A variety of drugs are used in the treatment of musculoskeletal (bone and muscle) disorders. Examples of the musculoskeletal disorders discussed in this chapter include osteoarthritis, rheumatoid arthritis, gout, and Paget's disease. A description of these and other musculoskeletal disorders is given in Table 21-1. The drug selected is based on the musculoskeletal disorder being treated, the severity of the disorder, and the patient's positive or negative response to past therapy. For example, early cases of rheumatoid arthritis may respond well to the salicylates, whereas advanced rheumatoid arthritis not responding to other drug therapies may require the use of one of the gold compounds.

The salicylates and nonsteroidal anti-inflammatory drugs (NSAIDs) are important in the treatment of arthritic conditions. For example, the salicylates and NSAIDs are used in the treatment of rheumatoid arthritis (a chronic disease characterized by inflammatory changes within the body's connective tissue) and osteoarthritis (a noninflammatory joint disease resulting in degeneration of the articular cartilage and changes in the synovial membrane), as well as relief of pain or discomfort resulting from musculoskeletal injuries such as sprains. The reader is referred to Chapters 17 and 18, where these drugs are discussed in detail.

**GOLD COMPOUNDS**

Gold suppresses or prevents but, but does not cure, arthritis and synovitis. The therapeutic effects from gold compounds occur slowly. Early improvement is often limited to reduction in morning stiffness. The full effects of gold therapy are not known for 6 to 8 weeks or in some cases after 6 months of therapy.

**ACTIONS**

The exact mechanism of action of the gold compounds (for example, gold sodium thiomalate, aurothioglucose, and auranofin) in the suppression or prevention of
inflammation is unknown. Gold compounds decrease synovial inflammation and retard cartilage and bone destruction. Gold decreases the concentration of rheumatoid factor and immunoglobulins.

**USES**

Gold compounds are used to treat active juvenile and adult rheumatoid arthritis not controlled by other anti-inflammatory drugs. It is important to note that when cartilage and bone damage has already occurred, gold cannot reverse structural changes to the joints. The greatest benefit appears to occur in patients in the early stages of disease.

**ADVERSE REACTIONS**

Adverse reactions to the gold compounds may occur any time during therapy, as well as many months after therapy has been discontinued. Dermatitis (inflammation of the skin) and stomatitis (inflammation of mucosa of the mouth, gums, and possibly the tongue) are the most common adverse reactions seen. Pruritus (itching) often occurs before the skin eruption becomes apparent. Photosensitivity reactions (exaggerated sunburn reaction when the skin is exposed to sunlight or ultraviolet light) may also occur. Chrysiasis (grey to blue pigmentation of the skin) may occur and is caused by gold deposits in tissues. Gold dermatitis is exacerbated by exposure to sunlight.

**CONTRAINDICATIONS**

The gold compounds are contraindicated in patients with known hypersensitivity to any component of the drug. Parenteral administration is contraindicated in patients with uncontrolled diabetes, hepatic disease, uncontrolled hypertension, uncontrolled congestive heart failure, systemic lupus erythematosus, and blood dyscrasias and in those with recent radiotherapy. Oral administration is contraindicated in patients with necrotizing enterocolitis, pulmonary fibrosis, and hematologic disorders and during pregnancy (Category C) and lactation.

**PRECAUTIONS**

The gold compounds are used cautiously in patients with a history of hypersensitivity to other drugs, previous kidney or liver disease, diabetes, or hypertension.
Concurrent administration of auranofin with phenytoin may increase phenytoin blood levels.

**DRUGS USED IN THE TREATMENT OF GOUT**

**Gout** is a form of arthritis in which uric acid accumulates in increased amounts in the blood and often is deposited in the joints. The deposit or collection of urate crystals in the joints causes the symptoms (pain, redness, swelling, joint deformity) of gout.

**ACTIONS**

Allopurinol (Zyloprim) reduces the production of uric acid, thus decreasing serum uric acid levels and the deposit of urate crystals in joints. The exact mechanism of action of colchicine is unknown, but it does reduce the inflammation associated with the deposit of urate crystals in the joints. This probably accounts for its ability to relieve the severe pain of acute gout. Colchicine has no effect on uric acid metabolism.

In those with gout, the serum uric acid level is usually elevated. Sulfinpyrazone increases the excretion of uric acid by the kidneys, which lowers serum uric acid levels and consequently retards the deposit of urate crystals in the joints. Probenecid (Benemid) works in the same manner and may be given alone or with colchicine as combination therapy when there are frequent, recurrent attacks of gout. Probenecid also has been used to prolong the plasma levels of the penicillins and cephalosporins.

**USES**

Drugs indicated for treatment of gout may be used to manage acute attacks of gout or in preventing acute attacks of gout (prophylaxis).

**ADVERSE REACTIONS**

One adverse reaction associated with allopurinol is skin rash, which in some cases has been followed by serious hypersensitivity reactions such as exfoliative dermatitis and Stevens-Johnson syndrome (see Chap. 6 for a description of this syndrome). Other adverse reactions include nausea, vomiting, diarrhea, abdominal pain, and hematoLOGIC changes.

Colchicine administration may result in nausea, vomiting, diarrhea, abdominal pain, and bone marrow depression. When this drug is given to patients with an acute attack of gout, the primary health care provider may order the drug given at frequent intervals until gastrointestinal symptoms occur. Probenecid administration may cause headache, gastrointestinal symptoms, urinary frequency, and hypersensitivity reactions. Upper gastrointestinal disturbances may be seen with the administration of sulfinpyrazone. Even when the drug is given with food, milk, or antacids, gastrointestinal distress may persist and the drug therapy may need to be discontinued. The adverse reactions seen with other agents used in the treatment of gout are listed in the Summary Drug Table: Drugs Used to Treat Musculoskeletal Disorders.

