

AN ONGOING CE PROGRAM of the University of Connecticut School of Pharmacy

#### **EDUCATIONAL OBJECTIVES**

After completing the continuing education activity, pharmacists will be able to

- Outline the causes of pet allergies in dogs, cats, and other less common species
- Differentiate between allergic sensitization, allergy, and cross sensitivity
- Paraphrase facts that prove that currently, hypoallergenic dogs and cats are a myth
- Compare nonpharmacologic, over the counter, and prescription treatments in terms of dosing, effectiveness, and cost

After completing the continuing education activity, pharmacy technicians will be able to

- Outline the causes of pet allergies in dogs, cats, and other less common species
- Differentiate between allergic sensitization, allergy, and cross sensitivity
- Paraphrase facts that prove that currently, hypoallergenic dogs and cats are a myth
- Identify patients whose complaints indicate they may need referral to a pharmacist



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ACPE UAN: 0009-0000-23-008-H01-P 0009-0000-23-008-H01-T

Grant funding: None Cost: FREE

INITIAL RELEASE DATE: March 15, 2023 EXPIRATION DATE: March 15, 2026

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# **Pet Allergies**

**TARGET AUDIENCE:** Pharmacists and Pharmacy technicians who hope to build or refresh their basic clinical skills

**ABSTRACT:** Many American households have pets, and many others would like to have pets but family members have pet allergies. Allergies to cats and dogs are common (an estimated 15% to 30% of people are allergic to companion pets), and allergies to unusual or exotic pets have increased over the last decade. Pet allergy is an allergic reaction to proteins (allergens) found in animals' skin cells (dander), saliva, urine, or sweat on their fur. Most animal allergens belong to one of three primary protein families. Pet allergies are currently incurable. The treatment goal is to control symptoms and improve patients' functional status and well-being. Options include nonpharmacologic interventions like cleaning and bathing the pet and pharmacologic management with antihistamines, corticosteroids, anticholinergic nasal sprays, mast cell stabilizers, or leukotriene modifiers. Allergists will consider allergy-specific immunotherapy when medications and/or avoidance measures fail.

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#### **INTRODUCTION and EPIDEMIOLOGY**

The American Pet Products Association (APPA) estimates that approximately 70% of Americans keep pets in their household, equating to 90.5 million homes. Dogs and cats are the most popular and live in around 69.0 and 45.3 million U.S. households, respectively, followed by 11.8 million households for freshwater fish, 9.9 million households for birds, and 3.5 million households for horses.<sup>1</sup> Public, residential, leisure, and specific occupational environments (e.g., farms, laborato-

TO REGISTER and PAY FOR THIS CE, go to: https://pharmacyce.uconn.edu/program\_register.php ries, pet shops) have high concentrations of pet allergens because of the high prevalence of community pet-keeping and Americans' tendency to live indoors. Allergic reactions to pets have been recognized for at least 100 years.<sup>2</sup> Risk factors for developing asthma and rhinitis include allergies to furry animals, especially cats and dogs.<sup>3</sup> Direct or second-hand pet exposure increases the likelihood of exacerbating disease in pet-sensitive people. However, evidence also shows that early childhood exposure to dogs or cats before one year of age may have protective effects in preventing allergic sensitization.<sup>4</sup>

Notably, allergies to unusual or exotic pets have increased over the last decade.<sup>5</sup> In many urban areas, apartment complexes prevent owning large pets or charge a fee for owning cats and dogs, leading to the choice of smaller, more unusual animals. Some examples of uncommon pets are rodents (mice, rats [which allegedly make very good pets], guinea pigs, and other mammals like ferrets, pigs), amphibians (axolotl [a Mexican salamander], dart frogs, and fire belly newts), and reptiles (snakes).<sup>6</sup> The allergic signs and symptoms or diseases associated with uncommon pets are like those manifested in cat and dog allergies. In addition, patients may present with respiratory symptoms induced by bird allergens and gastrointestinal symptoms after consuming bird eggs; this is called a bird-egg syndrome.<sup>7</sup>

