BC Centre for Palliative Care

B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

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SEVERE BLEEDING

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DEFINITION

Bleeding is the loss of blood or blood escaping from the circulatory system. Associated symptoms depend on the duration and rate of bleeding.[1] The terms **'massive' or 'catastrophic' are sometimes preferred over the term 'terminal' hemorrhage** because not all large bleeds result in death.2 This guideline will refer to **severe bleeding** which is a large amount of blood loss. The clinical presentation of bleeding in the palliative care setting is variable. It may be visible or invisible; volumes may vary from low-grade oozing to massive and catastrophic, continuous or intermittent. It may be localized or from multiple sites.[2] **Exsanguination** is defined as the blood loss of >150 mL per minute or loss of entire blood volume in 24 hours.[3, 4]

PREVALENCE

Massive hemorrhage has been estimated to affect less than 2% of patients in the palliative care setting.[3] In cancer patients, the nature of the bleeding depends on type of primary cancer and location of the metastases with tumour erosion of aorta, pulmonary, carotid and femoral arteries being the greatest likelihood.[3, 5, 6] Bleeding also occurs in terminally ill patients with non-cancer diagnoses, e.g., variceal hemorrhage occurs in 25-35% of patients with cirrhosis.[2]

IMPACT

Catastrophic, massive bleeding warrants special attention because of its dramatic and traumatic clinical presentation and the profound distress it causes to patients, families and caregivers.[2] While a catastrophic bleed is not painful for the patient, it is often described as a terrifying experience for the patient, the family and staff.[7, 8] This affects not only the family's experience at the time of death but runs the risk of affecting the nature of their grief and bereavement.

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ("**Additional Resources for Management of Severe Bleeding" on page 9**) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

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Step 2 | Assessment

Severe bleeding Assessment: Using Mnemonic O, P, Q, R, S, T, U and V[32]

Mnemonic Letter	**Assessment Questions** *Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.*
Onset	Has herald or sentinel bleeding occurred, i.e., have you had any bleeding or oozing at this point? When did it begin? How long does it last? How often does it occur?
Provoking /Palliating	Is there any action/movement that provokes bleeding? Is there anything that makes it worse? Or better?
Quality	If there is bleeding, how would you describe it? Is it gradual and slow? Does it ooze, gush or spurt?
Region/Radiation	Where is the bleeding located? Is there more than one site of bleeding?
Severity	How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g., pain, dyspnea, anxiety)? Approximately how much blood is lost in 24 hours (depending on site ask about soaked bed linen, number of saturated gauzes, color of water in the toilet)?
Treatment	What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? Have any special dressings been used to absorb bleeding?
Understanding	What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you?
Values	What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family?

Symptom Assessment: Physical assessment as appropriate for symptom

A comprehensive history and physical examination is required to determine the risk of a severe bleed, potential origins and the potential for multiple sites. Massive bleeding may take place in the lung without the presence of hemoptysis so listening to lung sounds is very important.9 Initial bleeding in the form of hemoptysis or bleeding from a malignant neck wound may signal an impending severe bleed.

Diagnostics: consider goals of care before ordering diagnostic testing

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see **Underlying causes of severe bleeding in palliative care**)

Bleeding causes can be classified within six categories

(1) cancer invasion and destruction, (2) treatment-related causes, (3) thrombocytopenia/marrow failure, (4) nutritional deficits, (5) drugs, and (6) coagulation disturbances.[2] See **Underlying causes of severe bleeding in palliative care** for further specific primary causes.

PRINCIPLES OF MANAGEMENT

When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?).

- Assess risks and need for anticipatory management
    - Develop an anticipatory care plan (see **Severe bleeding extra resources or assessment tools** for more detail) where possible and appropriate
    - Make sure all professionals and services involved are aware of the care plan, including out-of-hours services.[7]
- Manage bleed event
    - Keep calm, be present, comfort, reposition, shield visual trauma with dark towels, summon help, be supportive with help of medications and warm blankets. See further details in section 5 and 6.
- Post bleed management [10]
    - Offer de-briefing to family and health care team. This is critical
    - Provide ongoing support as necessary for relatives and staff members.
    - Dispose of clinical waste appropriately.