**CONTRAINDICATIONS**

The drugs used for gout are contraindicated in patients with known hypersensitivity. Probenecid is contraindicated in patients with blood dyscrasias or uric acid kidney stones and in children younger than 2 years. Sulfinpyrazone is contraindicated in patients with peptic ulcer disease and gastrointestinal inflammation. Colchicine is contraindicated in patients with serious gastrointestinal, renal, hepatic, or cardiac disorders and those with blood dyscrasias.

**PRECAUTIONS**

Allopurinol is used cautiously in patients with liver and renal impairment and during pregnancy (Pregnancy Category C) and lactation. Probenecid is used cautiously in patients with renal impairment, previous hypersensitivity to sulfa drugs, peptic ulcer disease, and those who are pregnant (Pregnancy Category B). Sulfinpyrazone is used cautiously in patients with renal function impairment and those who are pregnant (category unknown). Colchicine is used with caution in older adults and during pregnancy (Pregnancy Category C) and lactation.
## SUMMARY DRUG TABLE
### DRUGS USED TO TREAT MUSCULOSKELETAL DISORDERS

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>TRADE NAME*</th>
<th>USES</th>
<th>ADVERSE REACTIONS</th>
<th>DOSAGE RANGES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bisphosphonates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>alendronate sodium</td>
<td>Fosamax</td>
<td>Treatment and prevention of postmenopausal osteoporosis; glucocorticoid-induced osteoporosis; osteoporosis in men; Paget's disease</td>
<td>Headache, abdominal pain, arthralgia, recurrent bone pain, nausea, diarrhea</td>
<td>Postmenopausal osteoporosis, osteoporosis in men: 35—70 mg/wk or 10 mg/d PO; in glucocorticoid-induced osteoporosis: 5—10 mg/d PO; Paget’s disease: 40 mg/d PO</td>
</tr>
<tr>
<td>etidronate</td>
<td>Didronel, Didronel IV</td>
<td>Paget’s disease, postoperative treatment after total hip replacement</td>
<td>Headache, abdominal pain, arthralgia, recurrent bone pain, nausea, diarrhea</td>
<td>5–10 mg/kg/d PO (not to exceed 6 months) or 11 mg/d PO, if retreatment is necessary wait at least 90 days; 7.5 mg/kg/d IV; postop total hip replacement: 20 mg/kg/d PO</td>
</tr>
<tr>
<td>risedronate sodium</td>
<td>Actonel</td>
<td>Treatment and prevention of postmenopausal osteoporosis, glucocorticoid-induced osteoporosis, Paget’s disease</td>
<td>Headache, abdominal pain, arthralgia, recurrent bone pain, nausea, diarrhea</td>
<td>Osteoporosis: 5 mg/d PO; Paget’s disease: 30 mg/d PO for 2 months</td>
</tr>
<tr>
<td><strong>Gold Compounds</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>auranofin</td>
<td>Ridaura</td>
<td>Rheumatoid arthritis</td>
<td>Dermatitis, stomatitis, photosensitivity, pruritus, hematologic changes, nausea, vomiting, anorexia, rash, urticaria, metallic taste</td>
<td>6–9 mg/d PO (may give 3 mg BID or 6 mg QD)</td>
</tr>
<tr>
<td>aurothioglucose</td>
<td>Solganal</td>
<td>Rheumatoid arthritis</td>
<td>Dermatitis, stomatitis, photosensitivity, pruritus, hematologic changes, nausea, vomiting, anorexia, rash, urticaria, metallic taste</td>
<td>10–50 mg IM; initial dose: 10 mg IM; 2nd &amp; 3rd doses, 25 mg IM; 4th &amp; subsequent doses, 50 mg IM until 0.8–1g is given; dosage may be continued at 50 mg IM q3–4wk</td>
</tr>
<tr>
<td>gold sodium thioglate</td>
<td>Aurolate, generic</td>
<td>Rheumatoid arthritis</td>
<td>Dermatitis, stomatitis, photosensitivity, pruritus, hematologic changes, nausea, vomiting, anorexia, rash, urticaria, metallic taste</td>
<td>10–50 mg IM; initial dose: 10 mg IM; dosage increased weekly until 1 g is reached; dose may be continued at 25–50 mg IM every other week for 2–20 wk</td>
</tr>
</tbody>
</table>
### SUMMARY DRUG TABLE

**Drugs Used to Treat Gout**

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>TRADE NAME*</th>
<th>USES</th>
<th>ADVERSE REACTIONS</th>
<th>DOSAGE RANGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>allopurinol</td>
<td>Zyloprim, generic</td>
<td>Management of symptoms of gout</td>
<td>Rash, exfoliative dermatitis, Stevens-Johnson syndrome, nausea, vomiting, diarrhea, abdominal pain, hematologic changes</td>
<td>100–800 mg/d PO</td>
</tr>
<tr>
<td>colchicine</td>
<td>generic</td>
<td>Relief of acute attacks of gout, prevention of gout attacks</td>
<td>Nausea, vomiting, diarrhea, abdominal pain, bone marrow depression</td>
<td>Acute attack: Initial dose 0.5−1.2 mg PO or 2 mg IV then 0.5−1.2 mg PO q1–2h or 0.5 mg IV q6h until attack aborted or adverse effects occur; prophylaxis: 0.5−0.6 mg/d PO</td>
</tr>
<tr>
<td>probenecid</td>
<td>Benemid, generic</td>
<td>Treatment of hyperuricemia of gout and gouty arthritis</td>
<td>Headache, anorexia, nausea, vomiting, urinary frequency, flushing, dizziness</td>
<td>0.25 mg PO BID for 1 wk then 0.5 mg PO BID</td>
</tr>
<tr>
<td>sulfipyrazone</td>
<td>generic</td>
<td>Treatment of gout arthritis</td>
<td>Upper GI disturbances, rash, blood dyscrasias</td>
<td>200−400 mg/d PO in 2 divided doses</td>
</tr>
</tbody>
</table>