Overall, the incidence of specific allergy to exotic or uncommon pets is unknown because literature only includes isolated cases or small series. In the United States, an estimated 15% to 30% of people are allergic to their pets.<sup>8</sup> Among people with pet allergies, a fraction is sensitized to more than one animal. Moreover, according to the Asthma and Allergy Foundation of America, cat allergies are reported twice as often as dog allergies. Animals are also recognized as the third leading cause of allergic asthma, after mites and pollens.<sup>8</sup> Many people adopt ferrets or rabbits, believing they are hypoallergenic. They are not, and pharmacy staff should be aware of that fact.<sup>9,10</sup> The most frequent allergic reactions result from inhalation, contact, or bites.

This continuing education activity summarizes knowledge of pet allergens, including those from uncommon pets; the allergy reaction mechanism and its signs and symptoms; current advances in diagnosis and treatment methods such as immunotherapy; and recommendations for patient education and counseling.

**PAUSE and PONDER:** When patients ask about medication for pet allergies, what kinds of questions should you ask?

## PET ALLERGENS Allergy Mechanisms

Compared with other conditions' mechanisms, allergy mechanisms are simple and encompass three specific paths: allergic sensitization, allergy, and cross-reactivity.<sup>11</sup>

- Allergic sensitization is the presence of immunoglobulin E (IgE) antibodies to an allergen.
- Allergy is the occurrence of reproducible symptoms or signs initiated by exposure to a defined stimulus at a dose tolerated by nonallergic persons and mediated by specific immunologic mechanisms. If no symptoms develop, a person could be sensitizing to a particular allergen but not be allergic.
- Cross-reactivity occurs when IgE antibodies (originally developed against a given allergen) binding to homologous molecules originating from a different allergen source.

## **Characterizing Pet Allergens**

Allergies to pets are common. Pet allergy is an allergic reaction to proteins (allergens) found in animals' skin cells (dander), saliva, urine, or sweat on their fur.<sup>5</sup> Allergens within the same protein family can cause cross-reactivity. Most allergens are spread via airborne particles. Dander contains allergens formed in sebaceous gland secretions and saliva. Secretions containing allergens adhere to the hair and stratum corneum of the skin. When an animal sheds, tiny particles disperse into the air and remain buoyant for an extended period of time. After the particles slow-ly settle onto the floor, furniture, or other items, they can be easily re-dispersed into the air. As a result, pet-sensitive people could experience allergy symptoms in the nose, eyes, and respiratory tract even if the pet is not present.<sup>5</sup> Additionally, people can carry pet allergens that settled onto their clothing or hair.

For cats and dogs, the primary allergen sources are dander and saliva. Similarly, the primary allergen source in rabbits is saliva. In contrast, the primary allergen source is urine in rodents (e.g., mouse, rat,) and Mustelidae (ferrets and minks).

Rodents are an interesting case study. Most research laboratories experience a very high rate of staff turnover because lab workers develop allergies to rodents. Children who are exposed to rodent urine can develop this allergy, too. Male rodents produce a larger quantity of and more condensed urine than female rodents. This explains why people who commonly come in contact with male rodents are more likely to develop allergic symptoms. Allergy to rodents acts as an occupational hazard for researchers. Mouse urine is the most concentrated of all urines—far more concentrated than any other species.<sup>12</sup> One study showed that 30% of people exposed to mice and 13.7% of people exposed to rats suffered from allergy symptoms.<sup>12</sup> Symptoms range from conjunctivitis to asthma to skin reactions, which makes working with these animals difficult.

