**PHARMACY GUIDELINE**

# Rituximab Administration Guideline

## DOCUMENT REF: GPHARITAD
## (Version No. 1.0)

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| Approved by (committee, group, manager) | Drug and Therapeutics Committee |
| Approving signature | Minutes of meeting received |
| Date approved | 10th July 2020 |
| Review date | July 2023 |
| Review type (annual, three yearly) | Three yearly |
| Target audience | Nursing, medical and pharmacy staff |
| Links to other strategies, policies, procedures | |
| Protective Marking Classification | Internal |
| This document replaces | N/A |

## Consultation:

| | Authorised by | Date Authorised | Comments |
|---|---|---|---|
| Impact Assessment | N/A | N/A | N/A |
| Fraud Assessment | N/A | N/A | N/A |

## Circulation/Dissemination:

| | |
|---|---|
| **Date added into Q-Pulse** | 15th September 2020 |
| **Date notice posted in the Team Brief** | 15th September 2020 |
| **Date document posted on the intranet** | 15th September 2020 |

## Version History:

| Date | Version | Author name and designation | Summary of main changes |
|---|---|---|---|
| March 2020 | 1.0 | Aileen McCaughey Advanced Pharmacist – Haem-Oncology | New document |
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## 1.0 Introduction

Rituximab is a systemic anti-cancer therapy that is commonly prescribed within haematology and is associated with infusion related reactions (IRRs). IRRs are usually caused by cytokine release syndrome and up to 77% of patients can be affected. Most reactions are mild but fatalities have been reported. This policy aims to reduce the frequency of IRRs, provide guidance on the treatment of IRRs and improve patient experience and day ward capacity by introducing a rapid infusion rate for rituximab.

NB this guideline does *not* cover the use of sub-cutaneous rituximab.

## 2.0 Infusion rates

There are four different infusion rates that Rituximab can be given at:-

1. **First infusion rate for low risk patients**

   The recommended initial rate for infusion is 50 mg/hour; after the first 30 minutes, it can be escalated in 50 mg/hour increments every 30 minutes, to a maximum of 400 mg/hour (see appendix A)

2. **First infusion rate for high risk patients:-**
   - Chronic Lymphocytic Leukaemia (CLL) and/ or patients with a lymphocyte count ≥ $25x10^9$/L
   - very bulky or high grade Non-Hodgkin's lymphoma (NHL)
   - lymphoplasmocytic lymphoma

   Split dose of 100mg rituximab over 2 hours on day 1 and then the remainder of the 375mg/$m^2$ dose on day 2 as per first infusion rate for low risk patients (Appendix A).

3. **Second and subsequent infusion rate**

   **For patients not suitable for the rapid infusion rate:-**

   - Cycle 2 CLL patients (if well tolerated their fourth infusion [i.e. cycle 3 day 1] can be as per the rapid infusion rate)
   - patients with a lymphocyte count ≥ 25 x $10^9$/L (rapid infusion rate can be initiated once lymphocyte count is <25 x $10^9$/L)
   - patients who suffered a grade 2 or greater adverse reaction with their first infusion should have their second infusion as per the **first infusion rate for low risk patients**; if this is tolerated then their third infusion can be as per the second and subsequent infusion rate. If the third infusion is well tolerated then their fourth infusion can be as per the rapid infusion rate.
   - Clinical trial patients – trial protocol must be followed (note most trials permit a fast infusion rate).
   - Patients with cardiac or respiratory insufficiency.

   Initial rate of 100 mg/hour, and increased by 100 mg/hour increments at 30 minute intervals, to a maximum of 400 mg/hour (see appendix B).

4. **Rapid infusion rate**

   - Patients *must* be counselled by a clinician that this rate is off-label and verbal consent for the rapid infusion rate *must* be documented in the patient's notes.

   Initial rate of 200ml/hour for 30 minutes then 400ml/hour for 60 minutes - total infusion time 90 minutes irrespective of dose (see Appendix C).

## 3.0 Pre Infusion Medication

To be administered at least 30 minutes prior to rituximab

- Paracetamol 1000mg PO
- Chlorphenamine 10mg IV or 4mg PO depending on protocol

- Corticosteroids;
  - Patients having steroids as part of their chemotherapy regimen should have the dose they are due at least 30 minutes prior to their rituximab.
  - Patients not receiving steroids as part of their chemotherapy regimen should have hydrocortisone 100mg IV bolus as least 30 minutes prior to rituximab (but see next bullet point).
  - Patients with CLL and with a lymphocyte count ≥ 25 $x10^9$/L may be given prednisolone 100mg PO in place of hydrocortisone at the treating physician's discretion. In addition, these patients should receive antiuraemic treatment for 2 days prior to rituximab treatment and maintain adequate hydration.

