

Provincial Clinical Knowledge Topic

Fludarabine Cyclophosphamide ATG +/- TBI, Adult BMT - Inpatient V 1.0

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Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	December 27, 2018	Topic Completed	See Acknowledgments

Important Information Before you Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

Guidelines

This topic is based on the following guideline(s): [Alberta Blood and Marrow Transplant Program \(ABMTP\) Standard Practice Manual](#)

Please refer to [ABMTP Standard Practice Manual](#) for more information and recommendations about this topic.

Keywords

Topic Name: Fludarabine Cyclophosphamide ATG TBI, Adult BMT - Inpatient

- Alberta Blood and Marrow Transplant Program (ABMTP)
- Blood and Marrow Transplant (BMT)
- Anti-thymocyte Globulin (ATG)
- Total Body Irradiation (TBI)
- Stem Cell Transplant
- Allogeneic Transplant
- Conditioning

Clinical Decision Support

Guides:

- Order set should include access to the [ABMTP Standard Practice Manual](#)

References:

- Reference in other order groups as indicated in each protocol once developed
 - Stem Cell Infusion - Allogeneic

Alerts:

- Methotrexate drug orders within the *GVHD Prophylaxis: Methotrexate Leucovorin* are not to be signed until the day each dose is to be administered. If possible, prefer configuration of a hard stop preventing methotrexate from being signed prior to the day each dose is to be administered

Fludarabine Cyclophosphamide ATG TBI, Adult BMT Inpatient Order Set

Order Set Keywords: bone marrow transplant, blood and marrow transplant, BMT, allogeneic, conditioning, anti-thymocyte globulin (RABBIT), total body irradiation, fludarabine, cyclophosphamide, mesna, cyclosporine, methotrexate, leucovorin calcium

Order Set Requirements

Most recent:

- Height _____ cm
- Weight
 - actual _____ kg
 - ideal _____ kg
- BSA _____ m²
- Estimated Creatinine Clearance (CrCl) _____
- Bilirubin and creatinine lab results

Link patient weight with recommended dose of ursodiol

- For patient weighing less than 75 kg: ursodiol 250 mg PO TID
- For patient weighing 75 – 100 kg: ursodiol 500 mg PO BID
- For patient weighing more than 100 kg: ursodiol 500 mg PO TID

Indication

Conditioning for Allogeneic Stem Cell Transplant

Treatment Cycle and Dates

Stem Cell Infusion date: Day 0 _____ (dd-Mon-yyyy)

Protocol DAY -6, -5, -4, -3

fludarabine 30 mg/m²/dose

Protocol DAY -4 and -3

mesna 60 mg/kg/dose

cyclophosphamide 60 mg/kg/dose

Protocol Day -2

GVHD Prophylaxis: Anti-thymocyte globulin (RABBIT) 0.5 mg/kg/dose

Protocol Day -1, 0

GVHD Prophylaxis: Anti-thymocyte globulin (RABBIT) 2 mg/kg/dose

Protocol Day -1

GVHD Prophylaxis: Cyclosporine

Protocol Day -1 or 0

Total Body Irradiation 200 cGy (for unrelated or mismatched sibling donor)

Protocol Day 0

Allogeneic Stem Cell Infusion

Protocol Day 1 to 12

GVHD Prophylaxis: Methotrexate/Leucovorin

~Start of Order Panel~ BMT Laboratory Investigation – ONCE - Inpatient

****BMT Laboratory Investigation – ONCE - Inpatient**

Keywords: Admission, labs, one time

ONCE – Day of Admission/Pre-Treatment - STAT

Unit to Collect Lab to Collect

Hematology

- Complete Blood Count (CBC) with Differential
- PTT
- PT (INR)
- Retic count

Chemistry

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Electrolytes (Na, K, Cl, CO2) | <input checked="" type="checkbox"/> Albumin | <input type="checkbox"/> LD |
| <input checked="" type="checkbox"/> Creatinine | <input checked="" type="checkbox"/> ALP | <input checked="" type="checkbox"/> Protein Total |
| <input checked="" type="checkbox"/> Glucose Random | <input checked="" type="checkbox"/> ALT | <input checked="" type="checkbox"/> Urea |
| <input checked="" type="checkbox"/> Calcium (Ca) | <input checked="" type="checkbox"/> Bilirubin Total | <input checked="" type="checkbox"/> Urate (uric acid) |
| <input checked="" type="checkbox"/> Magnesium (Mg) | <input checked="" type="checkbox"/> Bilirubin Direct | |
| <input checked="" type="checkbox"/> Phosphate | <input checked="" type="checkbox"/> GGT | |