Common Name of	Source	Allergen	Family
Animal			
Dog	Dander, saliva, hair	Can f 1 (major allergen)	Lipocalin
		Can f 2	Lipocalin
		Can f 4	Lipocalin
		Can f 6	Lipocalin
		Can f 3	Albumin
		Can f 5 Can f 7	Arginine esterase (kallikrein) Epididymal secretory protein E1 or Niemann Pick type C2 protein
		Can f 8	Cystatin
Cat	Sebaceous, anal, and salivary gland	Fel d 1 (major allergen)	Uteroglobin
		Fel d 2	Albumin
		Fel d 4	Lipocalin
		Fel d 7	Von Ebner gland protein
		Fel d 3	Cystatin
		Fel d 5w	Cat IgA
		Fel d 8	Latherin-like
		Fed d 6w	IgM
Horse	Dander, sublingual, submaxillary salivary glands, and urine	Equ c 1 (major allergen)	Lipocalin
		Equ c 2	Lipocalin
		Equ c 4 Equ c 3	Latherin Albumin
		Equ c 6	Lysozyme
Chinchilla	Epithelia, saliva, urine	Chi La	Protein kinase inhibitor
Crimerinia		Chi Lb	Lipocalin
Guinea pig		Cav p 1 (major allergen)	Lipocalin
		Cap p 2 (major allergen)	Lipocalin
		Cap p 3	Lipocalin
		Cap p 4	Serum albumin
		Саррб	Lipocalin
Gerbil	Epithelial, salvia,	Mer un 23kDa	Lipocalin
Cile a sia a la successa a	urine, sleep bed	Mer un 4	Serum albumin
Siberian hamster	Epithelial, saliva, urine	Phod s 1	Lipocalin
Rat		Rat n 1 (major allergen) Rat n 4	Lipocalin; alpha-2u-glubulin Serum albumin
		Rat n 7	Immunoglobulin
Mouse		Mus m 1 (major allergen)	Lipocalin; urinary prealbumin
		Mus m 2	Unknown
		Mus m 4	Serum albumin
		Mus m 7	Immunoglobulin
Rabbit		Ory c 1	Lipocalin
		Ory c 2	Lipocalin
		Ory c 3	Secretoglobin
		Ory c 4	Lipocalin
Ferret		Mus p 17	Unknown
		Mus p 66	Serum albumin
Pig	Meat	Sus s 1	Serum albumin
		Sus s 5	Lipocalin
	1	Sus s 6	Serum albumin

Most animal allergens belong to one of three primary protein families. Within the three families, lipocalin-like proteins and the serum albumin family are the two most widely studied. Other identified allergens are considered minor, including gelatins, immunoglobulins, and transferrins presented in secretions and dandruff. Knowledge of these allergens' allergenicity and cross-activity is essential to improve treatment and prevent allergic reactions. **Table 1** summarizes partially characterized pet allergens, including those generated by exotic pets, because not all allergens are fully characterized.<sup>5</sup>

## **Lipocalin Superfamily**

More than 50% of allergens identified from furry animals belong to the lipocalin superfamily and are found in animal dander, saliva, and urine.<sup>23</sup> Lipocalins are large proteins and can induce IgE production in a large proportion of atopic individuals (people

who have enhanced immune response to common allergens) who are exposed to the allergen source.<sup>24</sup>

#### **Serum Albumin Family**

Serum albumin is a globular protein prone to participation in IgEmediated cross-reactions.<sup>24</sup> Serum albumin is commonly found in pet dander and saliva and causes an allergic reaction by inhalation and ingestion.

## Secretoglobin Superfamily

Secretoglobins are the most potent allergens in cats (e.g., Fel d 1) and other pets (e.g., rabbit Ory c 3). Produced by the skin, salivary and lacrimal glands, these proteins have an unknown function. Dried saliva and dandruff are spread as airborne particles and cause sensitization in susceptible people.<sup>25</sup>

#### SIGNS AND SYMPTOMS OF PET ALLERGIES

The most frequently observed pet allergies result from inhalation, contact, and bites. The main allergic symptoms are similar across both common and uncommon pet types. They present as rhinitis, conjunctivitis, urticaria (red, itchy welts that result from a skin reaction), and lower and upper respiratory symptoms, which can be mild to severe and rarely cause anaphylactic shock.<sup>5</sup>

### **Hypoallergenic Pets**

"Hypoallergenic" is defined as possessing decreased risk of causing an allergy in people, which means that hypoallergenic animals could still elicit allergies in humans.<sup>9</sup> To make hypoallergenic animals, breeders or researchers combine breeds that produce less allergen (in dogs, breeders use breeds that shed less than other breeds, or have hair rather than fur). However, animals often have different mechanisms of allergenicity, so infrequent shedding does not solve all allergy problems.

