R-BAC-800 CHEMOTHERAPY REGIME FOR THE TREATMENT OF MANTLE CELL LYMPHOMA (Rituximab, Bendamustine, Cytarabine)

Regimen	**R-BAC (800)**

Indication	First line therapy in patients considered unsuitable for standard treatment of Mantle Cell Lymphoma Relapsed Mantle cell lymphoma
Cycle Frequency	Every 28 days for four to six cycles. To restage of after cycle two
Tests required prior to initiation of course	Full blood count, renal, liver, bone, glucose, LDH, serum immunoglobulins and electrophoresis, virology screen Undertake relevant staging. Consider cardiac function tests WHO performance status
Tests required prior to individual cycle	Full blood count, U&E's, LFT's, calcium.
Concurrent Medication	Predsol eye drops Co-Trimoxazole 480 mg orally once a day Acyclovir 400 mg twice daily As per local protocol

Day 1

Day	Medication	Dose	Route	Administration Details
1	Chlorphenamine	10 mg	IV	30 mins prior to Rituximab
1	Hydrocortisone	100 mg	IV	30 mins prior to Rituximab
1	Paracetamol	1 g	Oral	30 mins prior to Rituximab
1	Rituximab	375 mg/m^2	IV	Infusion in 500 mls sodium chloride 0.9%. Use local protocol
1	Cotrimoxazole	480 mg	Oral	For 28 days
1	Acyclovir	400 mg	Oral	Twice daily for 28 days

Day 2

Day	Medication	Dose	Route	Administration Details
2	Ondansetron	8 mg	IV	
2	Dexamethasone	8 mg	IV	
2	Bendamustine	70 mg/m^2	IV	Infusion in 500 mls 0.9% sodium chloride over 30 minutes
2	Cytarabine	800 mg/m^2	IV	**Starting two hours after completion of bendamustine** **Intravenous infusion in 500 mls sodium chloride 0.9% over two hours**
2	Predsol eye drops	0.5% one drop		Eye drops four times a day in each eye for five days
2	Metoclopramide	10 mg	Oral	Three times daily as required
2	Ondansetron	8 mg	Oral	Twice daily for five days

Day 3

Day	Medication	Dose	Route	Administration Details
3	Dexamethasone	8 mg	IV	As a single dose prior to Bendamustine
3	Bendamustine	70 mg/m^2	IV	500 mls 0.9% sodium chloride over 30 to 60 mins
3	Cytarabine	800 mg/m^2	IV	**Starting two hours after completion of bendamustine** **Intravenous infusion in 500 mls sodium chloride 0.9% over two hours**

Day 4

Day	Medication	Dose	Route	Administration Details
4	Dexamethasone	8 mg	IV	As a single dose prior to Cytarabine
4	Cytarabine	800 mg/m^2	IV	Intravenous infusion in 500 mls sodium chloride 0.9% over two hours
4	Dexamethasone	8 mg	Oral	Once daily for three days
4	Allopurinol	300 mg	Oral	Once a day for seven days, reduce in renal impairment

Day 7

Day	Medication	Dose	Route	Administration Details
7	Filgrastim/biosimilar	5mcg/kg	subcut	For seven days/at clinician discretion

Notes: All patients who receive Bendamustine should receive **irradiated blood products** throughout their chemotherapy and for life.

Blood transfusion must be informed and patient must be issued with a requirement for irradiated blood products card.

Risk of cytokine release syndrome is increased when the peripheral blood lymphocyte is greater than 30. Clinicians may wish to pre-medicate patients with high tumour burden with steroids prior to the first cycle or omit Rituximab from the first cycle of treatment.

There is a risk of Stevens-Johnson syndrome and toxic epidermal necrolysis when Bendamustine and Allopurinol are administered concomitantly. Clinicians should consider omitting Allopurinol on the days of Bendamustine for patients at low risk of tumour lysis syndrome. Consideration may be given to the use of Rasburicase.

<table>
<tr><td>Dose Modifications and toxicities</td><td>Neutrophil count less than 1 x 10^9/l or platelets less than 75 x 10^9/l</td></tr>
<tr><td></td><td>Delay until neutrophil count greater than 1 x 10^9/l and platelets greater than 75 x 10^9/l. Dose reduced to 75% doses.
If counts have not recovered after two weeks' delay, withdraw from treatment</td></tr>
<tr><td>Renal Impairment</td><td>Bendamustine – no dose adjustment is necessary in patients with a creatinine clearance of over 10 ml/min.

Cytarabine:<table><tr><th>GFR ml/min</th><th>Cytarabine dose</th></tr><tr><td>>60</td><td>100%</td></tr><tr><td>46-60</td><td>60%</td></tr><tr><td>31-45</td><td>50%</td></tr><tr><td><30</td><td>contraindicated</td></tr></table></td></tr>
<tr><td>Hepatic Impairment</td><td>Bendamustine:<table><tr><th>Bilirubin mIcromol/L</th><th>Dose</th></tr><tr><td><20</td><td>100%</td></tr><tr><td>20- 51</td><td>70%</td></tr><tr><td>>51</td><td>No data available</td></tr></table>If bilirubin is greater than 34 x 10^9/l give 50% dose Cytarabine, consider subsequent dose escalation if no detrimental effects.</td></tr>
<tr><td>Supportive Care</td><td>Patients at risk of tumour lysis syndrome must receive prophylaxis prior to initiation of therapy. Consider use of Rasburicase. Refer to BCSH Guidelines relating to tumour lysis.
All patients should receive pneumocystis Jiroveci and anti-viral prophylaxis throughout treatment and for at least three months post-treatment or until the lymphocyte count is greater than 1 x 10^9/l. Septrin 480 mg od.
In cases of Septrin allergy consider Pentamidine nebuliser or Dapsone 100 mg once a day.</td></tr>
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	Acyclovir 400 mg twice a day Prednisolone eye drops 0.5% for prevention of Cytarabine induced conjunctivitis. To continue beyond five days of recommended therapy if necessary.
Side Effects	Infusion related reactions associated with Rituximab. **Rituximab:** See separate protocol for administration of Rituximab. Most side effects relate to infusion related allergies. Immunosuppression: Progressive multifocal leukoencephalopathy. Delayed myelosuppression. **Cytarabine toxicity:** Cytarabine syndrome usually occurs six to 12 hours following infusion and is more common the higher the dose. Cytarabine syndrome characterised by fever, myalgia, bone pain, occasional chest pains, rash, malaise and conjunctivitis. Cerebral and cerebellar toxicity (usually reversible): Myelosuppression Infertility Hair loss **Bendamustine side effects:** Myelosuppression Infections Hepatitis B reactivation Skin reactions Cardiac disorders (patients with a history of cardiac disorders need to be monitored closely). Potassium supplementation must be given if potassium falls less than 3.5. Nausea, vomiting Tumour lysis syndrome Anaphylaxis

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