Steroid-Associated Side Effects
A symptom management update on multiple myeloma treatment

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BACKGROUND: One constant and relatively unaltered aspect of treatment of multiple myeloma (MM) is the use of glucocorticosteroids, or steroids, which can cause a wide range of adverse side effects and harm patients’ quality of life.

OBJECTIVES: The objective of this study was to provide updated recommendations on the management of steroid-associated side effects in patients with MM.

METHODS: A study of steroid-associated side effects in MM treatment regimens was reviewed to provide updated recommendations to healthcare professionals.

FINDINGS: Identifying the side effects of steroids and managing them promptly contribute to the success of steroid-containing regimens for patients with MM.

KEYWORDS: multiple myeloma; side effect management; steroids; neuropsychiatric

MULTIPLE MYELOMA (MM) IS A CHRONIC CANCER of the bone marrow plasma cells, which affects more than 114,000 people worldwide each year (International Agency for Research on Cancer, 2012). The American Cancer Society (2017) predicts 30,280 new cases of MM and 12,590 deaths related to MM in the United States this year. Significant improvements have been made in the diagnosis, treatment, and supportive care of MM, resulting in longer overall survival of patients. One aspect of treatment is the use of glucocorticosteroids, or steroids, such as dexamethasone (Decadron®), prednisone (Deltasone®), and prednisolone (Omnipred®); however, they have been known to cause a wide range of adverse side effects in almost every system of the body. Healthcare professionals can improve the efficacy of myeloma regimens by recognizing the negative side effects of steroids and treating them promptly.

Melphalan (Alkeran®) chemotherapy was introduced in 1958 to treat MM, and steroids were introduced later (Alexanian et al., 1969). In the past, little emphasis was placed on the side effects of steroids because few effective therapies for MM existed. High-dose (HD) melphalan with autologous stem cell support was introduced in the 1980s, and thalidomide (Thalomid®), bortezomib (Velcade®), and lenalidomide (Revlimid®) became available within the past 15 years. Carfilzomib (Kyprolis®), pomalidomide (Pomalyst®), panobinostat (Farydak®), ixazomib (Ninlaro®), elotuzumab (Empliciti®), and daratumumab (Darzalex®) recently have been approved for the treatment of MM in the United States (National Comprehensive Cancer Network [NCCN], 2016). In 2008, the Nurse Leadership Board published a consensus statement for the management of steroid-associated side effects in patients with multiple myeloma (Faiman, Bilotti, Mangan, Rogers, & International Myeloma Foundation Nurse Leadership Board, 2008) to raise awareness of steroid-associated side effects and to provide strategic recommendations.

Since that time, healthcare providers have had a greater awareness of the toxicities associated with steroid therapy, particularly the neuropsychiatric (NP) effects and adverse effects on health-related quality of life (HRQOL). Despite the side effects, corticosteroids remain useful for most patients with MM. Steroids are not classified as chemotherapeutic agents, but their use has improved the overall response rate and progression-free survival of patients in...
almost every clinical trial treating MM (Lonial et al., 2015; Palumbo et al., 2014; Stewart et al., 2015). The mechanisms of action of steroids are complex and include powerful anti-inflammatory properties and the ability to modify the body’s immune responses (Chrousos & Kino, 2007). Steroids inhibit a range of cytokines (e.g., interleukin-6) responsible for myeloma cell growth and the work of nuclear factor-kappa B, leading to myeloma cell death (Alexanian, Dimopoulos, Delasalle, & Barlogie, 1992; Berenson et al., 2002).

Unfortunately, for most individuals with MM, the effectiveness of steroids is counterbalanced by NP and other side effects, such as infection, venous thrombotic events (VTEs), hyperglycemia, mood swings, insomnia, and an overall decreased HRQOL. Steroids, particularly high doses of dexamethasone, have multiple deleterious side effects that disturb almost every body system (see Figure 1). In fact, the effects of steroids can be so severe that some people cannot tolerate even very low doses or short courses of therapy. Dose-limiting effects include elevated blood glucose levels and blood pressure, fluid retention in older adults, and NP complications (Dubovsky, Arvikar, Stern, & Axelrod, 2012; Larocca & Palumbo, 2015; Sher et al., 2011). In the 2000s, newer agents with sophisticated mechanisms of action became available and, when used, resulted in improved response rates of combination therapies (Stewart, Richardson, & San-Miguel, 2009). However, clinicians began to question whether high doses of steroids improved survival and whether high doses of dexamethasone were still necessary.