In a dog allergen study, homes that included hypoallergenic dogs had no statistically significant difference in dog allergen levels compared to homes that included non-hypoallergenic dogs. The common allergen in dogs, Can f 1, was reported at similar levels in all groups.<sup>25</sup> The frequency of shedding varies in different dog breeds, but all dogs can elicit allergies in humans.

The main allergen in cats, Fel d 1 protein, comes from their saliva and sweat glands. Because of its small size and adhesiveness, Fel d 1 floats around and sticks to everything, making it almost impossible to remove physically. In fact, Fel d 1 measures in at less than one-tenth the size of ribosome; it's so small, it easily navigates its way deep into the lungs and can precipitate asthma.<sup>26</sup> For this reason, making a completely hypoallergenic cat has proven impossible, however vaccines to decrease the production of Fel d 1 protein have been studied; one vaccine is a combination of recombinant Fel d 1, tetanus toxoid protein, and a snippet of the coat of a plant virus.<sup>27</sup> Researchers are unsure as to the purpose of Fel d 1 in cats or why levels of Fel d 1 vary.

Ferrets—which are related to otters, minks, weasels—are considered hypoallergenic because they are less likely to cause an allergic reaction compared to other animals. However, they can still provoke allergies in people. Allergies to ferrets come from their hair, saliva, and urine. Ferret hair and saliva is usually easy to control because they shed infrequently and do not lick people like dogs and cats often do. However, urine is harder to control and can cause allergies when owners clean crates.<sup>9</sup>

Rabbits produce allergens through dander, hair from shedding, and saliva. They tend to shed more often than ferrets, around every three months, so keeping up with cleaning may be difficult. Rabbit hair isn't naturally allergenic, but when rabbits lick their fur, they transfer a saliva protein that is contaminated with the protein allergen.<sup>10</sup>

## DIAGNOSIS Skin Prick Test

Allergists (allergy specialists) use skin prick tests together with medical history and physical examinations to rule out or confirm a suspected IgE-mediated animal allergy.<sup>28</sup> Manufacturers prepare skin prick tests by extracting natural allergens from animal hair, dander, and urine. The doctor or nurse will prick the patient's skin on the forearm or upper back and determine if an allergic reaction occurs within 15 minutes. If a patient develops a red, itchy bump where the pet allergen extract is pricked into the skin, the patient is allergic to that pet allergen. Diagnosticians should first use a skin prick test as it is inexpensive, easy to use, and quick to perform. However, allergen concentrations and components are inconsistent, varying among similar commercial tests from different manufacturers. Healthcare providers should be aware that patients' test as different times.<sup>28</sup>

## Serum-specific IgE Test

Allergists can use a serum-specific IgE (blood) test when patients' symptoms and skin test results are contradictory or when patients' skin conditions prevent a skin test. Serum-specific IgE tests can only determine if a patient is sensitized to a specific pet allergen, but it cannot determine if a patient is allergic to that allergen. Serum-specific IgE tests are highly sensitive, but prone to false-positive results. From this perspective, serum-specific IgE tests may be less accurate than skin prick tests.<sup>29</sup>

#### **Molecular Diagnosis**

Recent scientific advances have allowed molecular diagnosis to differentiate patients who are allergic to a single species or sensitized due to cross-reactivity. This method can aid targeted recommendations for avoidance and assess the choice and composition of immunotherapy.<sup>28</sup>

## PET ALLERGY MANAGEMENT

Pet allergies cannot currently be cured. The treatment goal is to control symptoms and improve patients' functional status and well-being.

