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Medications in Dermatology, Part 2: Immunosuppressives

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The author reports no conflict of interest.

Drug (Pregnancy Category[a])	Mechanism of Action	Uses	Sides Effects	Standard Dosages	Monitoring Guidelines
MTX (X)	Antimetabolite, inhibits DHFR, inhibits DNA synthesis in immunocompetent cells capable of mitosis	Psoriasis,[b] Sézary syndrome,[b] pityriasis rubra pilaris, PLEVA, lymphomatoid papulosis, atopic dermatitis, immunobullous dermatosis, vasculitis and neutrophilic dermatosis, autoimmune connective-tissue diseases, Reiter disease	Pancytopenia, hepatotoxicity (fibrosis and cirrhosis), GI intolerance, fatigue, radiation recall	Start with 5–10 mg/wk, increasing by 2.5–5 mg every 2–4 wk until satisfactory results	Baseline: CBC with differential, liver function tests, serology for hepatitis A and B, renal function tests; standard follow-up: 5–6 d after test dose, then 1–2 wk for 2–4 wk, then gradually decrease to every 3–4 mo; some recommend liver biopsy after 1.5 g cumulative dose; men should be off MTX for 3 mo and women for 1 menstrual cycle before trying to conceive; folic acid supplementation 1 mg/d (for GI tolerability); folinic acid (leucovorin) can reverse the hematologic toxicity of MTX
Hydroxychloroquine (C)	Unclear for antimalarials; proposed: effects on light filtration, immunosuppressive actions, and anti-inflammatory actions (including reducing lysosome size and impairing chemotaxis)	Lupus erythematosus[b], photodermatoses, sarcoidosis, urticaria, granuloma annulare, lichen planus	GI distress, elevated liver enzymes, reversible premaculopathy and irreversible true retinopathy, high risk for retinopathy for those on medication >5 y, blue-gray to black discoloration, photosensitivity	200–400 mg/d	Baseline CBC, CMP, baseline ophthalmology examination; follow-up: CBC monthly for 3 mo then every 4–6 mo, CMP (after 1 mo, after 3 mo, then every 4–6 mo); eye examination every 6 mo for 1 y then every year
Colchicine (C)	Inhibits microtubular polymerization by binding to tubulin; suppresses LTB4 and diminishes leukocyte and granulocyte migration	Erythema nodosum, Behçet disease, granuloma annulare, vasculitis, urticaria	Acute: dose-dependent diarrhea and abdominal pain; chronic: hematuria, alopecia, myelosuppression, gastritis, peripheral neuropathy	0.6 mg twice daily to 3 times daily according to tolerance	CBC with differential, liver function, renal function, urinalysis at least every 3 mo

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Drug (Pregnancy Category[a])	Mechanism of Action	Uses	Sides Effects	Standard Dosages	Monitoring Guidelines
Mycophenolate mofetil (D)	Inhibitor of de novo synthesis of purines by inhibiting IMPDH leading to inhibition of DNA synthesis in T and B lymphocytes	Bullous diseases (pemphigus, pemphigoid), severe atopic dermatitis, vasculitis	GI side effects most common (eg, nausea, diarrhea, vomiting, abdominal cramps and tenderness), PML, bone marrow suppression, elevation of transaminases	Start 500 mg twice daily, increase to 1000–2000 mg/d	Baseline: CBC with differential, platelets, liver function; follow-up: CBC with differential biweekly for the first 2–3 mo, then monthly for the first year; serum transaminases at 1 mo then every 3 mo; avoid during lactation
Cyclosporine (C)	Bind to cyclophilins leading to reduced calcineurin; inhibits activation of T-cell transcription factors; reduction of IL-2, IL-3, and IFN-γ	Psoriasis,[b] severe atopic dermatitis, pyoderma gangrenosum, bullous dermatosis, autoimmune connective-tissue diseases, alopecia areata, granuloma annulare, sarcoidosis	Nephrotoxicity, reversible hypertension, gingival hyperplasia, hypertrichosis, hyperlipidemia, hypomagnesemia and hyperkalemia	Initiate with 2.5 mg/kg/d increased by 0.5–1 mg/kg/d every other week until maximum 5 mg/kg/d	Baseline BP and at every visit, creatinine, BUN, liver function tests, CBC, lipid panel, urinalysis, magnesium, uric acid (if risk of gout); if serum creatinine rises >30% above baseline, reduce dose by at least 1 mg/kg daily; follow-up: CBC, CMP, lipids, magnesium, uric acid every 2 wk for the first 1–2 mo, then monthly; should not use during lactation
Azathioprine (D)	Developed from 6-MP; purine analogue blocks purine synthesis (S-phase specific); suppress T-cell function and B-cell antibody production; decreases number of Langerhans cells and their ability to present antigens; inhibits purine metabolism and cell division	Nondermatologic uses[b] (eg, organ transplantation, severe rheumatoid arthritis) but dermatologists have used this drug for many years due to anti-inflammatory effects and as a corticosteroid-sparing agent in pemphigus vulgaris, bullous and cicatricial pemphigoid, leukocytoclastic vasculitis, severe atopic dermatitis, neutrophilic dermatosis	Malignancies (lymphoproliferative and SCCs of the skin), hypersensitivity reactions, hepatotoxicity, pancreatitis, myelosuppression	Starting at 50 mg/d, increasing to 2.5 mg/kg/d with careful monitoring; consider dosing based on TPMT level	CBC with differential, platelet count, CMP, urinalysis; pregnancy test, tuberculin test (depending on clinical situation); baseline TPMT level; allopurinol inhibits xanthine oxidase and increases toxicity; ACE inhibitors and folate antagonists increase myelosuppression