Other Labs

Order for ALL women of childbearing age

HCG Beta - serum

Urine Tests

Urinalysis

~End~

~Start of Order Panel~ BMT Laboratory Investigation – REPEATING - Inpatient

****BMT Laboratory Investigation – REPEATING - Inpatient**

Keywords: labs, repeat, Day 2

REPEATING - Starting on second day of protocol

Unit to Collect Lab to Collect

Draw the following labs daily for 35 occurrences:

- Complete Blood Count (CBC) with Differential
- Electrolytes (Na, K, Cl, CO2)
- Creatinine
- Magnesium (Mg)

Draw the following labs every Mon/Thurs for 5 weeks:

Hematology

- PTT
- PT (INR)
- Retic Count

Chemistry

- | | | |
|--|--|--|
| <input checked="" type="checkbox"/> Glucose Random | <input checked="" type="checkbox"/> ALT | <input type="checkbox"/> LD |
| <input checked="" type="checkbox"/> Calcium (Ca) | <input checked="" type="checkbox"/> Bilirubin Total | <input type="checkbox"/> Protein Total |
| <input checked="" type="checkbox"/> Phosphate | <input checked="" type="checkbox"/> Bilirubin Direct | <input checked="" type="checkbox"/> Urea |
| <input checked="" type="checkbox"/> Albumin | <input type="checkbox"/> GGT | <input type="checkbox"/> Urate (uric acid) |
| <input checked="" type="checkbox"/> ALP | | |

~End~

Patient Care

- Weight – BID at 0800 hours and 1600 hours starting on Day -4 to -2; Notify physician of weight as may require furosemide PRN for fluid overload
- Urine Dipstick Testing – POCT: for blood - BID starting on Day -4 to -2

Nurse Communication

- Nurse Communication: Initiate mouth care protocol
- Nurse Communication: Irradiated Blood Products only
- Nurse Communication: Ensure central venous access device is insitu and patent prior to initiating treatment protocol

Pre-Medication

- ondansetron 8 mg PO/IV once on Day -6 **AND THEN** ondansetron 8 mg PO/IV TID starting on Day -5 to Day 1; Give morning dose 30 to 60 minutes pre-chemotherapy
- aprepitant 125 mg PO once on Day -4 **AND THEN** aprepitant 80 mg PO daily on Day -3 and -2 for a total of 2 doses; Give dose 30 to 60 minutes pre-chemotherapy
- dexamethasone 12 mg IV/PO once on Day -4 **AND THEN** dexamethasone 8 mg IV/PO daily on Day -3; Give dose 60 minutes pre-chemotherapy; Dose has been reduced by 50% due to interaction with aprepitant

Intravenous Fluids

Pre-Cyclophosphamide Hydration

- 0.9% NaCl IV at 150 mL/hour starting at 2200 hours on Day -5 for a total of 10 hours; to run over 10 hours pre-cyclophosphamide

Cyclophosphamide Hydration

- 0.9% NaCl IV at 100 mL/hour starting at 0800 hours on Day -4 for a total of 3 days; Continue until 1200 hours on Day -2

Systemic Therapy

Use ideal body weight if less than actual body weight for dosing calculations

- fludarabine (30 mg/m²) _____mg IV daily starting 0900 hours on Day -6, -5, -4, -3 for a total of 4 doses; Infuse each dose over 1 hour
 - ❖ *Dosing adjustments: Dosage adjustments may be required for renal impairment*

Use ideal body weight if less than actual body weight for dosing calculations

- mesna (60 mg/kg) _____ mg IV daily starting 1000 hours on Day -4 and -3 for a total of 2 doses; Infuse each dose over 24 hours
 - ❖ *Dosing adjustments: Dosage adjustments may be required for body weight*