## Nonpharmacologic Treatment – Avoid & Minimize Allergen Exposure

Current recommendations for managing pet allergy symptoms start with exposure avoidance. Starting when animals are young, bathing them at least once weekly can reduce allergens and eliminate reactions in humans who are exposed to them (see SIDE-BAR, next page).<sup>30</sup> Immediate removal of animals from the household will not alleviate symptoms if the owner has carpeting and other pieces of furniture/items that the pet slept or sat on. Mammalian allergens are stable and can persist in house dust for up to six months.<sup>32</sup> Additionally, using high-efficiency particulate air (HEPA) filters and mattress encasement, vacuuming, and chemically treating carpet are alternative methods for reducing **PAUSE AND PONDER:** When patients have pet allergies, which symptoms are best treated with antihistamines?

exposure to contaminated materials, but may not reduce disease severity.  $^{\ensuremath{\mathsf{33}}}$ 

An allergen reducing cat food (Pro Plan LiveClear) is now available, and its manufacturer indicates it reduces the number of allergens in cat hair and dander by 47% after three weeks of feeding.<sup>34</sup> It is produced using eggs that contain an anti-Fel d1 antibody. When cats consume the food, the egg powder binds to and neutralizes Fel d1 in the cat's saliva.<sup>34</sup>

#### **Pharmacologic Treatment**

When avoidance and reducing allergens are not enough, depending on the severity of signs, over the counter (OTC) medications like antihistamines or local/topical steroids may provide temporary relief of allergy symptoms.<sup>35</sup> Those symptoms include runny/itchy nose or throat, sneezing, and itchy, red or watery eyes. Combination products that contain both an antihistamine and a decongestant or an analgesic are available but should be used with caution due to the increased risk of adverse effects. Other allergy medications, besides the ones mentioned above, are used less often, including mast cell stabilizers and leukotriene antagonists. **Table 2** (next page) summarizes common medications (both OTC and prescription) for treating mild to moderate allergy symptoms.<sup>35</sup>

In general, for conditions eligible for self-care, e.g., allergic rhinitis, patients should start taking OTC allergy medications one week before they expect symptoms from a predictable exposure or as soon as possible before allergen exposure (for episodic exposure).<sup>35</sup> Prescribers should tailor the pharmacologic therapy and length of treatment based on symptoms and severity. Usually, complete relief takes two to four weeks. Intranasal steroids control nasal symptoms more effectively than antihistamines, as they inhibit multiple cell types and mediators, and should be recommended for moderate or persistent allergic rhinitis. Decongestants are effective in nasal congestion but have little effect on other symptoms. Intranasal and ocular preparations are available for nasal and eye symptoms. Intranasal cromolyn is the preferred initial choice for pregnant or lactating patients, as the body does not absorb it based on the route of administration. As mentioned in the table, fluticasone and triamcinolone nasal sprays are available over the counter.35

If a patient has persistent allergies, allergy medication is more effective when taken regularly.<sup>35</sup> For example, if a patient with moderate or severe persistent allergic rhinitis has completed two to four weeks of treatment with intranasal corticosteroids or oral antihistamine and achieved symptomatic control, healthcare providers can optimize the treatment's effect by reducing the *Text continues on page 7* 

#### SIDEBAR: To Bathe or Not to Bathe...<sup>26,31</sup>

Bathing a cat or dog regularly appears to reduce the quantity of allergen harbored by the pet. To effectively lower Can f 1 concentrations, owners need to bathe the animal at least twice every week because Can f 1 concentrations rise rapidly, approaching baseline concentrations within three days after washing. Twice-weekly bathing can reduce the amount of recoverable Can f 1 on dogs by more than 80%, but researchers note that ideally, one would bathe the dog two to three times every week. Airborne Can f levels can fall by ruff-ly 40% but will quickly escalate.