A pivotal trial conducted by Rajkumar et al. (2010) (E4A03) determined that high doses of dexamethasone can reduce patients’ overall survival. The trial evaluated lenalidomide in combination with HD versus low-dose (LD) dexamethasone in patients with newly diagnosed MM. In the study, patients were randomized to receive either HD oral dexamethasone (40 mg on days 1–4, 9–12, and 17–20 [480 mg] of a 28-day cycle) versus LD dexamethasone (40 mg on days 1, 8, 15, and 22 [160 mg] of a 28-day cycle) in combination with lenalidomide. Those receiving HD dexamethasone demonstrated higher response rates; however, higher response rates in the HD dexamethasone arm did not result in a longer time to progression, progression-free survival, or overall survival compared to the LD dexamethasone arm (Rajkumar et al., 2010). The cause of inferior overall survival with HD dexamethasone was because of an increased number of deaths from toxicity (12 deaths [n = 222] compared to one death in the LD group [n = 220]) (NCCN, 2016; Rajkumar et al., 2010). One hundred seventeen patients in the HD steroid regimen compared to 76 in the LD regimen had grade 3 or higher toxic effects in the first four months, including deep vein thrombosis (57 of 223 versus 27 of 220); infections, such as pneumonia (35 of 223 versus 20 of 220); and fatigue (33 of 223 versus 20 of 220). The advent of novel, targeted, and more efficacious agents, such as lenalidomide, has allowed for widespread implementation of LD dexamethasone-based regimens (160 mg per month) (NCCN, 2016; Rajkumar et al., 2010). Since these findings were presented, a rapid shift in practice to incorporate LD dexamethasone schedules has taken place (NCCN, 2016).

Overriding Statement of Steroid-Associated Effects in Myeloma
Steroids have acute and chronic toxicities similar to those of Cushing’s disease. The antimaloma effect of steroid therapy must be balanced with the side-effect profile (Ghosh, Ye, Ferguson, Huff, & Borrello, 2011; Palumbo et al., 2014). Steroid-associated side effects occur in most body systems with varied incidence and have a heterogeneous and unpredictable nature (Chrousos & Kino, 2007). A recent Cochrane review of corticosteroids for the management of cancer-related pain in adults noted that the adverse events associated with steroid use, particularly long-term use, remain poorly described and documented, despite the wide use of steroids (Haywood et al., 2015). The most commonly reported steroid-associated effects in patients with MM include increased risk for hyperglycemia, infections, and VTEs (Boland & Headley, 1949). Although the NP side effects of steroids have been known for decades, only recently has the nature and impact of NP effects associated with steroid therapy been an area of focus (Dubovsky et al., 2012; Jenkins & Bruera, 2000; Judd et al., 2014; Kenna, Poon, de los Angeles, & Koran, 2011; McGrath & Holewa, 2010; McGrath, Pun, James, & Holewa, 2007).

Managing Side Effects
Increased Risk for Venous Thrombotic Events
HD dexamethasone (greater than or equal to 480 mg per month) is an independent risk factor for the development of VTEs in those with myeloma (Carrier, Gal, Tay, Wu, & Lee, 2011; Terpos et al., 2015). The risk for VTEs is higher when steroids are used with immunomodulatory drugs (IMiDs), such as thalidomide, lenalidomide, and pomalidomide, compared to IMiD monotherapy. A higher risk for VTEs also exists in the upfront setting and during the first 3–4 months of taking steroid-containing therapy (Dimopolous et al., 2011, 2014; Palumbo et al., 2007). Assessment of risk for VTEs is recommended in all patients with MM, and healthcare professionals should note that patient risk can change over time because of changes in treatment, disease, and health status.