Use ideal body weight if less than actual body weight for dosing calculations

- cyclophosphamide (60 mg/kg) _____ mg IV daily starting 1000 hours on Day -4 and -3 for a total of 2 doses; Infuse each dose over 2 hours
 - ❖ *Dosing adjustments: Dosage adjustments may be required for renal impairment and body weight*

Start of Order Panel~ GVHD Prophylaxis: Anti-Thymocyte Globulin (RABBIT) Adult Cancer - Inpatient

****GVHD Prophylaxis: Anti-Thymocyte Globulin (RABBIT) Adult Cancer - Inpatient**

Order Set Keywords: ATG, BMT, graft vs host disease

Order Set Requirements:

- Weight
 - actual _____ kg

Patient Care

- Vital Signs: For each anti-thymocyte globulin (RABBIT) infusion
 - Pre-ATG infusion initiation
 - Then every 15 minutes x 4
 - Then every hour for 3 hours and with rate changes
 - Then 15 minutes post end of infusion

Pre-Medications

- methylPREDNISolone sodium succinate 40 mg IV BID on Days -2, -1, 0 for a total of 6 doses; Give morning dose 30 minutes pre-anti-thymocyte globulin (RABBIT) at the following times:
 - To be given at 1130 hours on Day -2
 - To be given at 0830 hours on Day -1
 - To be given at 0430 hours on Day 0
- diphenhydrAMINE 50 mg IV daily on Days -2, -1, 0 for a total of 3 doses; Give dose 15 minutes pre-anti-thymocyte globulin (RABBIT):
 - To be given at 1145 hours on Day -2
 - To be given at 0845 hours on Day -1
 - To be given at 0445 hours on Day 0
- acetaminophen 1000 mg PO daily on Days -2, -1, 0 for a total of 3 doses; Give immediately pre-anti-thymocyte globulin (RABBIT):
 - To be given at 1200 hours on Day -2
 - To be given at 0900 hours on Day -1
 - To be given at 0500 hours on Day 0

Emergency Medications

- meperidine 25 mg IV every 4 hours PRN on Days -2, -1 and 0 for rigors with anti-thymocyte globulin (RABBIT) infusion

- meperidine 50 mg IV every 4 hours PRN on Days -2, -1 and 0 for rigors with anti-thymocyte globulin (RABBIT) infusion

Anti-thymocyte globulin (RABBIT)

Pre-medication with acetaminophen and antihistamines is recommended

- anti-thymocyte globulin (RABBIT) (0.5 mg/kg) _____mg IV once starting Hour 4 at 1200 hours on Day -2 for a total of 1 dose; Infuse over 4- 6 hours as per provincial parenteral monograph; Requires 0.2 to 1.2 micron filter on primary line
- anti-thymocyte globulin (RABBIT) (2 mg/kg) _____mg IV once starting Hour 0 at 0900 hours on Day -1 and Hour 0 at 0500 hours on Day 0 for a total of 2 doses; Infuse over 4 - 6 hours as per provincial parenteral monograph; Requires 0.2 to 0.22 micron filter on primary line

~End~

Day 0

~Start of Smart Group~ Total Body Irradiation (TBI) - Inpatient

*Total Body Irradiation (TBI) – Inpatient

Nurse Communication

- Nurse Communication: Total Body Irradiation must be completed **PRIOR** to hematopoietic progenitor cell (HPC) infusion
- Nurse Communication: Ensure patient has only **ONE** corticosteroid scheduled prior to morning Total Body Irradiation (i.e. methylPREDNISolone sodium succinate or dexamethasone)

Pre-medication (first fraction)

- LORazepam 1 mg PO/SUBLING once immediately prior to first fraction Total Body Irradiation

DO NOT order if corticosteroid already ordered in protocol

- methylPREDNISolone sodium succinate 40 mg IV once immediately prior to second fraction Total Body Irradiation

Pre-medication (second fraction)

- LORazepam 1 mg PO/SUBLING once immediately prior to second fraction Total Body Irradiation