**Skeletal Muscle Relaxants**

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>TRADE NAME*</th>
<th>USES</th>
<th>ADVERSE REACTIONS</th>
<th>DOSAGE RANGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>baclofen</td>
<td>Lioresal, generic</td>
<td>Spasticity due to multiple sclerosis, spinal cord injuries</td>
<td>Drowsiness, dizziness, nausea, urinary, frequency, weakness, rash, hypotension, headache, confusion</td>
<td>15−80 mg/d PO in divided doses</td>
</tr>
<tr>
<td>carisoprodol</td>
<td>Soma, generic</td>
<td>Relief of discomfort due to acute, painful musculoskeletal conditions</td>
<td>Dizziness, drowsiness, tachycardia, nausea, vomiting</td>
<td>350 mg PO TID, QID</td>
</tr>
<tr>
<td>chlorphenesin</td>
<td>Maolate</td>
<td>Discomfort due to musculoskeletal disorders</td>
<td>Drowsiness, dizziness, light-headedness, confusion, headache, rash, blurred vision, GI upset</td>
<td>400−800 mg/d PO in divided doses</td>
</tr>
<tr>
<td>chlorzoxazone</td>
<td>Paraflex, generic</td>
<td>Relief of discomfort due to acute, painful musculoskeletal conditions</td>
<td>GI disturbances, drowsiness, dizziness, rash</td>
<td>250−750 mg PO TID, QID</td>
</tr>
<tr>
<td>cyclobenzaprine</td>
<td>Flexeril, generic</td>
<td>Relieff of discomfort due to acute, painful musculoskeletal conditions</td>
<td>Drowsiness, dizziness, dry mouth, nausea, constipation</td>
<td>10−60 mg/d PO in divided doses</td>
</tr>
<tr>
<td>dantrolene sodium</td>
<td>Dantrium</td>
<td>Spasticity due to spinal cord injury, stroke, cerebral palsy, multiple sclerosis</td>
<td>Drowsiness, dizziness, weakness, constipation, tachycardia, malaise</td>
<td>Initial dose: 25 mg/d PO then 50−400 mg/d PO in divided doses</td>
</tr>
<tr>
<td>diazepam</td>
<td>Valium, generic</td>
<td>Relief of skeletal muscle spasm, spasticity due to cerebral palsy, epilepsy, paraplegia, anxiety</td>
<td>Drowsiness, sedation, sleepiness, lethargy, constipation, diarrhea, bradycardia, tachycardia, rash</td>
<td>2−10 mg PO BID-QID; 2−20 mg IM, IV; sustained release, 15−30 mg qd PO</td>
</tr>
</tbody>
</table>

(continued)
### SUMMARY DRUG TABLE  DRUGS USED TO TREAT MUSCULOSKELETAL DISORDERS  (Continued)

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>TRADE NAME*</th>
<th>USES</th>
<th>ADVERSE REACTIONS</th>
<th>DOSAGE RANGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>methocarbamol meth-oh-kar’-ba-mol</td>
<td>Robaxin, generic</td>
<td>Discomfort due to musculoskeletal disorders</td>
<td>Drowsiness, dizziness, light-headedness, confusion, headache, rash, blurred vision, GI upset</td>
<td>1–1.5 g QID PO; up to 3 g/d IM, IV</td>
</tr>
<tr>
<td>orphenadrine citrate or-fen’-a-dreen</td>
<td>Banflex, Flexojet, Flexon, Norflex, generic</td>
<td>Discomfort due to musculoskeletal disorders</td>
<td>Drowsiness, dizziness, light-headedness, confusion, headache, rash, blurred vision, GI upset</td>
<td>100 mg BID PO; 60 mg IV or IM q12h</td>
</tr>
<tr>
<td>prednisolone pred-niss’-oh-lone</td>
<td>Delta-Cortef, generic</td>
<td>Ankylosing spondylitis, bursitis, acute gouty arthritis, rheumatoid arthritis</td>
<td>See Chap. 50</td>
<td>5–60 mg/d PO</td>
</tr>
<tr>
<td>prednisone pred’-ni-sone</td>
<td>Deltasone, Orasone, generic</td>
<td>Ankylosing spondylitis, bursitis, acute gouty arthritis, rheumatoid arthritis</td>
<td>See Chap. 50</td>
<td>5–60 mg/d PO</td>
</tr>
<tr>
<td>etanercept ee-tah-ner’-sept</td>
<td>Enbrel</td>
<td>Rheumatoid arthritis</td>
<td>Congestion, abdominal pain, dyspepsia, irritation at injection site, increased risk of infections, optic neuritis, pancytopenia</td>
<td>25 mg SC twice weekly</td>
</tr>
<tr>
<td>hylan G-F 20 (hyaluronic acid derivatives)</td>
<td>Synvisc, Hyalgon</td>
<td>Treatment of osteoarthritic knee pain in patients with no response to other treatment</td>
<td>Temporary pain, swelling and/or fluid accumulation in the injected knee, nausea, rash</td>
<td>2 mL by intra-articular injections once weekly for 3 wk</td>
</tr>
<tr>
<td>hydroxychloroquine sulfate hye-drox-ee-klor’-oh-kwin</td>
<td>Plaquenil Sulfate, generic</td>
<td>Rheumatoid arthritis-antimalarial</td>
<td>Irritability, nervousness, retinal and corneal changes, anorexia, nausea, vomiting, hematologic effects</td>
<td>200-600 mg/d PO</td>
</tr>
<tr>
<td>leflunomide le-flu’-no-mide</td>
<td>Arava</td>
<td>Rheumatoid arthritis</td>
<td>Hypertension, alopecia, rash, nausea</td>
<td>Initial dose: 100 mg for 3d; maintenance dose: 20 mg/d</td>
</tr>
<tr>
<td>methotrexate meth-oh-trex’-ate</td>
<td>Rheumatrex Dose Pak, generic</td>
<td>Rheumatoid arthritis, antineoplastic</td>
<td>Nausea, vomiting, anorexia, severe bone marrow depression, nephrotoxicity, leukopenia, stomatitis, blurred vision</td>
<td>Initial dose: 7.5 mg PO once a wk or 2.5 mg at 12-h intervals for 3 doses once a week</td>
</tr>
<tr>
<td>penicillamine pen-i-sill’-a-meen</td>
<td>Cuprimine, Depen</td>
<td>Rheumatoid arthritis</td>
<td>Pruritus, rash, anorexia, nausea, vomiting, epigastric pain, bone marrow depression, proteinuria, hematuria, increased skin friability, tinnitus</td>
<td>Initial dose: 125–250 mg/d PO and increased to obtain remission. Maximum daily dose is 1.0 g PO</td>
</tr>
<tr>
<td>sulfasalazine sul-fa-sal’-a-zeen</td>
<td>Azulfidine, generic</td>
<td>Rheumatoid arthritis, ulcerative colitis</td>
<td>Nausea, emesis, abdominal pains, crystalluria, hematuria, Stevens-Johnson syndrome, rash, headache, drowsiness, diarrhea</td>
<td>2–4 g/d PO in divided doses</td>
</tr>
</tbody>
</table>