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

	**Use with confidence:** recommendations are supported by moderate to high levels of empirical evidence.
	**Use if benefits outweigh potential harm:** recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence.
	**Use with caution:** Evidence for recommendations is conflicting or insufficient, requiring further study
	**Not recommended:** high level empirical evidence of no benefit or potential harm

Non-pharmacological interventions[2, 4, 6, 8, 10, 12-14]:

Interventions available in the home and residential care facilities

It may be possible to manage a severe bleed in the home or residential care facility with appropriate planning and support for the patient, family and staff; all of these interventions do not necessarily require additional equipment or admission to acute care.

ABCD Response	
A - Assure	**Assure patient** this event has been anticipated. Reassure that you will stay with them throughout.
B - Be Present	**Stay with patient. Considered the most important intervention.** Ensure that someone is with the patient at all times.
C - Calm, Comfort	**Employ intensive calmness**. Comfort: verbally soothe, hold, touch or hug them.
D - Dignity	**Maintain patient dignity.** Minimize visual impact. Cover patient with dark towels or sheets. Use basins, sheets or absorptive dressings with an impermeable backing. Clean patient face with moist cloths often.
Management of the Bleed	
REPOSITION	Adjust body position for blood flow, comfort, minimize sighting of blood: Use recovery position to keep airway clear. For hematemesis - place in left lateral decubitis position. For hemoptysis - position onto the side in which the presumed bleeding lung is in the dependent position, e.g., place a patient whose right lung is bleeding on their right side.
SUMMON HELP	Call for help.
APPLY PRESSURE	Assess individual circumstances; use direct pressure cautiously with friable tissue. Local pressure **may** be appropriate for an external wound.
MEDICATIONS	Midazolam use when required; see below and Medications for management of severe bleeding**.**
WARMTH	Warm blankets can offset hypothermia from rapid bleed.
SUPPORT	Goals of care, plan a debrief for all who were present.
NOTIFY	Inform family, physician, others.

Pharmacological Interventions

(see **Medications for management of severe bleeding** for Medication table)

- Use sedation as quickly as possible to relieve distress, when practical and timely.[13, 14]
- **Midazolam 10 mg dose is most commonly used for major bleeds.**[2, 10, 12-17]
  - Give midazolam IV (preferred) bolus, if IV access is possible.[6, 10]
  - Alternatively give SC, IM (large deltoid or gluteal muscle),or buccal. [7, 12, 14, 18]
  - Repeat dose if needed. IV within 5 minutes, SC, IM, buccal within 5 to 15 minutes.[13]
- Alternatives include: Lorazepam 4 mg IV/SC/sublingual10 and Ketamine 150 to 250 mg IV, or 500 mg IM (large deltoid or gluteal muscle). [13, 16]
- Opioids are indicated for pain or dyspnea.[14] Hemorrhage is usually not painful.[6, 13, 16]

Patient and family education

- Ask if they want to know about risks, potential developments; ask if they are willing to participate in anticipatory planning for a potential bleed event.
  - As appropriate, involve patient and family in the plan creation.
  - As appropriate, share the supportive anticipatory care plan.
  - Reassure that in the event of a bleed, the person WILL be kept comfortable and will not be left alone; unconsciousness could occur quickly.[3]
  - Remind patient and family that not all anticipated bleeds materialize.
- Anticipatory plan should
  - Provide awareness and supportive information, and enhance patient/ family coping.
  - Include a NO CPR order and/or NO CPR advance directive.
  - Teach calm approach and value of comforting presence to patient.
  - Identify who to call; unprepared caregivers may panic, calling emergency services that are required to institute resuscitative measures. Include after hours nurse phone line if available in your region.
  - Ensure family and caregivers understand intent of medication is solely to relieve distress and anxiety, not to hasten death.[11]
    - Inform that if anti-anxiety drugs help, they will need time to prepare and work, which could be too slow if bleed is large or very rapid.
  - Consider the implications of asking a caregiver and family member to administer prefilled syringes of sedatives in the event of a massive bleed if they are alone when it begins.[2]

See Severe bleeding extra resources or assessment tools for further specifics about anticipatory planning.