## 4.0 Monitoring

Patients should have their vital signs (pulse, temperature, respiratory rate and blood pressure) monitored at baseline and then with each incremental increase in their infusion rate.

## 5.0 Infusion related reactions

Infusion related toxicities should be graded using the table in Appendix D.

Patients experiencing a grade 1 reaction should be monitored every 30 minutes until symptoms subside.

If patients experience a grade 2 reaction or higher;

1. Stop the infusion.
2. Urgently contact the relevant doctor/ANP. It may be necessary to give further supportive care at this point.
3. Once the reaction has subsided, restart the rituximab infusion **if appropriate** at **half** the rate that was being given prior to the reaction.

4. Further attempts may be made to increase the rate as per the infusion protocol in use at the time for that patient.
5. Monitor and record vital signs every 30 minutes until the end of the infusion
6. If the patient reacts again, stop the infusion, contact the relevant doctor/ANP and if appropriate to do so, at the clearance of symptoms restart the infusion at one infusion rate below that rate at which the reaction occurred
7. Continue at this rate **without** further escalation and continue to record vital signs every 30 minutes until the end of the infusion

## 6.0 References


1. https://www.medicines.org.uk/emc Mabthera (rituximab). Accessed Feb 2020.
2. Thames Valley Strategic Network. Guidelines for administration of rapid infusion Rituximab. Accessed Feb 2020.
3. Sehn LH, Donaldson J, Filewich A, Fitzgerald C, Gill KK, Runzer N, Searle B, Souliere S, Spinelli JJ, Sutherland J, & Connors JM (2007) Rapid infusion rituximab in combination with corticosteroid-containing chemotherapy or as maintenance therapy is well tolerated and can safely be delivered in the community setting. Blood. 109(10):4171.
4. Common Terminology Criteria for Adverse Events (CTCAE) Version 5, available at https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf

## Appendix A

**First** infusion rate for low risk patients

| Dose | Rate (mg/hr) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 50 | 100 | 150 | 200 | 250 | 300 | 350 | 400 |
| | Infusion rate (ml/hr, increase rate every 30 minutes) | | | | | | | |
| **500mg** | 50 | 100 | 150 | 200 | 250 | 300 | 350 | 400 |
| **550mg** | 45 | 90 | 135 | 180 | 225 | 270 | 315 | 360 |
| **600mg** | 40 | 82 | 124 | 166 | 208 | 248 | 290 | 332 |
| **650mg** | 38 | 77 | 115 | 153 | 192 | 231 | 269 | 308 |
| **700mg** | 34 | 70 | 104 | 140 | 176 | 212 | 248 | 284 |
| **800mg** | 30 | 62 | 92 | 124 | 154 | 186 | 216 | 248 |
| **900mg** | 28 | 56 | 84 | 112 | 140 | 168 | 196 | 224 |
| **1000mg** | 24 | 50 | 74 | 100 | 124 | 150 | 174 | 200 |

## Appendix B

**Second** and subsequent infusion rate

| Dose | Rate (mg/hr) | | | |
|---|---|---|---|---|
| | 100 | 200 | 300 | 400 |
| | Infusion rate (ml/hr, increase rate every 30 minutes) | | | |
| **500mg** | 100 | 200 | 300 | 400 |
| **550mg** | 90 | 180 | 270 | 360 |
| **600mg** | 82 | 166 | 248 | 332 |
| **650mg** | 77 | 153 | 228 | 304 |
| **700mg** | 70 | 140 | 212 | 284 |
| **800mg** | 62 | 124 | 186 | 248 |
| **900mg** | 56 | 112 | 168 | 224 |
| **1000mg** | 50 | 100 | 150 | 200 |
| **1100mg** | 45 | 90 | 135 | 180 |
| **1200mg** | 40 | 80 | 120 | 160 |

## Appendix C

**Rapid** infusion rate

| INFUSION DURATION | INFUSION RATE (ml/hr) |
|---|---|
| 30 MINUTES | 200 |
| 60 MINUTES | 400 |

## Appendix D

IRR toxicity grading

| Adverse Event | Grade | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| Allergic reaction/ Hypersensitivity | Transient flushing or rash, fever $<38^0$C | Rash, flushing, urticaria, dyspnoea, drug fever ≥ $38^0$C | Symptomatic bronchospasm with or without urticaria, parenteral medications indicated, allergy related oedema/ angioedema, hypotension | Anaphylaxis |
| Cytokine release syndrome/ acute infusion reaction | Symptoms are not life threatening and require symptomatic treatment only, e.g., fever, nausea, fatigue, headache, myalgia, malaise | Symptoms require moderate intervention or greater and may include (but not limited to) dyspnoea, hypoxia, bronchospasm and hypotension. | | |