Aspirin (100 mg by mouth daily) is widely considered an adequate anticoagulation therapy in patients at risk for VTEs and even in those without risk for VTEs (NCCN, 2016; Terpos et al., 2015). For those with two or more risk factors for VTEs, low molecular weight heparin (Hemochron®) or full-dose warfarin (Coumadin®) can be used (NCCN, 2016; Terpos et al., 2015). Major risk factors for VTEs include hyperviscosity; history of VTEs; a body mass index greater than or equal to 30; recent surgery; comorbidities, such as cardiac comorbidities, diabetes, renal insufficiency, chronic inflammatory disease, immobility, thrombophilia, myeloproliferative disorders, and
### FIGURE 1
**COMMON SIDE EFFECTS OF CORTICOSTEROIDS AND MANAGEMENT RECOMMENDATIONS**

#### IMMUNE
- **Leukocytosis**
  - Consider evaluating adrenal function in those with signs of AI (i.e., fatigue, hypotension, nausea, abdominal pain, hyponatremia, hyperkalemia).
- **Infection**
  - Increased incidence and severity of infection is dependent on the dose and duration of steroid use (cumulative dose). Risk is further increased in those taking concomitant immunomodulatory drugs.
  - Educate patients on the signs and symptoms of infection and how to act on findings (e.g., access to medical advice, seeking attention in a timely manner).
  - Consider prophylactic antimicrobial agents and using IV immunoglobulin if patient experiences hypogammaglobulinemia or recurrent infections.

#### ENDOCRINE
- **Adrenal insufficiency (AI)**
  - Consider evaluating adrenal function in those with signs of AI (i.e., fatigue, hypotension, nausea, abdominal pain, hyponatremia, hyperkalemia).
  - Higher risk for AI when steroids are stopped abruptly after a lengthy course.
  - AI may require a course of corticosteroid replacement therapy.
- **Hyperglycemia**
  - Monitor for signs of raised glucose level.
  - Educate patients and caregivers on the signs and symptoms of hypo- and hyperglycemia.

#### NEUROPSYCHIATRIC (NP)
- **Cognitive, behavioral, and mood changes**
  - Risk factors include high doses, previous history of NP effects from steroids, and older age.
  - Mania-like symptoms are more commonly associated with short-term use and depressive symptoms with long-term use.
  - Hyperactivity and jitters may be present on the days patients are taking steroids and abate on days they do not take steroids.
  - Steroid psychosis is rare, but monitor for risk of suicidal tendencies in those with overt mood changes.
  - Early recognition, diagnosis, and treatment of NP complications in patients receiving steroids is key to management.
  - Educate patient and family on possible NP effects.
  - Monitor patients for changes in mood, cognition, or behavior using an appropriate screening tool, such as the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983).
  - Dose reduction or discontinuation in presence of NP effects is the most effective management.
  - Tapering of doses can be useful to minimize the severity of mood changes (steroid “highs” and “lows”).
  - The use of antipsychotic or mood stabilizers may be indicated.
  - Avoid concomitant clarithromycin, which can increase circulating levels of corticosteroids and increase the risk for NP effects.
  - Consider referral to support groups and psychosocial services to aid coping.
  - Relaxation, mindfulness techniques, and exercise may aid coping.

#### CONSTITUTIONAL
- **“Let-down effect”**
  - More commonly associated with days immediately following steroid doses.
  - Characterized by weakness and fatigue.
  - Tapering steroid doses may help.
  - Educate patients on adapting lifestyles and activities to energy levels.
  - Flushing or sweating
  - Assess for other causes, such as infection or cardiovascular abnormalities, and manage appropriately.
  - Educate patients on appropriate clothing and maintaining hydration.
- **Insomnia**
  - More common on nights following steroid dose.
  - Tell patients to take the dose in the morning.
  - Educate patients on “sleep hygiene” practices (e.g., avoiding caffeine and alcohol, viewing monitors and screens before bedtime, appropriate sleep environment, use of meditation, relaxation techniques).
  - Consider pharmacologic interventions if insomnia is severe or ongoing.

#### MUSCULOSKELETAL
- **Myopathy**
  - Weakness and fatigue caused by muscle wasting.
  - Common proximal myopathy.
  - Encourage physical activity and exercise to prevent worsening.
  - May benefit from exercise physiology input.
  - May require dose reduction in severe cases.
  - Muscle cramping
  - Exercise, massage.
  - Magnesium supplements.
  - Electrolyte drinks.