However, the beneficial effects of reducing allergen levels by regular bathing are more likely associated with dogs, because their allergen burden returns faster than that of cats. So, bathing animals reduces the amount of allergen far better than vacuuming.

But should companion animals be bathed so often?

Most cats are notoriously averse to bathing, although some breeds like water (i.e., the Bengal). Dogs vary in the response to bathing—some like it, others do not. People who plan to bathe their cats or dogs regularly should do three things:

- Check with a veterinarian or a breed advocacy group. The American Kennel Club indicates that how often an owner should bathe a dog depends on the dog's coat type and presence or absence of an undercoat (in the latter case, frequent bathing can affect a dog's temperature regulation). Bathing an animal is not just about a human's allergies, the animal's health and welfare should be a primary concern.
- Consider the labor and time involved in bathing a pet often, safely, and well.
- Start when the animal is young.



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Medication	Mechanism of Action	Adverse Effects	Notes
medication	1		Notes
<ul> <li>1<sup>st</sup> generation (nonselective, more sedating)*: diphenhydramine, chlorpheniramine, clemas- tine</li> <li>2<sup>nd</sup> generation (less sedating, less drowsi- ness): cetirizine,* desloratadine,* fexofena- dine,* levocetirizine,* and loratadine*</li> <li>Azelastine has nasal spray* and eye drop for- mulations. Epinastine and olopatadine* are formulated as eye drops.</li> </ul>	Antihistami Blocks histamine and its binding to receptors, prevents histamine- caused redness, swelling, itching, and changes in secretions during an allergic response	nes Drowsiness, fatigue, headache	The 2 <sup>nd</sup> generation antihista- mines are preferred over 1 <sup>st</sup> gen- eration based on safety and efficacy data.
	Corticoster	bids	
Available as tablets, liquids, nasal spray, topi- cal creams for skin allergies, topical eye drops for conjunctivitis. Some steroids include beclomethasone, cicle- sonide, fluticasone furoate,* mometasone, budesonide,* triamcinolone,* dexametha- sone ophthalmic, prednisone, etc.	Anti-inflammatory effect	Short-term use: Weight gain, fluid reten- tion, high blood pressure Long-term use: Growth suppression, di- abetes, cataracts of the eye, osteoporo- sis, muscle weakness Adverse effects of inhaled steroids: Cough, hoarseness, fungal infection of the mouth	Highly effective for allergies but must be taken regularly. It may take 1 to 2 weeks before the full effect.
	Decongesta	Ints	
Available as nasal sprays, eye drops, liquids, and tablets Some decongestants include pseudoephedrine,* phenylephrine,* and oxymetazoline* nasal sprays	Shrinks swollen nasal tissues and blood vessels to relieve the symp- toms of nasal swelling, congestion, mucus secretion, and redness	<ul> <li>Increased blood pressure, insomnia. anxiety, feeling nervous, restless ness</li> </ul>	Relieve congestion and are often prescribed with antihistamines <b>Contraindicated</b> in patients with severe coronary artery disease, severe hypertension, and who concomitantly use monoamine oxidase inhibitors. <b>Short-term use only</b> (~5 days). Long-term use can make symp- toms worse.
	Combination Alle	rgy Drugs	
Some combination drugs include cetirizine/pseudoephedrine,* fexofenadine/ pseudoephedrine,* diphenhydramine/ pseu- doephedrine,* loratadine/pseudoephedrine,* pseudoephedrine/triprolidine* for nasal aller- gies, and naphazoline/pheniramine* for aller- gic conjunctivitis	Effects from each component	Adverse effects from each component	Use with caution due to in- creased risk of adverse effects
	Anticholinergic Na	asal Spray	
Ipratropium bromide nasal spray to control nasal discharge	Antisecretory properties in the nasal mucosa	<ul> <li>Bitterness in the mouth; dry nose, nosebleeds, or irritation; dizziness; headache; sore throat; respiratory tract infection</li> <li>Eye drops may cause blurred vision, stinging, and burning.</li> </ul>	For mild to moderate symptoms Not as effective as steroids
	Mast Cell Stab	ilizers	
Available as eye drops for allergic conjunctivi- tis and nasal sprays for nasal allergy symp- toms Some mast cell stabilizers include cromolyn sodium,* lodoxamide-tromethamine, nedo- cromil, pemirolast, etc.	Prevents histamine release from mast cells	<ul> <li>Throat irritation, coughing, skin rash For eye drops may cause blurred vision, stinging, and burning.</li> </ul>	For mild to moderate symptoms Not as effective as steroids
	Leukotriene Me	odifiers	
Montelukast*: Indicated for adults and pedi- atric patients six months or older with peren- nial allergic rhinitis. May be less effective than loratadine or ceti- rizine for reducing daytime nasal symptoms	Montelukast binds to leukotriene receptors in the human airway (smooth muscle cells and mac- rophages), preventing airway ede- ma, smooth muscle contraction, and other respiratory inflammation.	<ul> <li>Stomach pain or upset, headache, stuffy nose, cough, fever, rash, irrita- bility</li> </ul>	Warn patients to report behavior changes, including suicidal ide- ation or suicidal behavior Avoid concomitant use of aspirin or NSAIDs in aspirin-sensitive pa- tients