*The term generic indicates the drug is available in generic form.*
increases the risk of theophylline toxicity. When angiotensin-converting enzyme inhibitors or the thiazide diuretics are administered with allopurinol, there is an increased risk of hypersensitivity reactions. Administration of allopurinol with aluminum salts may decrease the effectiveness of allopurinol.

Salicylates antagonize probenecid's uricosuric action. Concurrent administration of probenecid increases the effects of acyclovir, barbiturates, benzodiazepines, dapsone, methotrexate, NSAIDs, rifampin, and the sulfonamides.

Sulfinpyrazone may increase the anticoagulant activity of oral anticoagulants. There is an increased risk of hypoglycemia when sulfinpyrazone is administered with tolbutamide. Concurrent administration of sulfinpyrazone with verapamil may decrease the effectiveness of verapamil.

**SKELETAL MUSCLE RELAXANTS**

**ACTIONS**

The mode of action of many skeletal muscle relaxants, for example carisoprodol (Soma), baclofen (Lioresal), and chlorzoxazone (Paraflex), is not clearly understood. Many of these drugs do not directly relax skeletal muscles, but their ability to relieve acute painful musculoskeletal conditions may be due to their sedative action. Cyclobenzaprine (Flexeril) appears to have an effect on muscle tone, thus reducing muscle spasm.

The exact mode of action of diazepam (Valium), an antianxiety drug (see Chap. 30), in the relief of painful musculoskeletal conditions is unknown. The drug does have a sedative action, which may account for some of its ability to relieve muscle spasm and pain.

**USES**

Skeletal muscle relaxants are used in various acute, painful musculoskeletal conditions, such as muscle strains and back pain.

**ADVERSE REACTIONS**

Drowsiness is the most common reaction seen with the use of skeletal muscle relaxants. Additional adverse reactions are given in the Summary Drug Table: Drugs Used to Treat Musculoskeletal Disorders. Some of the adverse reactions that may be seen with the administration of diazepam include drowsiness, sedation, sleepiness, lethargy, constipation or diarrhea, bradycardia or tachycardia, and rash.

**CONTRAINDICATIONS**

The skeletal muscle relaxants are contraindicated in patients with known hypersensitivity. Baclofen is contraindicated in skeletal muscle spasms caused by rheumatic disorders. Carisoprodol is contraindicated in patients with a known hypersensitivity to meprobamate. Cyclobenzaprine is contraindicated in patients with a recent myocardial infarction, cardiac conduction disorders, and hyperthyroidism. In addition, cyclobenzaprine is contraindicated within 14 days of the administration of a monoamine oxidase inhibitor. Oral dantrolene is contraindicated in patients with active hepatic disease and muscle spasm caused by rheumatic disorders and during lactation. See Chapter 30 for information on diazepam.

**PRECAUTIONS**

The skeletal muscle relaxants are used with caution in patients with a history of cerebrovascular accident, cerebral palsy, parkinsonism, or seizure disorders and during pregnancy (Pregnancy Category C) and lactation. Carisoprodol is used with caution in patients with severe liver or kidney disease and during pregnancy (category unknown) and lactation. Cyclobenzaprine is used cautiously in patients with cardiovascular disease and during pregnancy (Pregnancy Category B) and lactation. Dantrolene is a Pregnancy Category C drug and is used with caution during pregnancy. See Chapter 25 for information on diazepam.

**INTERACTIONS**

There is an increased central nervous system (CNS) depressant effect when the skeletal muscle relaxants are administered with other CNS depressants, such as alcohol, antihistamines, opiates, and sedatives. There is an additive anticholinergic effect when cyclobenzaprine is administered with other drugs with anticholinergic effects (eg, antihistamines, antidepressants, atropine, haloperidol). See Chapter 30 for information on diazepam.

**BISPHOSPHONATES**

The bisphosphonates are drugs used to treat musculoskeletal disorders such as osteoporosis and Paget’s disease. This chapter will discuss the use of these drugs in the treatment of osteoporosis.
ACTIONS

Alendronate, etidronate, and risedronate act primarily on the bone by inhibiting normal and abnormal bone resorption. This results in increased bone mineral density, reversing the progression of osteoporosis.

USES

The bisphosphonates are used to treat osteoporosis in postmenopausal women, Paget’s disease of the bone, and postoperative treatment after total hip replacement (etidronate).

ADVERSE REACTIONS

Adverse reactions with the bisphosphonates include nausea, diarrhea, increased or recurrent bone pain, headache, dyspepsia, acid regurgitation, dysphagia, and abdominal pain.

CONTRAINDICATIONS

These drugs are contraindicated in patients who are hypersensitive to the bisphosphonates. Alendronate and risedronate are contraindicated in patients with hypocalcemia. Alendronate is a pregnancy Category C drug and is contraindicated during pregnancy. These drugs are contraindicated in patients with renal impairment with serum creatinine less than 5 mg/dL. Concurrent use of these drugs with hormone replacement therapy is not recommended.

