

EXEMESTANE

Most patients treated with Exemestane 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 Exemestane are hot flushes, fatigue, arthralgia, headache, insomnia, and increased sweating.

ADVERSE DRUG REACTION MANAGEMENT GUIDE

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1. Diarrhea

Diarrhea is common in patients treated with Exemestane. 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

2. Nausea

Nausea may occur in up to 10% of patients on Exemestane. Unlike the nausea and vomiting often experienced by patients on cytotoxic chemotherapy (acute onset, more emesis than nausea), patients on Exemestane tend to have nausea of lesser severity and longer duration, 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 Exemestane 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. Gravol® 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. Insomnia

Insomnia, or the inability to fall asleep and/or stay asleep, may be a symptom of depression, a drug side effect, a reaction to unresolved pain, or a natural reaction to daily stress and worries (e.g. about the cancer). Many drugs can contribute to insomnia problems.

Prevention: Advise patients to:

- Avoid alcohol, nicotine (e.g. smoking, nicotine supplements) and caffeine intake, especially in the evening
- Avoid large meals late in the evening
- Use earplugs and/or eye masks if helpful. Turn the clock face away from sight and use the alarm daily.
- Try relaxation exercises
- Maintain a regular pattern of timing for going to bed and rising, 7 days a week. Limit mid-day naps. Do not sleep in on weekends or free days.

- Regular aerobic exercise (e.g. walking) during the day can help stimulate the need for sleep at night. Exercise should be enough to cause sweating, with a duration of 30 to 40 minutes daily. Do not overexert if there are other physical limitations to exercise

Management: There are many medications (prescription and OTC) used for insomnia. Try to start with the least potent options and limit use to short periods if possible.

- Common OTC products contain diphenhydramine or doxylamine. These products may help patients to fall asleep.
- Natural health products have limited evidence of effectiveness, but are often used. Products may contain Valerian or Melaton.

Prescription hypnotics may be considered. Options include benzodiazepines (e.g. lorazepam, flurazepam) and non-benzodiazepines (e.g. zopiclone).

4. Depression & anxiety

Depression is a mood disorder, which may include features such as diminished interest or pleasure in life, significant gain or loss of weight, sleep disturbances, agitation, fatigue, feelings of worthlessness or guilt, or reduced ability to concentrate. While depression is common in the general population, the incidence is higher in cancer patients. Several drugs can contribute to the severity of depression. Duration of symptoms may vary between patients.

Management: The following may provide relief from headaches and other general pain problems:

- Psychotherapeutic approaches are often used, including cognitive behavioral therapy and interpersonal therapy. These generally require a referral to a therapist, psychologist or psychiatrist.
- Antidepressant drugs- There are several antidepressant agents in use for this disorder. There are a number of classes of agents used. Pay particular attention to potential drug-drug interactions, to help determine if certain antidepressants should be avoided.

5. Hair loss

Up to 15% of patients will have hair loss while taking Exemestane. Most patients will lose a minimal amount of hair on the oral form of this agent.

Prevention:

- Although there is no way to prevent hair loss, you may advise the patient that hair will usually regrow, once the treatments are over. The replacement hair may have a different colour or consistency.

Management:

- If hair loss bothers the patient, a wig, hat, cap, scarf or hair piece may be worn

6. Hot flashes

Hot flashes (or hot flushes) can be very troublesome for many patients. Waves of heat sensation may occur without warning, similar to the hot flashes from female menopause.

Prevention: Advise the patient to:

- Keep room temperature lower, if possible
- Dress in layers, so layers can be removed if hot flushes become uncomfortable
- Natural health products may be tried, such as black cohosh, phytoestrogen supplements, evening primrose oil, dong quai, or ginseng. Evidence of benefit is lacking for most of these products. Watch for potential drug-drug interactions with the herbal product before advising use.
- Acupuncture has been tried for relief of hot flushes, but there is no evidence of effectiveness
- Psychoeducational interventions, as sometimes offered by psychosocial support teams in the cancer centres, may help patients to find ways to improve these symptoms

Management:

Try systemic treatment with clonidine, venlafaxine, paroxetine or gabapentin (prescription); evidence of benefit is minimal, and drug side effects may limit use for some patients.

7. Hyperhidrosis

Hyperhidrosis, or excessive sweating, can reduce quality of life for some patients. Sweating may be manageable for some patients by lifestyle options.

Prevention: Advise the patient to:

- Use strong antiperspirants (higher concentration of aluminum, e.g. DrySol 20% aluminum chloride)
- Bathe or shower with soap and water once or more daily
- Wear clothing from natural fibres- not synthetic fibres
- If scented products cause irritation, use unscented deodorant, soap and skin care products

Management:

Systemic anticholinergics, e.g. oxybutinin, glycopyrrolate or propantheline bromide (prescription)

8. Pain

Patients on Exemestane may experience other types of pain. About 10-15% of patients have headaches while on this treatment. Generalized pain maybe a drug side effect or may be related to the cancer.

Management: The following may provide relief from headaches and other general pain problems:

- Mild pain may respond to non-pharmacologic approaches, such as rest, distraction, cool cloth on the forehead
- Mild pain medications- Acetaminophen preferred; do NOT use non-steroidal anti-inflammatory agents, prescription or OTC due to risk of bleeding (e.g. ibuprofen, ASA, naproxen)
- Acetaminophen with codeine, either OTC (low dose) or on prescription (higher dose) may be considered for more severe pain.
- If there is a neuropathic component to the pain, consider a trial with a tricyclic antidepressant (e.g. low dose amitriptyline or imipramine) or gabapentin

- If acetaminophen is not sufficient to control pain, consider prescription opioid analgesics for management of more severe pain (possibly due to tumor)

9. Fatigue & weakness

About 10-15% of patients on Exemestane will experience fatigue. While fatigue is not life-threatening it can significantly reduce quality of life.

Management: The following may provide relief from fatigue:

- There are no medications that have demonstrated an effect to relieve fatigue
- Mild exercise is very helpful to reduce fatigue, but must be manageable if there is also muscle weakness

10. Arthralgia

Aching joints or arthritic pain is a common co-morbidity in cancer patients and can be initiated or exacerbated by some medications.

Prevention:

- Some light exercise (e.g. walking, jogging) and regular physical activity will help reduce pain and discomfort, even if it is painful to start some activities.

Management:

- Acetaminophen on a regular basis may help to manage pain. Try the controlled-release product, 1 or 2 tablets every 8 hours. Be careful not to take too much Acetaminophen (i.e. limit Acetaminophen from other sources, such as PRN dosing or Acetaminophen-containing narcotic analgesics)
- Do NOT use systemic non-steroidal anti-inflammatory agents, prescription or OTC due to risk of bleeding (e.g. ibuprofen, ASA, naproxen)
- For joint pain, consider the use of heating pads, ice packs, or topical arthritis creams and liniments
- Mild exercise and/or massage therapy may help reduce joint pain

If the arthralgia persists, see a physician, and tell them about all medications, including the cancer treatment drugs

11. Osteoporosis

Osteoporosis is the loss of bone mineral density, resulting in skeletal fragility. It affects 1 in 4 women and 1 in 8 men, increasing in older adults. The more the bones thin out, the greater the risk of fracture. Osteoporosis may be increased with some medications.

Prevention:

- Take 1000 mg calcium and at least 400U (10 mcg) Vitamin D supplement daily. This is available OTC.
- Add weight-bearing exercise (e.g. walking, jogging) to daily activities.

Management:

- Prescription bisphosphonate therapy (e.g. alendronate, etidronate, risedronate) may be added to calcium and vitamin D.

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