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FDA-approved systemic therapies for atopic dermatitis

By Layan Al-Sukhni, MD, and Hannah R. Johns, MD

FDA-approved systemic therapies for atopic dermatitis						
Class and mechanism	**FDA-approved indications**	**Route and storage**	**Dosing**	**Monitoring**	**Side effects nd adverse events**	**Notes**
Dupilumab[1-3]						
IL-4 receptor inhibitor Humanized IgG4 monoclonal; Ab binds to and inhibits alpha subunit of the IL-4 receptor, which interferes with IL-4 and IL-13 cytokines.	Moderate-severe atopic dermatitis in adults and pediatric patients ≥ 6 months Other: - Asthma - Chronic rhinosinusitis with nasal polyps -Eosinophilic esophagitis - Chronic obstructive pulmonary disease - Prurigo nodularis - Chronic spontaneous urticaria -Bullous pemphigoid	SubQ Keep refrigerated. Keep away from heat or direct sunlight. Allow to reach room temperature for at least 45 minutes for 300 mg/ 2 mL auto-injector or prefilled syringe, and at least 30 minutes for 200 mg/ 1 mL auto-injector or prefilled syringe. Syringe may be used for ages ≥6 months; autoinjector only for use in ages ≥2 years	≥6 months to <6 yrs: - 5 to < 15 kg: 200mg q4wk - 15 to < 30kg: 300 mg q4wk ≥ 6 yrs to ≤17 yrs: - 15 to < 20kg: 600 mg then 300 mg q4wk - 30 to < 60 kg: 400 mg then 200 mg q2wk - ≥ 60 kg: 600 mg then 300 mg q2wk ≥18 yrs: 600 mg then 300 mg q2wk Can consider de-escalating frequency to 300 mg q4wks after 16 weeks if adequate response	Before starting: - Complete age-appropriate immunizations - Treat pre-existing helminth infections	Common: Injection site reactions, conjunctivitis, blepharitis, oral herpes, eye pruritus, other HSV infections, dry eye, eosinophilia Uncommon: Facial erythema, polyarthralgia Rare but serious: Keratitis, serum sickness-like reaction, hypersensitivity reaction. Use with caution in patients with acute asthma or possible helminth infection.	- Consider holding 1-2 dosing periods prior to administration of live vaccines - Dupilumab neutralizing antibodies may develop - Some reports of secondary psoriasiform dermatitis Missed doses: - q1wk dosing: administer missed dose as soon as possible; start new weekly schedule from date of last dose - q2wk dosing: administer missed dose within 7 days from missed dose and resume original schedule. If >7 days, wait until next dose on original schedule - q4wk dosing: administer missed dose within 7 days from missed dose and resume original schedule. If >7 days, start new schedule based on date of next dose given

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Lebrikizumab[4-5]						
IL-13 inhibitor Humanized IgG4 monoclonal antibody binds IL-13 → inhibits IL-13 bioavailability → inhibits IL-13 signaling through IL-13Rα1 receptor → prevents release of pro-inflammatory cytokines, chemokines, IgE	Moderate -severe atopic dermatitis in adults and pediatric patients ≥ 12 years	SubQ Keep refrigerated. Keep away from heat or direct sunlight. 250 mg / 2 mL auto-injector or prefilled syringe Allow to reach room temperature for at least 45 minutes.	500mg at week 0 and week 2, then 250 mg q2wk - Consider discontinuation if no clinical benefit by week 16 - After 16 weeks, 250 mg q4wks	Before starting: - Complete age-appropriate immunizations - Treat pre-existing helminth infections	Common: Conjunctivitis, injection site reaction Rare: Eosinophilia, HSV infection, keratitis	- Avoid live vaccines during therapy - Lebrikizumab-neutralizing antibodies may develop - Unlike tralokinumab, lebrikizumab, does not block the interaction between IL-13 and the decoy receptor (IL-13Rα2) → allows for further clearance of IL-13
Tralokinumab[6-9]						
IL-13 inhibitor Humanized anti-IL13 monoclonal IgG4 antibody that sterically hinders IL-13 from interacting with both IL-13Rα1 and IL-13Rα2 receptors → inhibits inflammatory cytokines, chemokines, IgE	Moderate-severe AD in adults and pediatric patients ≥ 12 years	SubQ Keep refrigerated. Keep away from heat or direct sunlight. 300 mg / 2 mL autoinjector: for ages ≥ 18 yr; allow to reach room temperature for at least 45 minutes. 150 mg/1mL prefilled syringe: for ages ≥ 12 yr; allow to reach room temperature for at least 30 minutes.	Children ≥ 12 yrs - < 18 yrs: 300 mg once (Two 150 mg prefilled syringes), then 150 mg q2wk Adults ≥ 18 yrs: 600 mg once, then 300 mg once q2wk Weight < 100 kg who achieve clear - Almost clear skin after 16 weeks of therapy, can decrease dose to 300 mg q4 weeks	Before starting: - Complete age-appropriate immunizations - Treat pre-existing helminth infections	Conjunctivitis, keratitis, URTI, eosinophilia, injection site reaction 2 reports of tralokinumab-induced psoriasis	- Avoid live vaccines during therapy - Contains polysorbate 80 (risk of hypersensitivity reaction in some patients) - Tralokinumab-neutralizing antibodies can develop - Unlike lebrikizumab, tralokinumab sterically blocks IL-13 from interacting with both signaling receptor (IL-13Rα1) and the decoy receptor (IL-13Rα2) → theoretically blunts total anti-IL-13 efficacy of tralokinumab
Nemolizumab[10]						
IL-31 receptor α inhibitor Humanized IgG2 monoclonal antibody binds and inhibits IL-31 receptor α	Moderate-severe atopic dermatitis, ≥12 years Prurigo nodularis	SubQ 30 mg/0.49 mL prefilled dual chamber pen Keep refrigerated, away from heat and direct sunlight. Do not freeze. Allow to reach room temperature for at least 30 minutes. Must reconstitute prior to using. If not using within 4 hours of reconstitution, must be discarded	60 mg loading dose then 30 mg q4 weeks After 16 weeks of clear or almost clear skin, decrease frequency to 30 mg q8weeks	- Upon initiation or discontinuation, consider monitoring cytochrome p450 substrates	Common: Headache, arthralgia, urticaria, myalgia Uncommon: paradoxial eczematous eruptions, eosinophilia, hypersensitivity reactions, injection site reactions, herpes zoster infection	- Avoid live vaccines during therapy Discontinue if hypersensitivity reaction occurs Missed doses: Administer missed dose as soon as possible and resume scheduled dosing