**PAUSE AND PONDER:** Which providers in your area provide allergen-specific immunotherapy? What should patients expect if they take this route?

dose and continuing treatment for one additional month. If a patient's symptoms are uncontrolled after two to four weeks of OTC treatment, pharmacists should assess the patient's adherence and refer for prescription therapy if necessary.<sup>35</sup> Allergy Immunotherapy

Allergen-specific immunotherapy has been used in pet allergies for years and has proven efficacy to help control symptoms and prevent disease progression. Allergists will consider allergy-specific immunotherapy when symptoms are uncontrolled by medications and/or avoidance measures, when adverse drug effects are intolerable, or when patients want to reduce long-term use of allergy medications.<sup>37</sup>

The basis for allergen-specific immunotherapy is gradual reprogramming of the immune system to build a tolerance to allergens. The U.S. Food and Drug Administration (FDA) characterizes allergen-specific immunotherapies as biologics because they are produced from living cells, not synthesized by chemists, and regulated under the Center for Biologics Evaluation and Research (CBER).<sup>38</sup> This class comes in three forms:

- sublingual allergy immunotherapy (SLIT) tablets
- SLIT drops, and
- subcutaneous allergy immunotherapy (SCIT)

As of 2022, the FDA has approved four SLIT tablets to treat allergic rhinitis with or without allergic conjunctivitis caused by ragweed, northern pasture grasses, and dust mites in susceptible individuals; the FDA has not approved SLIT tablets for pet allergies.<sup>22</sup>

SLIT drops are made from FDA-approved allergy extracts used to make SCIT shots. However, these extracts are only FDA-approved for injection use under the skin, and they are not approved for use under the tongue. Therefore, SLIT drops are not FDA-approved and are off-label in the United States, and Medicare or Medicaid does not cover these treatments in most cases. Despite not having FDA approval, patients can still receive SLIT drops from some prescribers who prepare a custom-mixed formulation but must pay out of pocket. Research indicates SLIT is safe and effective.<sup>39</sup>

The FDA has approved SCIT for cat allergies, but not for other pet allergies. Patients who receive SCIT usually call it "allergy shots." One systematic review evaluated 88 trials that enrolled 3,459 asthmatic patients and exposed them to SCIT. One case of deterioration in asthma symptoms was avoided for every three patients treated with SCIT (95% CI, 3-5), and one patient would avoid increasing symptomatic medication use for every four patients treated (95% CI, 3-6).<sup>40</sup> Another study found that SCIT can reduce the need for systemic steroids in allergic rhinitis

patients.<sup>41</sup> Usually, the patient receives a solution for injection with 10,000 bioequivalent allergy units (BAUs) per milliliter (standardized extract) of lyophilized cat hair and dander added to glycerol and human serum albumin (0.03%). A clinician administers one to two subcutaneous injections every week starting at low doses (1:10,000 dilution) and titrating up to a seemingly effective maintenance dosing. Then, the prescriber extends the injection interval gradually to every 2 weeks to 4 weeks. For cat allergens, the effective maintenance dose usually falls within the 1000 to 4000 BAU range.<sup>42</sup>