#### GASTROINTESTINAL
- **Peptic ulcers and heartburn (dyspepsia)**
  - Take with food.
  - Use caution in those using concomitant nonsteroidal anti-inflammatory drugs.
  - Prophylactic use of over-the-counter H2 blockers or proton-pump inhibitors may be indicated.
  - May require dose reduction or omission if symptoms are severe.
  - Increased appetite
  - Educate patients on healthy eating practices.
  - Consider referral to dietitian if weight gain is problematic.
hemoglobinopathies; and the use of certain medications, such as erythropoiesis-stimulating agents, hormone replacement therapy, doxorubicin (Adriamycin®), and HD dexamethasone. The use of appropriate antiplatelet or anticoagulant therapy must be considered in all patients on HD dexamethasone or treatment regimens including an IMiD and a steroid (NCCN, 2016; Terpos et al., 2015).

Increased Risk for Infections
Infections are a major cause of morbidity and mortality in patients with MM (Blimark, 2014; Terpos et al., 2015). In a large population-based study, patients with MM experienced a 7-fold increase in bacterial infections and a 10-fold increase in viral infections compared to matched controls (Blimark et al., 2014). At the one-year follow-up, infection was the underlying cause of death in 22% of those with MM. The increased susceptibility of patients to infections is related to immunodeficiency, treatment with corticosteroids and alkylating agents, renal impairment, older age, and poor performance status (Blimark et al., 2014; Palumbo et al., 2011; Teh et al., 2015).

Risk factors for increased infection rates among patients with MM include poor performance status, hyperglycemia, being in the first two months of chemotherapy in de novo MM, and taking higher cumulative doses of corticosteroids, HD melphalan, IV cyclophosphamide, and intensive combination systemic chemotherapy (Jung et al., 2014; Snowden et al., 2011; Teh et al., 2015; Terpos et al., 2015).

In addition, steroids increase the risk for infections in those with MM by depressing cell-mediated immunity (Nucci & Anaissie, 2009). Overall risk for infection, including a higher incidence of severe grade 3–4 infections, is further increased in those receiving HD dexamethasone with a higher cumulative dose of steroids (Rajkumar et al., 2010; Teh et al., 2015), and in those on maintenance therapy with steroids after HD therapy and autologous stem cell transplantation (ASCT) (Nucci & Anaissie, 2009). Cumulative doses of steroids greater than 1,600 mg dexamethasone or 25 mg
Steroid-Associated Side Effects

Prednisolone equivalents (3.2 mg dexamethasone is equivalent to 20 mg prednisone) (Schimmer & Funder, 2011) per day for 60 days also have been shown to be independently associated with as much as six times the risk for developing a bacterial infection, and cumulative doses greater than 3,200 mg are associated with nine times the risk for developing a viral infection (Teh et al., 2015). Multiple lines of therapy result in cumulative immunosuppression and delayed immune recovery, further increasing patient risk for bacterial infections (Schütt et al., 2006; Teh et al., 2014). The increased risk for infections associated with steroid therapy further supports using lower doses (Rajkumar et al., 2010).

Patients with MM are particularly at a high risk for infections from gram-positive encapsulated organisms, such as pneumonias. Pneumococcal pneumonia is among the leading causes of preventable deaths (Dale, Fauci, & Wolff, 1974). Therefore, two pneumococcal vaccinations are recommended for patients with MM: the pneumococcal conjugate vaccine 13 (PCV13) and the pneumococcal polysaccharide vaccine (PPSV23). All adults aged 19 years or older with immunocompromising conditions (such as functional or anatomic asplenia, leukemia, lymphoma, or MM) or who are receiving chemotherapy should receive the PCV13 vaccine followed by the PPSV23 vaccine at least eight weeks later. Vaccinations should occur every five years (Centers for Disease Control and Prevention [CDC], 2016).

The role of prophylactic antibiotics in MM is yet to be established. Trimethoprim-sulfamethoxazole prophylaxis in those with pneumocystis jiroveci and antifungal prophylaxis in those taking HD dexamethasone (20 mg prednisone daily or the equivalent of 3.2 mg dexamethasone daily) is recommended (NCCN, 2016; Snowden et al., 2011; Terpos et al., 2015; Vesole et al., 2012). Antiviral prophylaxis against varicella zoster virus reactivation in patients receiving bortezomib, particularly when used in combination with dexamethasone, is recommended. Antibiotic prophylaxis may be considered for the first three months of therapy with IMiDs and steroids in patients with an increased risk for infection (Dimopoulos et al., 2011, 2014; Rajkumar et al., 2010; Terpos et al., 2015). Patients with MM have a functional immunoglobulin deficiency. IV immunoglobulin therapy should be considered in the case of recurrent life-threatening infections in these patients (NCCN, 2016; Snowden et al., 2011; Terpos et al., 2015).

