



PEDIATRIC BLOOD AND MARROW TRANSPLANT PROGRAM

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ADMINISTRATION OF HIGH DOSE CHEMOTHERAPY - BUSULFAN

1 PURPOSE

- 1.1 To outline the procedure required for administration of busulfan. Responsibilities of the nursing staff for administering and monitoring reactions to busulfan are described.

2 INTRODUCTION

- 2.1 Busulfan is a bi-functional alkylating agent that is not cell cycle specific. It is not a structural analog of the nitrogen mustards. Busulfan interacts with cellular thiol group's nucleic acids producing cross links primarily between DNA (deoxyribonucleic acid) and proteins and a small amount of DNA interstrand cross-linking.
- 2.2 Oral busulfan has variable absorption therefore intravenous (IV) busulfan is used. The elimination half-life is 2-3 hours. Peak plasma concentrations are reached within 0.5-4 hours.
- 2.3 Busulfan can cause myelosuppression, which is virtually universal and can include any combination of severe granulocytopenia, thrombocytopenia, and/or anemia. Seizures, veno-occlusive disease (sinusoidal obstructive syndrome), interstitial pneumonia, hemorrhagic cystitis, and permanent alopecia have been reported as complications with high dose chemotherapy in connection with bone marrow transplantation. Other complications include pulmonary fibrosis, endocardial and pericardial fibrosis, an Addisonian-like syndrome, and cataracts.

3 SCOPE AND RESPONSIBILITIES

- 3.1 Interdisciplinary: Attending physicians, advanced practice providers (APPs), pharmacists and registered nurses (RNs) are all responsible for the contents of this procedure.
 - 3.1.1 The nurse is responsible for administration of Busulfan, management of side effects and assessment of response.
 - 3.1.2 The attending physician is responsible for placing chemotherapy order in the medical records.
 - 3.1.3 The physician and advanced practice providers are responsible for assessment and direction of management of patient.
 - 3.1.4 The pharmacist is responsible for review of the chemotherapy order and all downstream pharmacy processes in compliance with chemotherapeutic policies and procedures.
- 3.2 RNs may administer Busulfan after successful completion of the medication administration test, the chemotherapy test, and demonstration of clinical competency with their preceptors.

4 DEFINITIONS/ACRONYMS

- 4.1 DNA Deoxyribonucleic acid
- 4.2 IV Intravenous
- 4.3 MD Medical Doctor
- 4.4 RN Registered Nurse
- 4.5 PK Pharmacokinetics

5 MATERIALS

- 5.1 See the health-system related policy: *Chemotherapy Administration Policy*.

6 EQUIPMENT

- 6.1 See the health-system related policy: *Chemotherapy Administration Policy*.

7 SAFETY

- 7.1 Use appropriate Personal Protective Equipment (PPE) when handling chemotherapy. See the health-system related policy: *Chemotherapy Administration Policy*.

8 PROCEDURE

- 8.1 See over-arching procedural steps, including steps for patient assessment and chemotherapy administration steps, in the health-system related policy: *Chemotherapy Administration Policy*.
- 8.2 Patient assessment will be performed as outlined in *Chemotherapy Administration Policy*.
- 8.3 Additionally:
 - 8.3.1 Patients will receive seizure prophylaxis medication immediately prior to the start of and during the Busulfan regimen.
 - 8.3.2 Monitor for seizure activity during dosing regimen.
 - 8.3.3 Busulfan must be given exactly at the time ordered. **The typical dosing times are 12am, 6am, 12pm, and 6pm.**
 - 8.3.4 **If patient is receiving oral Busulfan, educate family that patient may not eat or drink anything 1 hour before and 30 minutes after the administration of each dose of Busulfan.**
 - 8.3.5 Busulfan levels must be drawn with the first dose as follows:
 - 8.3.6 The pre-dose level is drawn prior to the administration of the first dose of Busulfan. This level may be drawn with the morning labs at 12 a.m.
 - 8.3.7 Additional levels must be drawn per admit orders and vary is schedule as to whether the Busulfan dose route of administration is oral or IV.
DO NOT GIVE THE SECOND DOSE OF BUSULFAN UNTIL ALL OF THE LEVELS ARE DRAWN.

- 8.3.8 The Busulfan Pharmacokinetic Flow Sheet is to be completed on each patient. The exact time of the blood draw is to be recorded.
- 8.3.9 All Busulfan levels should be placed in a 2 mL Lithium Heparin light green vacutainer. Call Phlebotomy to request the blood tubes if they are not available on the floor. Once drawn, the tubes should immediately go on ice or in an ice pack and then placed into the refrigerator in the dirty utility room.
- 8.3.10 After the final level is drawn, place the last specimen on ice or in an ice pack. Once all levels are collected and once ice, the RN hand delivers specimens with the completed Busulfan Pharmacokinetic Datasheet, with patient name label attached, to the 24/7 Central Collections lab drop off window.
- 8.4 Chemotherapy administration will be performed as outlined in *Chemotherapy Administration Policy*.

9 RELATED DOCUMENTS/FORMS

- 9.1 Busulfan Pharmacokinetic (PK) Flowsheet
- 9.2 Win-nolen PK Program - in Pharmacy
- 9.3 Duke University Health System *Chemotherapy Administration Policy*

10 REFERENCES

- 10.1 2003 Thompson Micromedex
- 10.2 Duke Hospital Process Standards for Chemotherapy Administration and Spills.
- 10.3 A pilot study of busulfan and melphalan as preparatory regimen prior to allogeneic bone marrow transplantation in refractory or relapsed hematological malignancies.
N Vey, B De Prijck, C Faucher, AM Stoppa, D Sainty, M Lafage, R Bouabdallah, C Chabannon, J Camerlo, JA Gastaut, D Maraninchi, and D Blaise
Bone Marrow Transplant, Sep 1996; 18: 495-9.
- 10.4 Busulphan kinetics and limited sampling model in children with leukemia and inherited disorders.
M Hassan, A Fasth, B Gerritsen, A Haraldsson, Z Syrucekova, H van den Berg, M Sandstrom, M Karlsson, S Kumlien, and J Vossen
Bone Marrow Transplant, Nov 1996; 18: 843-50.
- 10.5 High busulfan concentrations are associated with increased transplant-related mortality in allogeneic bone marrow transplant patients.
P Ljungman, M Hassan, AN Bekassy, O Ringden, and G Oberg
Bone Marrow Transplant, Dec 1997; 20: 909-13.
- 10.6 Association of busulfan area under the curve with veno-occlusive disease following BMT.
SP Dix, JR Wingard, RE Mullins, I Jerkunica, TG Davidson, CE Gilmore, RC York, LS Lin, SM Devine, RB Geller, LT Heffner, CD Hillyer, HK Holland, EF

Winton, and R Saral
Bone Marrow Transplant, Feb 1996; 17: 225-30.

11 REVISION HISTORY

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| 07 | S. McCollum | <ul style="list-style-type: none">• Scope and Responsibility section updated with job roles for better format uniformity across documents.• PBMT-GEN-069 was removed throughout the document as it will be archived soon and changed to the health system policy: Chemotherapy Administration Policy. |

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