

CHLORAMBUCIL

Most patients treated with Chlorambucil will experience adverse effects, but the effects will differ from one patient to the next. Symptoms may indicate that the underlying cancer is not under control or has relapses. Cancer patients may also have co-morbid diseases that require treatment and cause symptoms.

The most common adverse effects with Chlorambucil are myelosuppression and hyperuricemia.

ADVERSE DRUG REACTION MANAGEMENT GUIDE

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| 1. Myelosuppression | 4. Diarrhea |
| 2. Nausea & vomiting | 5. Rash |
| 3. Stomatitis | |

1. Myelosuppression

Chlorambucil may cause suppression of the blood cell production in the myeloid tissues of the bone marrow. This can result in lowering of white blood cells and platelets. It is important to have a Complete Blood Count (CBC) blood test prior to the start of each cycle of this agent. If any blood cell component is reduced below an acceptable level, the drug may need to be held until the blood cells recover. **Chlorambucil must NOT be dispensed** until the CBC test is completed and verified prior to each cycle of the treatment. Verification will be done by an oncology health professional.

2. Nausea & vomiting

Nausea and vomiting may occur in up to 30% of patients on Chlorambucil. Unlike the nausea and vomiting often experienced by patients on cytotoxic chemotherapy (acute onset, more emesis than nausea), patients on Chlorambucil tend to have nausea of lesser severity and longer duration, with or without emesis. This can be more distressing to patients' quality of life than acute nausea and vomiting. Often patients will have nausea without the relief that comes from emesis.

Management: The following may provide relief from nausea and vomiting:

- Prophylactic antiemetic agents (e.g. dopaminergic agents such as prochlorperazine, or promotility agents such as metoclopramide) given with each dose of Chlorambucil and repeated as needed for nausea control. While there is no evidence to support the use of dimenhydrinate, there is evidence that ginger products (e.g. Graval[®] Ginger) may be effective, with fewer adverse effects
- Avoid spicy or greasy foods that may contribute to the feeling of nausea. Bland foods, fresh air, and plenty of clear water may reduce the feelings of nausea

3. Stomatitis

Stomatitis (mouth sores) is a common side effect of Chlorambucil. Integrity of mucous membranes may be affected by Chlorambucil treatment, leading to the swelling and reddening of membranes lining the mouth. Mouth sores or cankers may develop. Patients may complain of changes on the inner cheeks or mouth surfaces, even when mouth sores are not present or only a mild redness is evident.

Patients may experience:

- Mouth pain
- Difficulty chewing
- Painful swallowing (dysphagia)

It is important to maintain good oral health during treatment. Aggressive prevention may reduce incidence and severity of stomatitis. Treatment during stomatitis event(s) can relieve symptoms (including oral pain, oral bleeding, dental complications, soft tissue infection and dietary restrictions) and restore oral health, often within 7 to 14 days.

Prevention and Management: Good oral care is the key to prevention of stomatitis. If possible, the patient should work with their dentist (and oncologist) to correct any pre-existing dental problems before starting Capecitabine treatment. Careful and thorough oral hygiene is important, and particularly irritating foods (e.g. very spicy foods, rough textures, alcohol-containing foods or liquids) should be avoided.

Management may be achieved in many patients without prescribed therapies. Most important is meticulous oral hygiene:

- Toothbrushing, 3-4 times daily with soft-bristle toothbrush. Soak toothbrush in warm water to soften bristles
- If brushing is painful, Toothettes (sponge-tipped stick with toothpaste), sponges, or gentle use of Waterpik®
- Biotene toothpaste is non-irritating contains natural salivary enzymes to control bacteria
- Floss gently once daily to avoid gum injury
- Salt and baking-soda rinses (1/2 teaspoon of each ingredient in 1 cup of warm water at least 4 times daily, especially after meals)
- Bland rinses, antimicrobial mouthwash (non-alcoholic)
- OTC analgesics, such as ibuprofen (e.g., Advil®, Motrin®) and acetaminophen (e.g., Tylenol®).

If the patient has difficulty eating or drinking sufficient fluids or if redness is associated with lesions on the inner cheeks, tongue or lips, contact the cancer care team at once and tell the patient to contact the oncology nurse or oncologist for immediate advice or a visit.

Topical preparations in widespread use for chemotherapy-induced stomatitis contain ingredients such as lidocaine, benzocaine, milk of magnesia, kaolin, pectin, and diphenhydramine. Although there is no significant evidence of the effectiveness or tolerability of these combinations, there may be a degree of symptom management (e.g. oral pain, improved ability to maintain a proper diet). Clinical trials in chemotherapy patients with stomatitis have shown no difference in the effectiveness of stomatitis resolution from chlorhexidine mouthwash, “magic” mouthwashes that contain lidocaine, and salt-and-baking soda rinses. Hydrogen peroxide may worsen mouth ulcers. In addition, mouthwash preparations containing *antifungals* (i.e. nystatin), broad-spectrum *antibiotics*, or *corticosteroids* have shown no benefit and possibly further worsening of stomatitis- **these combinations are not recommended!**

4. Diarrhea

Diarrhea is very common in patients treated with Chlorambucil. Dietary modifications are not recommended in anticipation of diarrhea, but must be considered if diarrhea occurs.