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Drug (Pregnancy Category[a])	Mechanism of Action	Uses	Sides Effects	Standard Dosages	Monitoring Guidelines
Thalidomide (X)	Anti-inflammatory and immunomodulatory effects leading to inhibition of TNF-α	Erythema nodosum leprosum[b]; several off-label uses: lupus, neutrophilic dermatosis, Behçet disease, GVHD, severe prurigo nodularis	Teratogenic (phocomelia), sedation, constipation, sensory peripheral neuropathy, leukopenia, exfoliative erythroderma, xerosis, pruritus, red palms	50–200 mg/d	Enroll patient in the STEPS program[c]; birth control method 1 mo prior to start therapy; pregnancy tests weekly for the first 4 wk then monthly (women with regular menses) or every 2 wk (women with irregular menses) every 28 d; follow-up: CBC with differential, platelet monthly until stable doses then every 2–3 mo, liver enzymes
Dapsone (C)	Inhibit neutrophilic, eosinophilic, and monocytic myeloperoxidase; inhibits neutrophil chemotaxis	Dermatitis herpetiformis,[b] leprosy, chronic idiopathic urticaria, neutrophilic dermatosis, autoimmune bullous diseases, vasculitis, acne, lichen planus, pyoderma gangrenosum	Methemoglobinemia, hemolytic anemia, agranulocytosis and peripheral (predominantly motor) neuropathy, dapsone hypersensitivity syndrome	Start with 50 mg/d; standard dose range: 50–200 mg/d	Prior to therapy: G6PD, CBC with differential, liver function tests, urinalysis; follow-up: CBC with differential, WBC count every week for 4 wk then every 2 wk until 12 wk then every 3–4 mo; reticulocyte count as needed to assess degree of response to dapsone hemolysis, liver and renal function tests and urinalysis every 3–4 mo; approved by the AAP for use during lactation; small risk for cross-reactivity with sulfonamide antibiotics

Abbreviations: MTX, methotrexate; DHFR, dihydrofolate reductase; PLEVA, pityriasis lichenoides et varioliformis acuta; GI, gastrointestinal; CBC, complete blood cell count; CMP, complete metabolic profile; LTB4, leukotriene B_4; IMPDH, inosine 5'-monophosphate dehydrogenase; PML, progressive multifocal leukoencephalopathy; BP, blood pressure; BUN, serum urea nitrogen; 6-MP, 6-mercaptopurine; SCC, squamous cell carcinoma; TPMT, thiopurine methyltransferase; ACE, angiotensin-converting enzyme; TNF-α, tumor necrosis factor α; GVHD, graft-versus-host disease; STEPS, System for Thalidomide Education and Prescribing Safety; G6PD, glucose-6-phosphate dehydrogenase; WBC, white blood cell; AAP, American Academy of Pediatrics.

[a]There are 5 categories used by the US Food and Drug Administration to indicate the potential of a drug to cause birth defects if used during pregnancy.

[b]Approved by the US Food and Drug Administration.

[c]The goal of this program is to achieve the lowest possible incidence of drug-associated teratogenicity by controlling access to the drug; educating prescribers, pharmacists, and patients; and monitoring compliance.

Practice Questions

1. A 40-year-old woman is diagnosed with systemic lupus erythematosus. You discuss treatment options and decide to start hydroxychloroquine. What laboratory tests and monitoring are required prior to starting this medication?

a. complete blood cell count with differential

b. complete blood cell count with differential and complete metabolic profile

c. ophthalmology evaluation

d. b and c

2. Two months ago you saw a 30-year-old woman with a history of severe atopic dermatitis. She had been using topical steroids with not much improvement. You decided to start a systemic medication. Within 1 month of drug initiation, she called your office to tell you that she is much better but has noticed unwanted hair on her face lately. Which medication is most likely implicated?

a. cyclosporine

b. dapsone

c. hydroxychloroquine

d. methotrexate

3. A 70-year-old man with type 2 diabetes mellitus who drinks 10 cans of beer per week presents to the emergency department with a 3-day history of diffuse tense bullae and pruritus on the legs and trunk. Direct immunofluorescence displayed linear deposition of IgG and C3 at the dermoepidermal junction, confirming your clinical diagnosis. What is the best long-term treatment option for this patient?

a. combination of oral steroids plus methotrexate

b. oral steroids and mycophenolate mofetil

c. oral steroids only

d. topical steroids only

4. A 45-year-old Venezuelan man presents with painful nodules on his bilateral lower legs. A biopsy demonstrates acid-fast bacilli, and a multidrug regimen is initiated for erythema nodosum leprosum. Which of the following is the mechanism of action of the treatment that is US Food and Drug Administration approved for this condition?

a. inhibits chemotaxis

b. inhibits dihydrofolate reductase

c. inhibits tumor necrosis factor α

d. suppresses T-cell function and B-cell antibody production

5. A patient consults her physician because of several side effects from a medication she started 2 weeks ago due to erythematous to violaceous papules on the legs from palpable purpura. She reports diarrhea, abdominal pain, and fatigue. Which medication is she taking?

a. azathioprine

b. colchicine

c. dapsone

d. methotrexate

Fact sheets and practice questions will be posted monthly. Answers are posted separately on www.cutis.com.