

# DASATINIB

Most patients treated with Dasatinib 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 Dasatinib are fluid retention, diarrhea, infections, musculoskeletal pain, headache, cough and rash.

### ADVERSE DRUG REACTION MANAGEMENT GUIDE

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|--------------------------------|-----------------------------------|
| 1. Diarrhea                    | 5. Other pain problems            |
| 2. Rash                        | 6. Nausea and Vomiting            |
| 3. Fluid Retention             | 7. Fatigue and Weakness           |
| 4. Joint, bone, or muscle pain | 8. Hand-foot skin reaction (HFSR) |

#### 1. Diarrhea

Diarrhea is a common side effect of Dasatinib, occurring in up to 45% of patients. 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 liters 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. **Rash**

Rash is a common adverse effect of Dasatinib, occurring 20% of patients. Rash symptoms often appear soon after starting treatment. This rash presents with spots and bumps on the forearms, trunk, and sometimes, the face. They are often itchy, but if scratched, may become infected and crusty. Most cases of this generalized skin rash are mild and go away on their own. Rash is more common in women and patients on higher doses, and may worsen after sun exposure. It is important to recognize rash symptoms early and start symptomatic therapy promptly.

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

You should advise your patient to:

- Cleanse with mild soaps or hypoallergenic cleaners or bath or shower oils to avoid skin dryness
- Take short showers with warm water.
- Moisturize twice a day with a colloidal oatmeal lotion, such as Aveeno® lotion, or thick, emollient-based creams, such as Neutrogena® Norwegian Formula hand cream or Vaseline Intensive Care® Advanced Healing Lotion
- Use only fragrance-, alcohol-, and dye-free lotions and cosmetics
- Use a dermatologist-approved cover-up, such as Dermablend® or Cover FX®
- Remove make-up with a gentle, skin-friendly cleanser (e.g., Neutrogena®, Dove®).
- Use a broad-spectrum sunscreen (SPF of 30 or more) that contains zinc oxide or titanium dioxide

**Management:** For Mild to moderate skin rash, there are some over-the-counter options you may consider:

- Antihistamine (diphenhydramine)
- Topical steroid (hydrocortisone 0.5%)
- Coal tar preparations

If the rash progresses to moderate to severe, the patient may need prescribed therapy:

### Counseling tips:

Reinforcement is important. Make a note to yourself (or book a time for a follow up call) to repeat these suggestions 2-3 weeks after the Dasatinib treatment initiation or any report of early rash symptoms.

- Oral corticosteroids (short course, with or without topical triamcinolone acetonide 0.1% ointment)
- Temporary interruption of therapy until the rash resolves, and then re-challenge at low dose

### **3. Fluid Retention**

Fluid retention (edema) is a common side effect, developing in 10-22% of patients taking Dasatinib. Peripheral fluid retention is usually superficial and mild to moderate in severity. The most common form of edema is swollen eyelids or swelling around the eyes (periorbital edema), which is worse in the morning and often associated with swelling of ankles, feet, and lower legs. This type of fluid retention tends to get better over time, occurring more frequently in women, adults older than 65, and patients with a history of heart or kidney problems.

Pleural effusion (excess fluid around the lungs) occurs in 14-30% of patients taking Dasatinib. It is more common on patients being treated with higher doses of Dasatinib, or with a history of heart disease, hypertension, rash, autoimmune disease, and high cholesterol. Pleural effusion may occur anytime from 5 weeks to 1 year after the start of treatment. Patients should be monitored for early signs of fluid retention: dry cough, shortness of breath, and tight chest.

Early intervention is critical; refer patient to a doctor for immediate care. Advise patients to weigh themselves regularly and report any weight gain greater than or equal to 5 lbs. Central fluid retention in or around the lungs, stomach, central body tissues, heart, or brain (often associated with rapid weight gain) is potentially life-threatening.

#### ***Prevention:***

- Limit salt intake.
- To prevent swollen eyelids or swelling around eyes, elevate head while sleeping.