PRECAUTIONS

These drugs are used cautiously in patients with gastrointestinal disorders, renal function impairment and those who are pregnant or lactating.

INTERACTIONS

When administered with ranitidine, alendronate bioavailability is increased. When calcium supplements or antacids are administered with risedronate or alendronate, absorption of the bisphosphonates is decreased. In addition, risedronate absorption is inhibited when the drug is administered with magnesium and aluminum. There is an increased risk of gastrointestinal effects when the bisphosphonates are administered with aspirin.

CORTICOSTEROIDS

ACTIONS

Corticosteroids are hormones secreted from the adrenal cortex. These hormones arise from the cortex of the adrenal gland and are made from the crystalline steroid alcohol cholesterol. Synthetic forms of the natural adrenal cortical hormones are available. The potent anti-inflammatory action of the corticosteroids makes these drugs useful in the treatment of many types of musculoskeletal disorders. The corticosteroids are discussed in Chapter 50.

USES

The corticosteroids may be used to treat rheumatic disorders such as ankylosing spondylitis, rheumatoid arthritis, gout, bursitis (inflammation of the bursa, usually the bursa of the shoulder), and osteoarthritis.

ADVERSE REACTIONS

Corticosteroids may be given in high doses for some arthritic disorders. Many adverse reactions are associated with high-dose and long-term corticosteroid therapy. Chapter 50 discusses some of the adverse reactions associated with corticosteroid therapy. A comprehensive list of adverse reactions is provided in Display 50-2. Contraindications, precautions, and interactions of the corticosteroids are discussed in Chapter 50.

MISCELLANEOUS DRUGS

The miscellaneous drugs are used to treat a variety of musculoskeletal disorders. Penicillamine, methotrexate (MTX), and hydroxychloroquine are used to treat rheumatoid arthritis in patients who have had an insufficient therapeutic response to or are intolerant of other antirheumatic drugs such as the salicylates and NSAIDs. The Summary Drug Table: Drugs Used to Treat Musculoskeletal Disorders provides additional information about these and other drugs. One compound, hylan G-F 20, listed in the Summary Drug Table is not used for rheumatoid arthritis, but rather, for osteoarthritis knee pain. It is a viscous, elastic
sterile mixture made of hylan A fluid, hylan B gel, and salt water that is administered directly into the knee.

**ACTIONS**

The mechanism of action of penicillamine, MTX, and hydroxychloroquine in the treatment of rheumatoid arthritis is unknown.

**USES**

Penicillamine, MTX, and hydroxychloroquine are used in the treatment of rheumatoid arthritis. The administration of MTX is reserved for severe, disabling disease that is not responsive to other treatment.

**ADVERSE REACTIONS**

Hydroxychloroquine administration may result in irritability, nervousness, anorexia, nausea, vomiting, and diarrhea. This drug also may have adverse effects on the eye, including blurred vision, corneal edema, halos around lights, and retinal damage. Hematologic effects, such as aplastic anemia and leukopenia, may also be seen.

The adverse reactions seen with penicillamine include pruritus, rash, anorexia, nausea, vomiting, epigastric pain, bone marrow depression, proteinuria, hematuria, increased skin friability, and tinnitus. Penicillamine is capable of causing severe toxic reactions.

MTX is a potentially toxic drug that is also used in the treatment of malignancies and psoriasis. Nausea, vomiting, a decreased platelet count, leukopenia (decreased white blood cell count), stomatitis (inflammation of the oral cavity), rash, pruritus, dermatitis, diarrhea, alopecia (loss of hair), and diarrhea may be seen with the administration of this drug.

**CONTRAINDICATIONS**

These drugs are contraindicated in patients with known hypersensitivity. Hydroxychloroquine is contraindicated in patients with porphyria (a group of serious inherited disorders affecting the bone marrow or the liver), psoriasis (chronic skin disorder), and retinal disease (may cause irreversible retinal damage). MTX is contraindicated during pregnancy because it is a Pregnancy Category X drug and may cause birth defects in the developing fetus. Penicillamine is contraindicated in patients with a history of allergy to penicillin.

**PRECAUTIONS**

Hydroxychloroquine is used cautiously in patients with hepatic disease or alcoholism and during pregnancy (Pregnancy Category C) and lactation. MTX is used cautiously in patients with renal impairment, women of childbearing age, and older adults or individuals who are chronically ill or debilitated. Penicillamine is used with extreme caution during pregnancy (Pregnancy Category C) and lactation.

**INTERACTIONS**

There is an increased risk of toxicity of MTX when administered with the NSAIDs, salicylates, oral antidiabetic drugs, phenytoin, tetracycline, and probenecid. There is an additive bone marrow depressant effect when administered with other drugs known to depress the bone marrow or with radiation therapy. There is an increased risk for nephrotoxicity when MTX is administered with other drugs that cause nephrotoxicity. When penicillamine is administered with digoxin, decreased blood levels of digoxin may occur. There is a decreased absorption of penicillamine when the drug is administered with food, iron preparations, and antacids.

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**Health Supplement Alert: Glucosamine and Chondroitin**

Both glucosamine and chondroitin are used, in combination or alone, to treat arthritis, particularly osteoarthritis. Chondroitin acts as the flexible connecting matrix between the protein filaments in cartilage. Chondroitin can be produced in the laboratory or can come from natural sources (eg, shark cartilage). Some studies suggest that if chondroitin sulfate is available to the cell matrix, synthesis of the matrix can occur. For this reason it is used to treat arthritis. Although there is not much information on chondroitin’s long-term effects, it is generally not considered to be harmful.