ADDITIONAL RESOURCES FOR MANAGEMENT OF SEVERE BLEEDING

Resources specific to Severe Bleeding: No additional resources specific to severe bleeding included in this document

General resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide

  https://www.bc-cpc.ca/cpc/serious-illness-conversations/
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease

  http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care
- BC Palliative Care Benefits: Information for prescribers

  https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions

  https://nccih.nih.gov/
- Canadian Association of Psychosocial Oncology: Algorithms for Cancer-related Distress, Depression and Global Anxiety

  https://www.capo.ca/resources/Documents/Guidelines/4.%20Algorithms%20for%20Cancer-related%20Distress,%20Depression%20and%20Global%20Anxiety.pdf
- Fraser Health psychosocial care guideline

  https://www.fraserhealth.ca/employees/clinical-resources/hospice-palliative-care#.W-by_pNKg2w

Resources specific to health organization/region

- Fraser Health

  https://www.fraserhealth.ca/employees/clinical-resources/hospice-palliative-care#.XDU8UFVKjb1

- First Nations Health Authority

  http://www.fnha.ca/

- Interior Health

  https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx

- Island Health

  https://www.islandhealth.ca/our-services/end-of-life-hospice-palliative-services/hospice-palliative-end-of-life-care

- Northern Health

  https://www.northernhealth.ca/for-health-professionals/palliative-care- end-life-care

- Providence Health

  http://hpc.providencehealthcare.org/

- Vancouver Coastal Health

  http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians

  https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care- For-Primary-Care-Physicians-English.pdf

- ALS Society of British Columbia 1-800-708-3228

  www.alsbc.ca

- BC Cancer Agency: Symptom management guidelines

  http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management

- BC Renal Agency: Conservative care pathway and symptom management

  http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care

- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management

  http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life- tools/

- Canuck Place Children's Hospice

  https://www.canuckplace.org/resources/for-health-professionals/

  - 24 hr line – 1.877.882.2288
  - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)

- Together for short lives: Basic symptom control in pediatric palliative care

  http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

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UNDERLYING CAUSES OF SEVERE BLEEDING IN PALLIATIVE CARE[2,6]

1. Overall risk factors for bleeding in cancer patients	
Thrombocytopenia<20,000/uL	Myelodysplasia
Large head and neck cancers	Severe liver disease and metastatic liver disease
Large centrally located lung cancers	High-dose radiation therapy
Refractory chronic and acute leukemias	Oral anticoagulants
Risk factors for severe hemorrhaging in head and neck cancers	
Radical neck dissection	Fungating tumours with arterial invasion
High-dose radiotherapy	Sentinel bleed
Postop healing problems	Direct observation during surgery or imaging (e.g. magnetic resonance imaging) of artery wall invasion
Visible arterial pulsation	
2. Drug Causes	***Using references[2, 6]***
Drugs - Drug Classes	**Specific Causative Examples***
Anticoagulants, Antiplatelet drugs	ASA, Apixiban 0.1-2.1% (major), Clopidogrel 0.8-3.7% (major), Dabigatran 0.3-3.3%, Dalteparin up to 13.6% (major), Danaparoid up to 45%, Dipyridamole, Enoxaparin up to 4% (major), Heparin, Rivaroxaban 17.4-28.3% (treatment of deep vein thrombosis or pulmonary embolism), Ticagrelor 1.7-3.9% (major), Ticlopidine %, Tinzaparin 0.8% (major), Warfarin
Antidepressants	Citalopram, Desvenlafaxine, Doxepin, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline <0.1%, Venlafaxine
Antiretrovirals	Indinavir 2.7-39%, Ritonavir 2.7-46%, Saquinavir 2.7-14%