#### ***Management:***

- For mild swelling around eyes, elevate head during sleep or use skin-tightening agents (e.g. topical Preparation H®) containing phenylephrine or lanolin (avoid eye contact). This is available OTC.
- For mild periorbital fluid retention, topical eye ointments with phenylephrine 0.25% or topical corticosteroids (e.g. hydrocortisone 1%)
- For moderate fluid retention, consider a low-dose loop diuretic (e.g. furosemide with calcium and magnesium supplements) and close electrolyte monitoring

### **4. Joint, bone, or muscle pain**

Aching bones or muscle and muscle cramps occur in 12-35% of patients taking Dasatinib. Muscle cramps may occur in the hands, feet, calves, or thighs. Cramps have been described as sustained muscular contractions that follow a consistent pattern, frequency, and severity. Muscle cramps may be related to exertion or could happen at night. Patients should avoid using quinine or drinking tonic water (contains quinine).

Bone and joint pain may begin in the first month of therapy and commonly subside after a few months. Pain may affect the leg bones, hips, and knees, and may appear in an asymmetrical pattern. Although there are no evidence-based guidelines for prevention or treatment, anecdotal reports and expert experience suggest that some patients' pain could be eased by using mineral supplements.

**Management:** The following may provide relief from muscle aches or cramps:

- Calcium and magnesium supplements
- 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)
- For bone or 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 bone and joint pain
- Avoid using quinine or drinking tonic water.

### 5. Other pain problems

Patients on Dasatinib may experience other types of pain. About 40% 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 acetaminophen is not sufficient to control pain, consider prescription opioid analgesics for management of more severe pain (possibly due to tumor)
- 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

### 6. Nausea and Vomiting

Nausea and vomiting may occur in up to 30% of patients on Dasatinib. Unlike the nausea and vomiting often experienced by patients on cytotoxic chemotherapy (acute onset, more emesis than nausea), patients on Dasatinib 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 Dasatinib 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<sup>®</sup> 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

### **7. Fatigue and Weakness**

About one third of patients on Dasatinib will experience fatigue and one in five will have asthenia (or general weakness). These symptoms are not life-threatening but will 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

### **8. Hand-foot skin reaction (HFSR)**

Hand-foot skin reaction (HFSR), also known as hand-foot syndrome and palmar-plantar erythrodysesthesia, is an uncommon side effect of Dasatinib. HFSR is a potentially dose-limiting, skin-related side effect if not managed and prevented at an early stage.

If the patient tells you on the call back phone call he/she is bothered by pain in the hands or feet, you might want to **have the patient drop by the pharmacy** for you to have a look and determine if any prevention or management is required.

**Prevention:** Prevention of traumatic activity and rest are crucial.

Urge your patients to:

- Have a manicure or pedicure to remove thickened skin or calluses; follow with moisturizing cream
- Use a moisturizing cream (e.g. Udderly Smooth<sup>®</sup>, Bag Balm<sup>®</sup>)
- Wear loose-fitting, soft shoes or slippers, foam absorbing soles, gel inserts to cushion pressure points, cotton socks
- Cushion callused areas with soft or padded shoes
- Reduce exposure of hands and feet to hot water (showers, dishwashing, etc.)
- Avoid excessive friction to hands or feet when performing tasks
- Avoid vigorous exercise or activities that place undue stress on the hands and feet
- Wear thick cotton gloves or socks to protect hands and feet and keep them dry
- Report any signs or symptoms immediately to ensure early-stage treatment

**Management:** For *Mild* HFSR, there are several management strategies you may consider:

- Avoid hot water; cool water or cold compresses may ease symptoms

#### **Counseling tips:**

Tell your patient about prevention of HFSR early in the treatment. If the patient is not prepared for detailed counselling on the day the prescription is picked up, plan a follow up call in a couple of days.

- Diligently apply moisturizers to keep palms and soles soft and pliable to prevent cracks or breaks in skin integrity- Use moisturizing creams twice daily; also use aloe vera lotion as needed and use 20% to 40% urea cream or 6% salicylic acid on callused areas
- Soak feet in magnesium sulfate (Epsom salts) to soften calluses and reduce pressure pain
- Use low to moderate dose pain killers
- Advise patients to consult their doctor about reducing their dosage of Dasatinib, if symptoms of HFSR worsen after being treated for 2 weeks

For *Moderate to Severe* HFSR, the patient will likely need prescribed therapy, such as:

- Topical corticosteroid (e.g., clobetasol 0.05% ointment)
- 2% lidocaine topical ointment
- For thick, tender sores after acute rash with/without blisters resolves: 40% urea cream; or Tazarotene 0.1% cream; or Fluorouracil 5% cream
- Dose modification of the Dasatinib

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