

#### a. Drug presentation and handling

All transfer procedures require strict adherence to aseptic techniques. The study drug vials are to be kept refrigerated (2-8°C) prior to dosage preparation.

The ocrelizumab drug product is supplied as a liquid at a concentration of 30 mg/mL ocrelizumab in 15 mL single-use vials, which contain a nominal 10 mL (300 mg) of ocrelizumab per vial.

The drug is a protein. It is therefore important to handle the drug gently and to avoid foaming during product handling, dosage preparation and drug administration, as foaming may lead to denaturing of the protein. The drug must be diluted with 0.9% Sodium Chloride Injection prior to infusion.

**Please remember that vials of Ocrelizumab are for single use only.**

#### b. Kit Configuration and Study Drug Assignment:

Each study drug kit will contain one 15 mL single-use liquid vial with ocrelizumab. At the randomization visit and week 2, one study drug kit will be assigned (each visit). For subsequent visits two study drug kits will be assigned each time. Each drug kit will be identified by the batch number.

#### c. Storage of Ocrelizumab Vials:

Ocrelizumab vials are stable at 2–8°C (refrigerated storage). They should not be used beyond the expiration date stamped on the carton unless there is documented expiry date extension from the Sponsor. Ocrelizumab vials should not be frozen or shaken and should be protected from direct sunlight. All study drug should be stored in a locked and secured area.

## II. Infusions

### a. General Remarks

**Please note that the entire content of the infusion bag must be administered to the patient to deliver the complete dose. Please refer to the protocol on guidance in the event of infusion reactions.**

### b. Storage of Infusion Bags Containing Diluted Study Drug

Ideally, IV bags should be prepared on the day of infusion, but may be prepared one day prior. Because ocrelizumab solutions for infusion do not contain a preservative, store prepared infusion bags containing ocrelizumab solutions refrigerated at 2-8°C for up to 24 hours.

The infusion solution must be administered using an infusion set with an in-line, sterile, non-pyrogenic, low-protein-binding filter (pore size of 0.2 micrometer or less). The dose solution should be used immediately. If not used immediately, the total storage time of the dose solution prior to administration should not exceed 24 hours to limit the risk of microbial growth in case of accidental contamination. The recommended storage condition for the dose solution is 2 to 8°C, but dose solutions may be stored at room temperature for up to a maximum of 8 hours.

To avoid an infusion reaction associated with the administration of a low temperature solution, the bag must be brought to room temperature before infusion. To do this, place the bag at room temperature for approximately one hour.

### c. General Instructions for Preparation:

For the preparation of doses use a sterile needle and a syringe no larger than 10 cc/mL to remove the appropriate volume of study drug from the vials (there is an overage in each vial). Please refer to the step by step instructions below for exact quantities.

**DO NOT USE A VACUUM APPARATUS** to transfer study drug from the syringe to the infusion bag.

Ocrelizumab infusions should be given as a slow i.v. infusion. It must not be administered as an i.v. push or bolus. Infusion pumps should be used to control the infusion rate and the study drug should be infused through a dedicated iv-line. Use sterile, non-pyrogenic, disposable containers, syringes, needles, stopcocks, and transfer tubing, etc., during dosage preparation and infusion. There are no restrictions on using PVC or PO infusion bags.

**Please note that each vial contains a small overage in accordance with standard manufacturing processes.**

## Ocrelizumab Drug Preparation Instructions (with vials à 300 mg Ocrelizumab)

### **Dual Infusions (Cycle 1)**

For the dual infusions (300 mg ocrelizumab infusion), it is necessary to prepare a 250-mL 0.9% Sodium Chloride Injection for each infusion.

### **Preparation of Dual Infusion Cycle Doses**

- 1) Using a 10 cc/mL syringe, remove **10.0 mL** of study drug (ocrelizumab) from the first vial and add to the 250-mL infusion bag.
- 2) Gently invert bag to mix, do not shake.

A total of **10.0 mL** of study drug will be added to the IV infusion bag.

THE REMAINS OF EACH VIAL ARE NOT TO BE USED.

Both used and unused vials (as applicable) should be kept for the drug accountability of the monitor; they can be destroyed locally afterwards.

### **Dual Infusion Rates Table**

<b>Time (Minutes)</b>	<b>Infusion Rate (mL/hr)</b>	<b>Maximum Dose per Interval (mg)</b>	<b>Cumulative Dose (mg)</b>
0-30	32	18.75	18.75
31-60	65	37.5	56.25
61-90	97	56.25	112.5
91-120	129	75	187.5
121-150	194	112.5	300

Infusion of 300 mg of ocrelizumab should be completed at approximately 150 minutes (~2.5 hours).

## Ocrelizumab Drug Preparation Instructions (with vials à 300 mg Ocrelizumab)

### **Single Infusions (commencing cycle 2)**

For single infusion cycles (600 mg ocrelizumab infusion), it is necessary to prepare a 500-mL 0.9% Sodium Chloride Injection. To prepare a single infusion two vials will be used.

### **Preparation of Single Infusion Cycle Doses**

- 1) Using a new 10 cc/mL syringe, remove **10 mL** of study drug (ocrelizumab) from the first vial and add to a 500 mL IV Bag.
- 2) Using a new 10 cc/mL syringe, remove **10 mL** of study drug (ocrelizumab) from the second vial and add to the same 500 mL IV Bag.
- 3) Gently invert bag to mix, do not shake.

A total of **20.0 mL** of study drug will be added to a 500 mL IV Bag.

THE REMAINS OF EACH VIAL ARE NOT TO BE USED;

The used vials should be kept for the drug accountability of the monitor; they can be destroyed locally afterwards.

### **Single Infusion Rates Table**

<b>Time (Minutes)</b>	<b>Infusion Rate (mL/hr)</b>	<b>Maximum Dose per Interval (mg)</b>	<b>Cumulative Dose (mg)</b>
0-30	40	23.18	23.18
31-60	85	49.27	72.45
61-90	130	75.36	147.81
91-120	169	98.05	245.86
121-215*	200	354.14	600

*\*This last interval is approximately 95 minutes, delivering a max dose of 115.94 mg per 0.5 hour.*

The infusion of 600 mg Ocrelizumab should be completed at approximately 215 minutes (~3.6 hours).