Increased Risk for Hyperglycemia

Treatment with steroids can cause hyperglycemia because of an increase in peripheral insulin resistance and glucose production as well as suppression of insulin production (Ranta et al., 2006; Schimmer & Funder, 2011). Steroids may cause hyperglycemia in patients with or without diabetes. Steroid-induced hyperglycemia further increases risk for infection in patients with MM (Jung et al., 2014; Khordori, Adamski, & Khordori, 2007; Nucci & Anaissie, 2009).

The incidence of diabetes is increasing in the population as a whole. From 1980 to 2014, the rate of diabetes among adults in the United States aged 18–79 years more than doubled from 3.3 to 6.9 per 1,000 adults (CDC, 2015). The risk for MM increases with age, and the median age of patients with MM is 69 years (Howlader et al., 2016). In an analysis of older adults (N = 869) who were not eligible to receive a transplantation, the most common comorbidities were diabetes (13%), cardiopulmonary disease (10%), mild renal failure (7%), and peripheral vascular disease (6%) (Palumbo et al., 2015).

With an increasing number of older adults affected by MM, the greater incidence of diabetes in the general population, and the frequency of steroid use in the treatment of MM, nurses should take extra care and be extra attentive in monitoring blood glucose levels in at-risk groups. Routine blood glucose monitoring should be considered for all patients on steroids, with increased surveillance of those with known glucose intolerance or preexisting diabetes.

Adrenal Insufficiency

Adrenal insufficiency (AI) may be associated with steroid treatment and is characterized by nausea, vomiting, abdominal pain, dehydration, hyponatremia, hyperkalemia, weakness, lethargy,
and hypotension (Schimmer & Funder, 2011). It can be acute or chronic and may occur following abrupt withdrawal of steroids. The administration of steroids for a few days to several weeks can be enough to induce AI (Krasner, 1999). Studies have demonstrated higher rates of AI in patients with MM (Mattour, Farhan, Janakiraman, & Peres, 2014; Ng, Kumar, Russell, Rajkumar, & Drake, 2009). The incidence of hypotension during ASCT may be increased in those with AI (66%) compared to those without AI (10%) (Mattour et al., 2014). These findings illustrate the importance of adrenal function evaluation in patients who receive dexamethasone-based treatment regimens for MM.

Testing for AI requires measuring serum cortisol levels at 8 am using the adrenocorticotropic hormone stimulation test.

**FIGURE 2. PATIENT EDUCATION TOOL: MANAGING STEROID-ASSOCIATED SIDE EFFECTS**

**POTENTIAL SIDE EFFECTS**

- Difficulty sleeping (insomnia)
- “Let down effect” or withdrawal effect
- Personality changes or mood alterations
- Anxiety
- Depression
- Hyperactivity and jitters
- Difficulty concentrating
- Ulcers and heartburn
- Gas (flatulence)
- Hiccoughs
- Increased appetite
- Changes in taste
- Weight gain in body or face
- Higher blood sugar levels
- Temporary diabetes or thyroid issues
- Temporary decrease in testicular size
- Sexual dysfunction
- Acne or rashes
- Swelling in hands, legs, or feet
- Flushing and sweating
- Thinning of skin (can more easily tear)
- Changes affecting hair
- Blurred vision
- Cataract formation
- Muscle cramps
- Muscle weakness (myopathy)
- Decrease in bone strength (osteopenia or osteoporosis)
- Death of bone tissue (avascular necrosis)
- Increased number of white blood cells
- Increased risk for infections

**STRATEGIES FOR CONTINUING TREATMENT**

- Steroids are commonly taken on a regular schedule (e.g., once a week). Side effects commonly follow a predictable pattern, particularly side effects that affect mood and energy.
- Maintain a journal of symptoms to help identify the pattern of any side effects, which will help you to remember side effects to discuss with your healthcare provider. Learn the pattern of your side effects so that you can adjust to your lifestyle to accommodate changing mood and energy levels.
- If you feel jittery, exercise may help. Try to remain active during the day. Focus on simple work or tasks to keep yourself busy. Relaxation, meditation, or mindfulness techniques can also help.
- Caregivers may identify mood and behavior changes before the patient. They should talk with healthcare providers if they are concerned about mood or behavioral changes.