Glucosamine is found in mucopolysaccharides, mucopolypeptides, and chitin. Chitin is found in various marine invertebrates and other lower animals and members of the plant family. In osteoarthritis there is a progressive degeneration of cartilage glycosaminoglycans. Oral glucosamine theoretically provides a building block for regeneration of damaged cartilage. The absorption of oral glucosamine is 90% to 98%, making it widely accepted for use. However, chondroitin molecules are very large (50–300 times larger than glucosamine), and only 0% to 13% of chondroitin is absorbed. There is speculation that these larger molecules are undeliverable to cartilage cells. Glucosamine is generally well tolerated, and no adverse reactions have been reported with its use.
The Patient Receiving a Drug for a Musculoskeletal Disorder

ASSESSMENT

Preadministration Assessment
The nurse obtains the patient's history, that is, a summary of the disorder, including onset, symptoms, and current treatment or therapy. In some instances, it may be necessary to question patients regarding their ability to carry out activities of daily living, including employment when applicable.

For the physical assessment, the nurse generally appraises the patient's physical condition and limitations. If the patient has arthritis (any type), the nurse examines the affected joints in the extremities for appearance of the skin over the joint, evidence of joint deformity, and mobility of the affected joint. Patients with osteoporosis are assessed for pain particularly in the upper and lower back or hip. Vital signs and weight are taken to provide a baseline for comparison during therapy. If the patient has gout, the nurse examines the affected joints and notes the appearance of the skin over the joints and any joint enlargement.

Ongoing Assessment
Periodic evaluation is an important part of therapy for musculoskeletal disorders. With some disorders such as acute gout, the patient can be expected to respond to therapy in hours. Therefore, it is important for the nurse to inspect the joints involved every 1 to 2 hours to identify immediately a response or nonresponse to therapy. At this time, the nurse questions the patient regarding the relief of pain, as well as adverse drug reactions. In other disorders, response is gradual and may take days, weeks, and even months of treatment. Depending on the drug administered and the disorder being treated, the evaluation of therapy may be daily or weekly. These recorded evaluations help the primary health care provider plan current and future therapy, including dosage changes, changes in the drug administered, and institution of physical therapy.

Some of these drugs are toxic. The nurse closely observes the patient for the development of adverse reactions. Should any one or more adverse reactions occur, the nurse notifies the primary health care provider before the next dose is due.

NURSING DIAGNOSES

Drug-specific nursing diagnoses are highlighted in the Nursing Diagnoses Checklist. Other nursing diagnoses applicable to these drugs are discussed in depth in Chapter 4.

Nursing Diagnoses Checklist

- Risk for Injury related to adverse drug reactions (dizziness, drowsiness)
- Risk for Impaired Skin Integrity related to adverse drug reactions (dermatitis, rash)
- Altered Oral Mucous Membranes related to adverse reactions (stomatitis)
- Diarrhea related to adverse drug reaction
- Constipation related to adverse drug reaction

PLANNING

The expected outcomes for the patient depend on the reason for administration but may include an optimal response to therapy, management of common adverse drug reactions, and an understanding of and compliance with the prescribed therapeutic regimen.

IMPLEMENTATION

Promoting an Optimal Response to Therapy
The patient with a musculoskeletal disorder may be in acute pain or have longstanding mild to moderate pain, which can be just as difficult to tolerate as severe pain. Along with pain, there may be skeletal deformities, such as the joint deformities seen with advanced rheumatoid arthritis. For many musculoskeletal conditions, drug therapy is a major treatment modality. Therapy with these drugs may keep the disorder under control (e.g., therapy for gout), improve the patient's ability to carry out the activities of daily living, or make the pain and discomfort tolerable.

Patients on bed rest require position changes and good skin care every 2 hours. The patient with an arthritis disorder may experience much pain or discomfort and may require assistance with activities, such as ambulating, eating, and grooming. Patients with osteoporosis may require a brace or corset when out of bed.

Patients with a musculoskeletal disorder often have anxiety related to the symptoms and the chronicity of their disorder. In addition to physical care, these patients often require emotional support, especially when a disorder is disabling and chronic. The nurse explains to the patient that therapy may take weeks or longer before any benefit is noted. When this is explained before therapy is started, the patient is less likely to become discouraged over the slow results of drug therapy.

GOLD COMPOUNDS. Aurothioglucose and gold sodium thiomalate are given intramuscularly, preferably in the upper outer quadrant of the gluteus muscle. The nurse gives auranofin orally.
DRUGS USED FOR GOUT. The nurse gives allopurinol, probenecid, and sulfinpyrazone with, or immediately after, meals to minimize gastric distress. Colchicine usually can be given with food or milk. When this drug is used for the treatment of an acute gout attack, the nurse may give it every 1 to 2 hours until the pain is relieved. The primary health care provider writes specific orders for administration of the drug and when the drug is to be stopped. The nurse evaluates the patient carefully for relief of pain or the occurrence of nausea, vomiting, or diarrhea. After this evaluation, the nurse decides whether to administer or withhold the drug. Colchicine may be given intravenously for severe gout.

SKELETAL MUSCLE RELAXANTS. The nurse gives these drugs with food to minimize gastrointestinal distress. In addition to drug therapy, rest, physical therapy, and other measures may be part of treatment.

BISPHOSPHONATES. When administering alendronate or risedronate the nurse gives the drug orally in the morning before the first food or drink of the day. Risedronate and etidronate are administered once daily. Etidronate is not administered within 2 hours of food, vitamin and mineral supplements, or antacids.

Nursing Alert

Alendronate is administered orally each day or as a once-a-week dose. The nurse should check the physician’s order to be certain of the dosage and the times of administration. When administering the drug for treatment of osteoporosis in postmenopausal women, the dosage is 70 mg once weekly or 10 mg daily. When administering the drug for prevention of osteoporosis, 5 mg of the drug is given daily or 35 mg once a week.

When alendronate and risedronate are administered, serum calcium levels are monitored before, during, and after therapy.

To facilitate delivery of the drug to the stomach and minimize adverse gastrointestinal effects, the nurse administers the drug with 6 to 8 oz of water while the patient is in an upright position. The patient is instructed to remain upright (avoid lying down) for at least 30 minutes after taking the drug.

CORTICOSTEROIDS. When the patient is receiving one of these drugs on alternate days (alternate-day therapy), the drug must be given before 9 AM. It is extremely important that these drugs not be omitted or discontinued suddenly.