DO NOT order if corticosteroid already ordered in protocol

- methylPREDNISolone sodium succinate 40 mg IV once immediately prior to second fraction Total Body Irradiation

TBI

- Total Body Irradiation First Fraction
- Total Body Irradiation Second Fraction

~end~

Day 0

Required order set (Currently under development; to be referenced in upon completion)

➤ **Stem Cell Infusion - Allogeneic**

~Start of Smart Group~ *GVHD Prophylaxis: Cyclosporine Adult Cancer - Inpatient*

***GVHD Prophylaxis: Cyclosporine Adult Cancer - Inpatient**

Cyclosporine LEVEL

- Unit to Collect Lab to Collect
- Cyclosporin LEVEL, pre-dose: every Mon/Wed/Fri X 35 occurrences starting on Day 0; **Target LEVEL 200 – 400 mcg/L**; Draw trough level PRIOR to AM dose of cyclosporine from a non-cyclosporine infusion line

Cyclosporine

Choose *ONE* of the following options:

Round PO cyclosporine dose to nearest 25 mg. If actual body weight is less than ideal body weight, use actual body weight for all dosing calculations

- cycloSPORINE (6.25 mg/kg-ideal/dose) _____ mg PO every 12 hours starting on Day -1; If administering cycloSPORINE by this route, suspend any other scheduled routes ordered for this drug
 - ❖ *Dosing adjustments: Dosage reduction may be required for renal and hepatic impairment*

OR

If actual body weight is less than ideal body weight, use actual body weight for all dosing calculations

- cycloSPORINE (2.5 mg/kg-ideal/dose) _____ mg IV every 12 hours starting on Day -1; Infuse over 2 to 6 hours; If administering cycloSPORINE by this route, suspend any other scheduled routes ordered for this drug
 - ❖ *Dosing adjustments: Dosage reduction may be required for renal and hepatic impairment*

~End~

~Start of Smart Group~ *GVHD Prophylaxis: Methotrexate / Leucovorin Adult Cancer - Inpatient*

***GVHD Prophylaxis: Methotrexate / Leucovorin Adult Cancer - Inpatient**

Methotrexate Monitoring

- Unit to Collect Lab to Collect
- Bilirubin Total daily on Day 1, 3, 6, and 11
- Bilirubin Direct daily on Day 1, 3, 6, and 11

Nurse Communication

- Nurse Communication: If creatinine rising or abnormal, ascites, effusions, mucositis, or increasing direct bilirubin, consult physician regarding holding/reducing methotrexate dose
- Nurse Communication: methotrexate orders to be signed by ordering clinician individually on each day of administration after patient has been assessed

Provider Communication

- Provider Communication: methotrexate orders are not to be signed until after patient has been assessed on each day of administration

Methotrexate (Held Orders: to be signed each day of dose administration)

Order both of the following methotrexate orders:

- methotrexate (15 mg/m²-ideal) _____ mg IV once on Day 1 for a total of one dose; Give dose 24 hours post **END** of stem cell infusion; Administer IV direct push over 2 to 5 minutes
 - ❖ *Dosing adjustments: Dosage reduction may be required for renal impairment, ascites, mucositis and elevated direct bilirubin*
- methotrexate (10 mg/m²-ideal) _____ mg IV daily starting 1200 hours on Day 3, 6, 11 for a total of 3 doses; Administer IV direct push over 2 to 5 minutes
 - ❖ *Dosing adjustments: Dosage reduction may be required for renal impairment, ascites, mucositis and elevated direct bilirubin*

Leucovorin Calcium

- leucovorin calcium 5 mg IV every 6 hours starting on Days 2, 4, 7, 12:
 - Start Day 2 dose 24 hours post last methotrexate dose for a total of 3 doses; Not to be given within 12 hours prior to next methotrexate dose; Due to timing of stem cell transplant and methotrexate dose, third leucovorin dose may need to be held
 - Start Day 4 at 1200h for a total of 7 doses; Not to be given within 12 hours prior to next methotrexate dose
 - Start Day 7 at 1200h for a total of 15 doses; Not to be given within 12 hours prior to next methotrexate dose
 - Start Day 12 dose at 1200h; MD to reassess when absolute neutrophil count (ANC) greater than or equal to $0.5 \times 10^9/L$