**POINTS TO REMEMBER**

- Steroids should be taken with food.
- Patients should take an over-the-counter or prescription medication to prevent stomach upset.
- Steroids can cause sleeplessness and, therefore, should be taken early in the morning. In some cases, increased energy caused by taking steroids has a delayed effect. As such, taking steroids in the evening may allow improved sleep patterns.
- Be aware of and act upon (contact your healthcare provider) signs and symptoms of infection. Signs of infection include a fever more than 100.5°F (38°C), shaking or chills even without a fever, dizziness, shortness of breath, and low blood pressure.
- Medications to prevent infections, such as shingles (small blisterlike rash anywhere on the body, usually painful with or without rash) and thrush (white coating on the tongue, bad taste, painful swallowing), may be prescribed. Discuss any medications you take with your healthcare provider.
- Know the signs and symptoms of high and low blood sugar: aggressiveness, confusion, difficulty waking, increased thirst, and frequent urination. If you have diabetes, consult your endocrinologist, diabetes educator, or whoever manages your care prior to starting treatment with steroids.
- Most of the side effects of steroids will resolve when the steroids are stopped. Remember that steroids should never be stopped abruptly. Any side effects should be discussed with your healthcare team. The dose of your steroids may be reduced over time or stopped.
- Always report any concerning symptoms to your healthcare team as soon as they occur.

Steroid-Associated Side Effects

Steroid-associated NP complications have been well recognized since steroids were first used in the late 1940s (Breitbart, Stiefel, Kornblith, & Pannullo, 1993; Dubovsky et al., 2012; Jenkins & Bruera, 2000; Kenna et al., 2011; McGrath & Holewa, 2010). Steroid-associated NP effects remain poorly characterized and understood compared to the known somatic effects (Halper, 2002), likely because of the heterogeneous mixture of NP effects, steroid dosing, indications for use, and duration of therapy (Dubovsky et al., 2012). Little empirical evidence on steroid-associated NP effects and their management exists, with case study reports making up the majority of published material.

NP effects of steroids involve affective, behavioral, and cognitive manifestations, but symptoms vary and are largely unpredictable (Dubovsky et al., 2012). They include mania, euphoria, agitation, panic, mood lability, anxiety, insomnia, depression, catatonia, depersonalization, distractibility, cognitive impairment, recall deficits, delirium, dementia, and psychosis (Dubovsky et al., 2012; Jenkins & Bruera, 2000; Kenna et al., 2011). Mild irritability or euphoria to acute psychosis with suicidal ideation may occur. Overall, the incidence of NP effects in populations without cancer is from about 2%-60%, and the incidence of major NP effects in populations with cancer is 5%-10% (Dubovsky et al., 2012; Steifel, Breitbart, & Holland, 1989). Other risk factors for NP effects include increased steroid doses, concomitant use of drugs that increase the circulating levels of steroids, and hypoalbuminuria (Dubovsky et al., 2012; Finkenbine & Frye, 1998; Kenna et al., 2011; Lewis & Smith, 1983; Nishimura, Harigai, Omori, Sato, & Hara, 2008).

The time of onset of NP symptoms varies; however, most reactions occur in the first two weeks of treatment with HD steroids (Lewis & Smith, 1983). Depressive symptoms are more commonly associated with long-term steroid therapy, as seen in patients with Cushing’s disease, and mania is associated with short-term steroid use (Bolanos et al., 2004). Not all steroid effects are negative, as demonstrated by reports of positive experiences of increased energy and reduced pain among patients with MM taking steroids (McGrath & Holewa, 2010). The duration of the NP effects is highly variable, although the majority of people recover within six weeks of cessation of steroids (Lewis & Smith, 1983). Family members are often more aware of changes than patients taking steroids (McGrath & Holewa, 2010; Patten & Neufel, 2000). Treatment of NP effects should start with steroid dose reduction or cessation when clinically possible; however, aside from stopping or tapering steroids, no clearly established treatment guidelines or recommendations exist (Dubovsky et al., 2012; Kenna et al., 2011). Treatment with mood stabilizers or antipsychotic agents is based on NP manifestation type. Clinical review of patients is advised soon after starting steroids because NP effects may occur quickly (Kenna et al., 2011).