MISCELLANEOUS DRUGS. The nurse administers hydroxychloroquine with food or milk to help prevent gastrointestinal upset. The nurse administers MTX orally. A therapeutic response usually begins within 3 to 6 weeks of therapy, and improvement may continue for another 12 weeks. Treatment with this drug may continue for as long as 2 years. Penicillamine must be given to a patient with an empty stomach, 1 hour before or 2 hours after a meal.

Monitoring and Managing Adverse Drug Reactions

GOLD COMPOUNDS. The nurse observes the patient closely for evidence of dermatitis. Itching may occur before a skin reaction and should be reported to the primary health care provider immediately. If itching occurs, the nurse may apply a soothing lotion or an antibiotic cream. The nurse also keeps the environment free of irritants that aggravate itching, such as rough fabrics, excessive warmth, or excessive dryness.

The nurse inspects the patient’s mouth daily for ulceration of the mucous membranes. A metallic taste may be noted before stomatitis becomes evident. The teeth should be brushed after each meal and the mouth rinsed with plain water to remove food particles. Mouthwash may also be used, but excessive use may result in oral infections due to the destruction of the normal bacteria present in the mouth.

Gerontologic Alert

Gold compounds are given cautiously to older adults. Tolerance for gold therapy decreases with advancing age.

While taking gold compounds the patient is monitored closely for thrombocytopenia (abnormally low numbers of platelets in the blood). The primary health care provider orders frequent blood studies (usually once a month or more frequently).

Nursing Alert

If the platelet count falls below 100,000/mm³ or if the patient experiences signs and symptoms of thrombocytopenia (eg, easy bruising, bleeding gums, epistaxis, melena), the nurse notifies the physician immediately.
DRUGS USED FOR GOUT. The nurse encourages a liberal fluid intake and measures the intake and output. The daily urine output should be at least 2 liters. An increase in urinary output is necessary to excrete the urates (uric acid) and prevent urate acid stone formation in the genitourinary tract.

The nurse provides adequate fluids and reminds the patient frequently of the importance of increasing fluid intake. If the patient fails to increase the oral intake, the nurse informs the primary health care provider. In some instances, it may be necessary to administer intravenous fluids to supplement the oral intake when the patient fails to drink about 3000 mL of fluid per day.

Administration of allopurinol may result in skin rash. This rash may precede a serious adverse reaction, Stevens-Johnson syndrome (see Chaps. 6 and 8). The nurse immediately reports to the primary health care provider the presence of any rash.

SKELETAL MUSCLE RELAXANTS. These drugs may cause drowsiness. Because of the risk of injury, the nurse evaluates the patient carefully before allowing the patient to ambulate alone. If drowsiness does occur, assistance with ambulatory activities is necessary. If drowsiness is severe, the nurse notifies the primary health care provider before the next dose is due.

BISPHOSPHONATES. The nurse monitors the patient taking the bisphosphonates for any adverse reactions such as nausea, diarrhea, increased or recurrent bone pain, headache, dyspepsia, acid regurgitation, dysphagia, and abdominal pain. A nalgesic may be administered for headache. Notify the primary health care provider of adverse reactions such as the return of bone pain or severe diarrhea.

MISCELLANEOUS DRUGS. The nurse closely observes the patient taking hydroxychloroquine for adverse reactions. It is important for the nurse to be alert to skin rash, fever, cough, easy bruising, or unusual bleeding, or the patient’s complaints of sore throat, visual changes, mood changes, loss of hair, tinnitus, or hearing loss. The nurse immediately reports adverse reactions. Particular attention is paid to visual changes because irreversible retinal damage may occur. The nurse observes the patient for signs of easy bruising and infection, which may indicate bone marrow depression, an adverse reaction related to the platelets and white blood cells. A decreased platelet count may cause the patient to bleed easily. The nurse applies pressure to all venipuncture puncture sites for at least 10 minutes and avoids intramuscular injections. The mouth is inspected daily for signs of inflammation or ulceration. The nurse also inspects each stool for diarrhea or signs of gastrointestinal bleeding.

Administration of penicillamine has been associated with many adverse reactions, some of which are potentially serious and even fatal. The nurse carefully evaluates any complaint or comment made by the patient and reports it to the primary health care provider. Increased skin friability may occur, which may result in easy breakdown of the skin at pressure sites, such as the hips, elbows, and shoulders. If the patient is unable to ambulate, the nurse changes the patient’s position and inspects pressure sites for skin breakdown every 2 hours.

MTX is potentially toxic. Therefore, the nurse observes closely for development of adverse reactions, such as thrombocytopenia (see Nursing Alert in Gold Compounds section) and leukopenia (see discussion of adverse reactions associated with hydroxychloroquine). Hematology, liver, and renal function studies are monitored every 1 to 3 months with MTX therapy. The primary care provider is notified of abnormal hematology, liver function, or kidney function findings. The nurse immediately brings all adverse reactions or suspected adverse reactions to the attention of the primary health care provider.

Educating the Patient and Family
To ensure compliance with the treatment regimen, the patient must understand the importance of complying with the prescribed treatment regimen and taking the drug exactly as directed to obtain the best results from therapy. To meet this goal, the nurse develops an effective plan of patient and family teaching.

The points included in a patient and family teaching plan depend on the type and severity of the musculoskeletal disorder being treated. The nurse must carefully explain that treatment for the disorder includes drug therapy, as well as other medical management, such as diet, exercise, limitations or nonlimitations of activity, and periodic physical therapy treatments. The nurse emphasizes the importance of not taking any nonprescription drugs unless their use has been approved by the primary health care provider. The following points for specific drugs are included in the teaching plan. Information included for the patient taking a corticosteroid is explained in Chapter 50.