Chemotherapy	Bevacizumab 40 % (glioblastoma any grade), Capecita-bine, Cyclophosphamide, Gemcitabine 9-17%, Hydroxy-urea, Ifosfamide, Imatinib 1-53% (chronic myeloid leuk-emia [CML] all grades), Irinotecan 1-5%, Nilotinib 1.1-1.8% (CML), Paclitaxel 10-14%, Sorafenib 15.3% (renal cell carcinoma [RCC]), 17.4% (thyroid carcinoma), Sunitinib 37% (RCC), 18% (GI stromal tumor) 22% (pancreatic neuroendocrine tumors), Thiotepa 28% (IV high dose)
Corticosteroids	Dexamethasone 2.5% (gastrointestinal), Prednisone
Non-Steroidal Anti-inflammatory Agents	Celecoxib, Diclofenac, Ibuprofen 4-10%, Indomethacin, Ketorolac, Meloxicam, Naproxen
Other	Dexmedetomidine 3%, Everolimus 3% (renal cell carcin-oma), Meropenem 1.2%, Sodium Valproate 1-27% (throm-bocytopenia), Sotalol 2%, Testosterone, Topiramate 4.4%

* There are many medications that are reported to cause bleeding, thrombocytopenia. If no specific percentage incidence shown for each drug, the known occurrence rate not reported.[6, 10] This table above provides some examples. Consult pharmacist if additional assistance is required.

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MEDICATIONS FOR MANAGEMENT OF SEVERE BLEEDING

Drug (classification)	Dose, Therapeutic range	Onset, Adverse Effects, Precautions and Dosing Concerns
Midazolam*† (benzodiazepine)	Stat dose: 10 mg IV, SC, IM, buccal Repeat dose 5 min IV 5 to 15 min SC, IM, buccal	**Onset:** 1 to 5 min IV,[20] 5 to 10 min SC,[21] 5 to 15 min IM into deltoid muscle[10, 18] **Adverse effects:** IV administration over 2 to 3 minutes suggested to minimize hypotensive effects, reported in up to 30% of patients.[22, 23] However, consider immediacy of bolus administration within clinical context. **Contraindicated** if hypersensitivity to benzodiazepines. **Precautions** in patients with prior paradoxical reaction history to benzodiazepines. Prior or concurrent opioid dosing may increase respiratory depressant effects. **Dosing:** Review dose, 10 mg commonly recommended.[2, 10, 12-17] A single dose in an emergency situation, must be sufficiently adequate for a rapid and predictable effect.[13] Lower doses, such as 2.5 to 5 mg may be appropriate if bleeding is brisk but not rapidly fatal.[2, 13] Weight based dosing of 0.2 mg/Kg dose IV or SC suggested for urgent palliative bleed sedation (where known).[4] Higher doses may be needed; if already on background benzodiazepines, heavy alcohol or substance use.[7, 10, 14] **Effectiveness of route of administration**: Peripheral circulation shutdown during hypovolemic shock has some experts suggesting that bioavailability will be especially compromised for IM and SC administration.[2, 10, 16] SC route may be unpredictable.[10] Most references continue to suggest SC use.[2, 4, 14, 17] For buccal administration, place dose between the patient's cheek and gum.[14] **Storage of prefilled syringes**: 5 mg/mL undiluted reported stable for 36 days at 25° C when protected from light.[24] Sterility assurance beyond 24 hours of preparation unknown, assess importance, duration of storage within clinical context. Recently, Health Canada has cautioned regarding storage of medications in disposable plastic syringes citing risk of potency concerns.[25] Replacement every 4 to 7 days has been suggested.[15, 26]

Drug (classification)	Dose, Therapeutic range	Onset, Adverse Effects, Precautions and Dosing Concerns
Lorazepam*† (benzodiazepine)	**4 mg x 1 dose** **IV, SL, SC, IM or buccal**	**Onset:** 5 minutes SL.[21, 27] May be as long as 20-30 minutes.[28] IV onset faster than SC or SL.[29] Sublingual onset similar to IM, SC. [28, 29] For buccal administration: in patients with a dry mouth, the tablet should be dissolved in a few drops of warm water, or drop SL tablet into a syringe, add water to dissolve, then place dose between the patient's cheek and gum.[27 30]
Ketamine*† (anesthetic)	150 to 250 mg IV x 1 dose 500 IM x 1 dose [13, 16]	**Onset:** 1 minute IV,[31] 5 min IM.[21] **Adverse effects** include paradoxical excitation. IM injection volume large, requiring multiple sites of injection.

* Dose effect for massive bleed treatment not studied, is expert opinion only.

†Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan https://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdfprovides province wide drug coverage for many of the recommended medications– check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

SEVERE BLEEDING MANAGEMENT ALGORITHM

No management algorithm included in this document.