Management:

For mild diarrhea (less than 4 loose stools per day)

- Follow instructions on loperamide (e.g., Imodium®) package insert: 2 tablets immediately, then 1 tablet after each liquid bowel movement (maximum: 8 tablets/24 hours)

For moderate diarrhea (more than 4 to 6 loose stools per day or night-time diarrhea), tell the patient to be more aggressive with loperamide (e.g., Imodium®) for early-onset diarrhea

- Take 2 tablets immediately, then 1 tablet every 2 hours during the day and 2 tablets every 4 hours during the night until bowel movements are normal for at least 12 hours
- This dosage is higher than packaging recommendations.

Replace lost fluids: Fluid intake is more important than eating in patients with diarrhea. To replace lost fluid, advise patients to increase fluids by up to 3 to 4 litres per day (unless there is a known contraindication to increased fluid intake). The patient may drink several types of fluid, including plain water and electrolyte-containing drinks, such as clear broth, gelatin desserts, sports drinks, flat soft drinks, or decaffeinated tea

Anal care: Recommend to your patient to:

- Clean the anal area with mild soap and warm water after each bowel movement to prevent irritation
- Apply a barrier cream or ointment, such as petroleum jelly or Isle's paste
- Soak in a warm bathtub or sitz bath to relieve discomfort

Dietary changes during diarrhea: Advise your patients to change their diet while diarrhea is a problem:

- Eat and drink small quantities of food often
- Avoid spicy, greasy, or fried foods
- Follow the BRAT (banana, rice, applesauce, toast) diet, along with clear liquids, until diarrhea begins to resolve
- Follow a lactose-free diet
- Avoid cabbage, brussel spouts, and broccoli, which may produce stomach gas, bloating and cramps

5. Rash

Rash is a common adverse effect of Chlorambucil. It is not uncommon for patients to develop a moderately severe rash. Preventive therapy is recommended to reduce the incidence of severe skin rashes in Chlorambucil-treated patients. Avoid exposure to sunlight and wear sunscreen that contains UVA filters (titanium dioxide) and has an SPF of 30 or greater.

Early recognition of symptoms and a prompt start to therapy are the mainstays of treating this rash. Mild to moderate symptoms may be managed while the patient continues therapy. Refer any patient who develops a severe rash to their doctor.

Prevention: Prevention should begin when Chlorambucil therapy is begun, and continue throughout treatment.

You should advise your patient:

- Cleanse with mild soaps or cleaners or bath or shower oils to avoid skin dryness
- Moisturize 2-3 times a day with a colloidal oatmeal lotion, such as Aveeno® lotion, or with thick, emollient-based creams, such as Aveeno® lotion, Neutrogena® Norwegian Formula hand cream, or Vaseline Intensive Care® Advanced Healing Lotion
- Use only fragrance-, alcohol-, and dye-free lotions and cosmetics
- Use a broad-spectrum sunscreen (SPF 30 or higher) that contains zinc oxide or titanium dioxide

6. Urticaria

Urticaria, or hives, is a common complication from many types of drugs. Hives are itchy, red, raised wheals of various sizes and shapes. They generally last for less than 24 hours and can be very irritating to patients (who tend to scratch the hives and cause broken skin and bleeding). New lesions may continue to erupt during drug therapy. Dry skin can exacerbate hives.

Prevention: Advise patients to:

- Avoid over bathing, bathing in very hot water, use of harsh soaps and bubble baths. Consider showering with tepid water or adding 4 tablespoons of baking soda to bath water.
- Use tap water compresses to relieve affected skin.

Management: In addition to management of dry skin, the patient may try one or more option below:

- Use a systemic antihistamine, either an H1 blocker (e.g. diphenhydramine) or a non-sedating antihistamine (e.g. loratidine, cetirizine, desloratidine). Consider adding an H2 blocker antihistamine (e.g. ranitidine, famotidine) for chronic urticaria
- Bathing with colloidal oatmeal preparations (e.g. Aveeno®) and use of unscented moisturizing creams after bathing may help with itchiness and dry skin
- Cooling salves, such as menthol or camphor-containing products (e.g. Gold Bond®) may provide relief. Keep products in the refrigerator for additional cooling effect.
- Topical corticosteroids, beginning with OTC Hydrocortisone 0.5% cream and progressing as needed to more potent prescription corticosteroid creams, are often used
- Acetaminophen may be added to the treatment of urticaria for more painful lesions.

REFERENCES:

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