GOLD COMPOUNDS
- Toxic reactions are possible when taking gold compounds. Report adverse reactions to the primary health care provider as soon as possible.
- Contact the primary health care provider if a metallic taste is noted.
- Arthralgia (pain in the joints) may be noted for 1 or 2 days after the parenteral form is given.
- Chryisiasis may occur, especially on areas exposed to sunlight. Avoid exposure to sunlight or ultraviolet light.
DRUGS USED FOR GOUT
• Drink at least 10 glasses of water a day until the acute attack has subsided.
• Take this drug with food to minimize gastrointestinal upset.
• If drowsiness occurs, avoid driving or performing other hazardous tasks.
• Acute gout—Notify the primary health care provider if pain is not relieved in a few days.
• Colchicine for acute gout—Take this drug at the intervals prescribed by the primary health care provider and stop taking the drug when the pain is relieved or when diarrhea or vomiting occurs. If the pain is not relieved in about 12 hours, notify the primary health care provider.
• Allopurinol—Notify the primary health care provider if a skin rash occurs.
• Colchicine—Notify the primary health care provider if skin rash, sore throat, fever, unusual bleeding or bruising, unusual fatigue, or weakness occurs.

SKELETAL MUSCLE RELAXANTS
• This drug may cause drowsiness. Do not drive or perform other hazardous tasks if drowsiness occurs.
• This drug is for short-term use. Do not use the drug for longer than 2 to 3 weeks.
• Avoid alcohol or other depressants while taking this drug.

BISPHOSPHONATES
Alendronate and risedronate. These drugs are taken with 6 to 8 oz of water first thing in the morning. Do not lie down for at least 30 minutes after taking the drug and wait at least 30 minutes before taking any other food or drink. The drugs are taken exactly as prescribed. The primary care provider may prescribe alendronate as a once weekly dose or to be taken daily. Risedronate is taken daily. Take supplemental calcium and vitamin D if dietary intake is inadequate. Take all medication, including vitamin and mineral supplements, at a different time of the day to prevent interference with absorption of the drug.

MISCELLANEOUS DRUGS
Penicillamine. The primary health care provider will explain the treatment regimen and adverse reactions before therapy is started. You must know which toxic reactions require contacting the primary health care provider immediately. Take penicillamine on an empty stomach, 1 hour before or 2 hours after a meal. If other drugs are prescribed, penicillamine is taken 1 hour apart from any other drug. Observe skin areas over the elbows, shoulders, and buttocks for evidence of bruising, bleeding, or break in the skin (delayed wound healing may occur). If these occur, do not self-treat the problem, but notify the primary health care provider immediately. An alteration in taste perception may occur. Taste perception should return to normal within 2 to 3 months.

Methotrexate. Take MTX exactly as directed. If a weekly dose is prescribed, use a calendar or some other method to take the drug on the same day each week. Never increase the prescribed dose of this drug. Mistaken daily use has led to fatal toxicity. Notify the primary health care provider immediately if any of the following occur: sore mouth, sores in the mouth, diarrhea, fever, sore throat, easy bruising, rash, itching, or nausea and vomiting. Women of childbearing age should use an effective contraceptive during therapy with MTX and for 8 weeks after therapy.

Hydroxychloroquine. Take hydroxychloroquine with food or milk. Contact the primary health care provider immediately if any of the following occur: hearing or visual changes, skin rash or severe itching, hair loss, change in the color of the hair (bleaching), changes in the color of the skin, easy bruising or bleeding, fever, sore throat, muscle weakness, or mood changes. It may be several weeks before symptoms are relieved.

EVALUATION
• The therapeutic drug effect is achieved.
• Adverse reactions are identified, reported to the primary health care provider, and managed using appropriate nursing interventions.
• The patient verbalizes the importance of complying with the prescribed therapeutic regimen.
• The patient and family demonstrate an understanding of the drug regimen.

Critical Thinking Exercises
1. Mary is a nurse who has returned to nursing after 15 years absence to raise a family. Mary asks you what should be included in a teaching plan for a patient with rheumatoid arthritis now taking high doses of salicylates. Discuss what information you would suggest Mary emphasize in a teaching plan.
2. Ms. Leeds is prescribed methotrexate for rheumatoid arthritis not responding to other therapies. She is nervous about starting the drug after she was told that the drug can cause many serious adverse reactions. Discuss what you could say to Ms. Leeds to relieve her anxiety. Identify specific instructions you would give her before she begins therapy with this drug.
3. Discuss important points the nurse should consider when administering colchicine to a patient with an acute attack of diarrhea.
4. Discuss the important points to include when educating a patient prescribed alendronate 35 mg once weekly.
What suggestions could you give the patient to help him remember when to take the drug?

**Review Questions**

1. When a patient is taking gold compound therapy on an outpatient basis, the nurse advises the patient to inform the primary care provider if ______.
   A. the appetite decreases
   B. a severe headache occurs
   C. a metallic taste is noted
   D. hair loss occurs

2. When administering a skeletal muscle relaxant the nurse observes the patient for the most common adverse reaction, which is ______.
   A. drowsiness
   B. gastrointestinal bleeding
   C. vomiting
   D. constipation

3. When a patient is prescribed a corticosteroid for arthritis and alternate-day therapy is used, the nurse administers the drug ______.
   A. with food or milk
   B. on an empty stomach
   C. before 9:00 AM
   D. at bedtime

4. When allopurinol (Zyloprim) is used for the treatment of gout, the nurse ______.
   A. administers the drug with juice or milk
   B. administers the drug after the evening meal
   C. restricts fluids during evening hours
   D. encourages a liberal fluid intake

5. What teaching points would the nurse include when educating the patient prescribed risedronate?
   A. The drug is administered once weekly.
   B. Take a daily laxative because the drug will likely cause constipation.
   C. Take the drug in the morning before breakfast and immediately lie down for 30 minutes to facilitate absorption.
   D. After taking the drug, remain upright for at least 30 minutes.

**Medication Dosage Problems**

1. A patient is to receive allopurinol 300 mg PO for gout. The nurse has 100-mg tablets available. How many tablets would the nurse administer?

2. The physician prescribes 1.5 g methocarbamol (Robaxin) PO for a musculoskeletal disorder. Available for administration are 500-mg tablets. The nurse administers ______.