SEVERE BLEEDING EXTRA RESOURCES OR ASSESSMENT TOOLS

Anticipatory Planning Review List for Bleed Risk Patients [2, 6, 10, 14, 16, 19]

Note: use the below checklist as a guide for creating a care plan

FOR ALL SETTINGS

☐ Discussion

- The discussion should be consistent with the patient's information, needs and preferences; the care plan needs to be compatible with the patient's wishes.[2]
- All patients with a potential bleed need a plan of care created for use by family and health care providers.
- Additionally, some patients may wish to create a Bleeding Plan specific to their situation (e.g., in the event of a bleed, music to be played, dim lights in room, persons to phone or be present, sedation to be initiated or not).
- Store plans and Bleed Kit in accessible, convenient locations. Ensure appropriate awareness of these locations.

☐ Contact Lists (individualized for this patient/family and this situation)

- 24 hr access in event of bleed at home, psychosocial counselling, other: Name, Telephone Number.

☐ Supportive Resources

- The primary objective in managing a severe bleed is to minimize distress and potential trauma for the patient, family and staff.[6]
- Create a Bleed Kit: Ensure a supply of dark sheets or towels along with other equipment (gloves, aprons, plastic sheet, and clinical waste bags) in one organized container. Keep readily available.
- Explain the rationale for dark towels – to reduce the visible impact and decrease distress anxiety from seeing large volumes of blood.[14, 19]
- Have several face cloths close to bedside to wipe patient's mouth, face.

☐ Provide for Emergency On-Demand Medication Care Orders

- Orders written, or initiate pre-printed facility orders.
- Consider route, pre-insertion and management of parenteral access device.
- Medication and doses should reflect pre-existing conditions, benzodiazepine exposure. **See Medications for management of severe bleeding**
- Parameters: When to initiate, sedation target or need for use of sedation scales.
- Review suitability of prefilled syringe of medication to be on-hand, or use of locked storage cabinet.[16]
- Clarify if opioids have an emergency role, usually limited to that of pain or dyspnea.

☐ Assess bleeding risk of Current Medications

- Anticoagulants, chemotherapy, corticosteroids, non-steroidal anti-inflammatory agents, selective serotonin receptor antagonists, sodium valproate. **See others in Underlying causes of severe bleeding in palliative care**.
- Modify risk factors; stop unnecessary drugs; appropriately reduce/stop suspected drug causes; and consider a switch to drug option of lower bleed risk propensity.
- Assess benefits versus burden of continuing prophylactic anticoagulation treatments.
- Consider consultation with a pharmacist for drug-related risk management.
- Assess if specific preventative medication measures could have a role (e.g., proton pump inhibitors, tranexamic acid, topicals). Discuss further with palliative team consultants.

☐ Team Planning, Communication

- Ensure there is multidisciplinary team involvement and documentation. Suitably share with other teams and involved care members.
- Confirm team understanding of action priorities. Acknowledge that crisis medications may have little role due to the speed of event, with a duration that last only minutes and insufficient time for therapeutic effect.[2, 19]

- Ensure clarity that medication intent is to relieve patient distress, not to hasten death.[2, 16]
- Reflect current care site in plans, and foresee if site transfers might occur.
- Provide staff education and awareness of patient's own management, goals of care.
- Plan for who will clean up after an event and how to contact them.[10]

☐ Other Anticipatory Management

- Acknowledge that any major bleed should be managed the same way, regardless of knowing which will be a terminal event.[16]
- Assess suitability of continuous subcutaneous midazolam infusion for other indications, such that an on-demand bolus dose could be administered.
- Assess need for the addition of an opioid (e.g., if patient has pre-existing pain or dyspnea).

FOR HOME (COMMUNITY) SETTINGS

☐ Discussion

- Ensure family (in home setting) have 24-hour contact number(s) and designate people who will be nearby for support.
- Confirm patient family acceptance and understanding that medications for distress are planned for and readily available should a severe bleed occur.
- Enquire if caregivers feel able to administer needed medication.
- Establish administration responsibility.
- Pre-plan at home for individual prescriptions or Palliative drug kits as appropriate.

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