No clear guidelines for tapering steroids in MM exist. Suggestions include reducing the dose in the presence of grade 2 or 3 toxicities, which is the established dose attenuation practice with other concomitant agents in MM (Larocca & Palumbo, 2015; Palumbo, 2012; Zweegman, Palumbo, Bringhen, & Sonneveld, 2014). Clinicians may consider using divided doses in those experiencing “let down effect” on a weekly dosing schedule (Paiman et al., 2008; Palumbo, 2012). To taper dexamethasone and prednisolone use, assess the patient’s level of frailty score with the the Myeloma Frailty Score Calculator (www.myeloma frailtycorecaluculator.net), which combines age, comorbidity, and functional status and identifies three categories of patients (fit, intermediate-fitness, and frail), and reduce the starting dose accordingly by 50% and 75% (Larocca & Palumbo, 2015; Zweegman et al., 2014). Patients of standard fitness would start at 40 mg of dexamethasone weekly or 60 mg/m² prednisolone on days 1–4. Patients of intermediate fitness would take either dexamethasone or prednisolone at a dose reduced by 50%. Patients of frail fitness would take either dexamethasone or prednisolone at a dose reduced by 75% (Larocca & Palumbo, 2015; Zweegman et al., 2014). Suggestions for tapering weekly dexamethasone can be found in Table 1. Other recommendations for management and patient education can be found in Figure 2.

Considerations for Steroid Use in Older Adults

MM is mainly a disease of older adults, with a median age of 69 years at diagnosis (Howlader et al., 2016), and aging is commonly associated with comorbidities (Palumbo et al., 2015). Frailty, “a state of increased vulnerability to stressors due to critical decline in physiologic reserves” (Larocca & Palumbo, 2015, p. 1), is present in a third of patients with MM at diagnosis (Palumbo & Anderson, 2011). Patients who are frail are more likely to discontinue MM treatment because of a reduced capacity to tolerate adverse side effects associated with steroids (Palumbo, Mateos, Bringhen, & San Miguel, 2011). The myeloma frailty score predicts mortality and the risk for toxicity in older adults with MM. In one report (Palumbo et al., 2015), the cumulative incidence of grade 3 or greater nonhematologic adverse events and treatment discontinuation at 12 months were associated with an increased frailty score. The authors suggested that the frailty score be used to determine appropriate dose attenuation.

**IMPLICATIONS FOR PRACTICE**
- Deliver appropriate, timely education of patients and their caregivers, allowing for earlier recognition of related symptoms.
- Closely monitor for and recognize steroid-associated side effects, allowing for application of relevant, timely interventions to minimize adverse effects of treatment and to enhance adherence.
- Improve outcomes for patients taking steroids for multiple myeloma through improved awareness and understanding of the side effects of steroids.
Implications for Nursing
The Eastern Cooperative Oncology Group E4Ac3 study (Rajkumar et al., 2010) demonstrated adverse survival outcomes in the HD dexamethasone plus lenalidomide group compared to the LD dexamethasone plus lenalidomide group. The shorter progression-free survival and overall survival seen in the study were directly attributed to increased toxicities in the HD dexamethasone group. Important steroid dosing and side effect considerations are not always discussed with patients or caregivers at the beginning of treatment because providers often focus on delivering education geared toward chemotherapy. When steroids are prescribed to patients with MM, healthcare professionals should discuss potential side effects, such as mood swings and hyperglycemia, and emphasize the importance of long-term health maintenance with patients, and patients should alert providers when they experience these side effects.

Conclusion
Steroids remain the backbone of effective MM treatment. Research has shed light on the importance of lowering steroid doses; various dosing schedules, such as the day and time of dosing; and the need for clinicians to tailor appropriate doses according to patient frailty and/or comorbid conditions. Newer drugs with more effective mechanisms of action allow for more flexibility with steroid dosing and schedules without compromising progression-free survival or quality of life. Clinicians should be aware of steroid-related side effects, discuss the effects with patients and caregivers, and intervene as necessary.

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