~End~

~Start of Order Panel~ **BMT Electrolyte Imbalance - Inpatient**

**** BMT Electrolyte Imbalance - Inpatient**

Order Set Keywords: potassium, K, KCl, magnesium, Mg

Nurse Communication:

- Nurse Communication: Ensure patient has no other IV potassium infusing while receiving PRN IV potassium doses

Potassium:

Choose **ONE** option based on site availability of product

- KCl 20 mmol in 100 mL sterile water IV bolus daily PRN if potassium level 3.0 to 3.3 mmol/L; infuse as per provincial parenteral monograph

OR

- KCl 10 mmol in 100 mL sterile water IV bolus daily PRN; Give 2 boluses for a total of 20 mmol if potassium level 3.0 to 3.3 mmol/L; Infuse as per provincial parenteral monograph

Magnesium:

- magnesium sulfate 4 grams IV daily PRN if magnesium level is LESS than 0.55 mmol/L; Infuse as per provincial parenteral monograph

~End~

~Start of Smart Group~ Allogeneic Prophylactic/Supportive Medication - Inpatient

***Allogeneic Prophylactic/Supportive Medication - Inpatient**

Prophylactic Medications

- valACYclovir 500 mg PO daily starting on day of admission
- fluCONazole 400 mg PO daily starting on Day 1 for a total of 30 days

Start Protocol Day 21 if neutrophils are greater than $1 \times 10^9/L$

- sulfamethoxazole - trimethoprim 400 mg - 80 mg 1 tab PO daily starting on Day 21

OR

If patient has allergy to sulfa or sulfamethoxazole/trimethoprim order both:

Start Protocol Day 21 if neutrophils are greater than $1 \times 10^9/L$

- dapsone 50 mg PO daily starting on Day 21
- penicillin V potassium 300 mg PO BID starting on Day 21

Supportive Medications

Only order for menstruating women

- norethindrone - ethinyl estradiol (Ortho 1/35®) 1 tab PO daily starting on day of admission

For patient weighing less than 75 kg

- ursodiol 250 mg PO TID with meals starting on day of admission

OR *for patient weighing 75 – 100 kg*

- ursodiol 500 mg PO BID with meals starting on day of admission

OR *for patient weighing more than 100 kg*

- ursodiol 500 mg PO TID with meals starting on day of admission

~End~

Transition Planning

Patient and Family Education

MyHealth.Alberta.ca

- [Cancer Resources](#)
- [Allogeneic Stem Cell Transplant](#)
- [Conditioning Phase When Having an Allogeneic Stem Cell Transplant](#)
- [Radiation Treatment: Video Series \(includes Total Body Irradiation\)](#)

YouTube: AHS Channel

- [CancerControl Alberta Playlist](#)

Transitions to Primary Care

Alberta Health Services Website (External)

- [Provider and Patient Resources](#)

Patient Medication Teaching Sheets

MyHealth.Alberta.ca

- [Cyclophosphamide](#)
- [Mesna](#)
- [Fludarabine](#)
- [Anti-thymocyte Globulin \(ATG\)](#)
- [Methotrexate](#)
- [Leucovorin Calcium](#)
- [Cyclosporine](#)
- [Ondansetron](#)
- [Dexamethasone](#)
- [Dapsone](#)
- [Sulfamethoxazole/Trimethoprim](#)
- [Penicillin V Potassium](#)
- [Fluconazole](#)
- [Valacyclovir](#)
- [Ursodiol](#)
- [Norethindrone/ethinyl estradiol](#)

Alberta Health Services Website (Internal)

- Total Body Irradiation: Please see Patient and Family Education Resources – Radiation Treatment on the CancerControl Alberta AHS Internal website

References

1. Cancer Control Alberta: Guideline Resource Unit: Alberta Blood and Marrow Transplant Program (ABMTP) Standard Practice Manual. Alberta, Canada.
<https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-bmt-manual.pdf>. Updated January 16, 2017. Accessed January 5, 2018.

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