SCIT sometimes can cause treatment-related systemic allergic reactions; however, near-fatal or severe reactions are rare, and most reactions are local and mild (swelling, pruritis, and redness at injection site).<sup>43</sup> SCIT should not be recommended to patients who have severe uncontrolled heart problems or asthma if they take beta-blockers, which are associated with more frequent reactions, more severe reactions, and reactions that are refractory to epinephrine. Additionally, allergy shots should not be recommended for pregnant women unless discussed with their obstetricians.<sup>43</sup>

Both SCIT and SLIT require gradual up-titration of dosages with ongoing and multiple treatments and may take three to five years to reach desensitization. Also, for SCIT, based on its route of administration (subcutaneous injections are invasive), patients will need to visit the doctor's office more frequently and may experience the treatment-associated side effects.

SLIT has been increasingly recommended because of its ability to modify the immune system for the long term while reducing allergy symptoms. SLIT also showed a safer profile, only associated with mild mouth symptoms, and improved adherence compared to SCIT.<sup>44</sup> When compared to traditional allergy treatments, SLIT tablets showed similar clinical efficacy to nasal corticosteroids and greater clinical efficacy than second-generation antihistamines and montelukast.<sup>45</sup>



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#### What About Cost?

In adherent patients, SCIT and SLIT have proven to be an economically viable option. The annual cost of using SCIT depends on patients' insurance: Medicare (\$1021.70), Medicaid (\$758.16), and the commercial average (\$1722.24). Yearly treatment costs for SLIT are self-pay because treatment is not FDA approved and costs around \$679.25.<sup>46</sup> Because SLIT drops are administered at home by patients, they tend to be more affordable than the cost of SCIT. Patient preference might be for a once monthly administration, rather than taking oral antihistamines daily.

OTC medications are less expensive than immunotherapy, but costs vary. In a comparison of second-generation antihistamines versus montelukast, levocetirizine (Xyzal) had the best efficacy per cost value. Generic fexofenadine (Allegra), although similar in efficacy, was more expensive than levocetirizine.<sup>44</sup>

#### CONCLUSION

Healthcare providers should counsel patients about reducing allergen exposure and help patients to choose OTC medications for self-care based on individual patient needs and conditions to optimize treatment effects. Pharmacy staff should refer patients to allergists when necessary to identify the cause of their allergy symptoms. If a patient's allergy does not allow him or her to have pets at home and the patient owns a pet, suggest that the patient ask family members or friends about placement before contacting the local animal shelters.

**Figure 1** reviews need-to-know information to elevate your practice.

#### Figure 1. Quick Review of Information Related to Pet Allergies

Best Be COMMUNITY CHAMPIONS and work with your local shelters and veterinarians to educate the community. Increasingly, pharmacy teams need to know about pets and animal care and its effect on families. **2** Dispel myths about hypoallergenic pets. Patients may still experience allergies when they adopt such pets. **3** Answer patients' questions when they are referred for allergen-specific immunotherapy so their expectations are in line with reality. Better **1** Ask patients to describe their symptoms and match the medication you recommend with the specific symptoms. 2 Remember that adverse effects can limit patients' choices; drowsiness is a primary concern for many people. **3 Review OTC product labeling** with patients so they know how to take the medicine and its components, especially if it's a

#### Good

**1** Know that pet allergies are common and many people experience symptoms.

combination product.

**2** Recognize the different types of proteins that can cause pet allergies

**3** Educate patients that pet allergies are incurable; regardless, good hygiene and medication can alleviate symptoms.

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