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Abrocitinib[11-12]						
JAK 1 inhibitor Inhibits JAK1 enzymatic activity, thereby reducing the phosphorylation and activation of STATs and downstream release of proinflammatory cytokines such as IL-4, IL-13, and IL-31	Moderate-to-severe atopic dermatitis in adults and pediatric patients ≥ 12 years	PO	50, 100, or 200 mg daily	Before starting: - Shingles vaccination and any live vaccines - Labs: hepatitis B/C serologies, pregnancy, QuantiFERON gold, CBC w/ diff, AST/ALT, lipid panel Repeat 4 weeks after initiation & with dose escalation: CBC w/diff, AST/ALT, lipid panel. No established lab monitoring guidelines	Common: Upper respiratory infections, headache, nausea/vomiting, diarrhea, elevated CPK, impetigo, thrombocytopenia Rare but serious: Elevated AST/ALT, lymphoma, anemia, neutropenia, lipid abnormalities Boxed warning: - Cardiovascular event - Thromboembolic events - Serious infections, including TB and herpes zoster	- Avoid live vaccines during therapy - Avoid use in severe renal or hepatic impairment - Higher dose is more efficacious, but it is recommended to start at lower dose and titrate up Discontinue if: - Platelets <50,000/mm3 - Absolute lymphocyte count <500/mm3 - Absolute neutrophil count <1,000/mm3 - Hemoglobin <8g/dL
Upadacitinib[11, 13]						
JAK1 inhibitor Inhibits JAK1 enzymatic activity, thereby reducing the phosphorylation and activation of STATs and downstream release of proinflammatory cytokines such as IL-4, IL-13, and IL-31	Moderate-to-severe atopic dermatitis in adults and pediatric patients ≥ 12 years Non-dermatologic: -Moderate-to-severe ulcerative colitis -Moderate-to-severe rheumatoid arthritis -Ankylosing spondylitis -Psoriatic arthritis	PO available in extended-release oral tablet or oral solution	15 or 30 mg daily	Before starting: - Shingles vaccination and any live vaccines - Labs: hepatitis B/C serologies, pregnancy, QuantiFERON gold, CBC w/ diff, AST/ALT, lipid panel Repeat 12 weeks after initiation & with dose escalation: CBC w/diff, AST/ALT, lipid panel No established lab monitoring guidelines	Common: Upper respiratory infections, headache, nausea/vomiting, diarrhea, elevated AST/ALT, acne, hypertension, fatigue Rare but serious: Lymphoma, anemia, neutropenia, thrombocytopenia, lipid abnormalities Boxed warning: - Cardiovascular event - Thromboembolic events - Serious infections, including TB and herpes zoster	- Avoid live vaccines during therapy - Avoid grapefruit while on therapy - Advise against breastfeeding - Higher dose is more efficacious, but it is recommended to start at lower dose and titrate up

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Oral corticosteroids[11, 14-16]						
Inhibition of multiple inflammatory enzymes. Binds to glucocorticoid receptors which then bind to Glucocorticoid Receptor Elements in the nucleus leading to an interaction with transcription factors such as nuclear factor kappa-B, resulting in modulation of gene transcription and ultimately leading to decreased pro-inflammatory cytokines and mediators and decreased recruitment and activation of lymphocytes. Inhibit phospholipase A2, leading to decreased arachidonic acid and decrease in prostaglandins and other pro-inflammatory mediators.	Dermatology: Atopic dermatitis, pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, Sjogren's syndrome, systemic lupus erythematosus, severe psoriasis, severe seborrheic dermatitis, drug hypersensitivity reaction	Commonly used formulations include prednisone (PO), prednisolone (PO), triamcinolone acetonide (IM)	0.5-1.0 mg/kg/day, with tapering (typically prednisone, prednisolone, or triamcinolone acetonide)	Blood pressure monitoring, blood glucose monitoring, ophthalmologic examination, HPA axis suppression testing, bone-density evaluation (adults), growth-velocity measurement (pediatrics)	Rebound flare and worsening disease after steroid cessation HTN, glucose intolerance, gastritis, weight gain, decreased bone density, adrenal suppression, emotional lability, acne Pediatric: Decreased linear growth	- Consider antibiotic prophylaxis for opportunistic infections, calcium and vitamin D supplementation, "booster" immunizations if on steroids long term. - Although FDA-approved, systemic steroids should generally be avoided to avoid short-term and long-term side effects

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