Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Chewable formulation improves administration ease and owner preference with oclacitinib in canine atopic dermatitis: findings from three complementary studies

Travis Street
University of Surrey
Georgina Tarrant
University of Surrey
Taranpreet Rai
University of Surrey
Margaret Gober
Zoetis Inc
Chiara Noli
Servizi Dermatologici Veterinari
Andrea Wright
Andrea.Wright@Zoetis.com
Zoetis Inc
Kevin Wells
University of Surrey

Research Article

Keywords: canine atopic dermatitis, oclacitinib, chewable tablet, adherence, palatability, owner satisfaction, caregiver burden, antimicrobial stewardship

Posted Date: May 26th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9587397/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: Competing interest reported. MG and AW are employees of Zoetis Inc. TS, GT, TR, and KW are affiliated with the University of Surrey. CN was compensated to conduct study 2. Zoetis

funded the studies reported in this manuscript and contributed to study design, data collection, analysis, interpretation, and manuscript review. The final decision on manuscript content remained with the authors.

Chewable formulation improves administration ease and owner preference with oclacitinib in canine atopic dermatitis: findings from three complementary studies

Travis Street[1*], Georgina Tarrant[1], Taranpreet Rai[1,2], Margaret Gober[3], Chiara Noli[4], Andrea Wright[3], Kevin Wells[1,2]

[1]Surrey DataHub, vHive, School of Veterinary Medicine, University of Surrey, Guildford, United Kingdom

[2]Centre for Vision, Speech and Signal Processing, University of Surrey, Guildford, United Kingdom

[3]Global Medical Affairs, Zoetis Inc., Parsippany, NJ, United States

[4]Servizi Dermatologici Veterinari, Peveragno (CN), Italy

*** Correspondence:**
Corresponding Author
Andrea.Wright@Zoetis.com

Abstract

Background

Canine atopic dermatitis is a chronic, pruritic, inflammatory skin disease that commonly requires sustained home administration of oral therapy, yet dosing difficulty may undermine adherence and disease control. Oclacitinib maleate is available as Apoquel® (oclacitinib tablet) and Apoquel® Chewable (oclacitinib chewable tablet). Three complementary studies evaluated whether these formulation differences were associated with administration ease, owner experience, and adherence under routine clinical conditions.

Results

In Study 1, 10/11 CHEW administrations (91%) were completed within 1 minute compared with 5/11 (45%) for FCT, and 2/11 dogs (18%) required food aids with CHEW compared with 9/11 (82%) for FCT; 10/11 owners (91%) preferred CHEW. In Study 2, 11/15 owners (73%) reported difficulty administering FCT, whereas 12/15 (80%) reported that CHEW administration was enjoyable for both owner and dog; mean administration time was 1.6 minutes for CHEW and 4.0 minutes for FCT. In Study 3, 57/60 dogs (95.00%) met the study-defined adherence criterion during CHEW administration compared with 49/60 (81.67%) during FCT administration. Owners reported lower administration difficulty with CHEW (mean score 1.4 vs 3.7), less need to hide the formulation in food (29% vs 96%), and greater future preference for CHEW (76% vs 18% for FCT; 5% no preference). Secondary clinical variables were summarized descriptively in Study 3.

Conclusion

Across three complementary studies, CHEW was consistently associated with easier administration than FCT, with faster dosing, fewer workaround strategies, and more favorable owner experience. These findings indicate that formulation is a clinically relevant factor influencing whether long-term oral therapy can be delivered reliably in the home setting.

Keywords: canine atopic dermatitis, oclacitinib, chewable tablet, adherence, palatability, owner satisfaction, caregiver burden, antimicrobial stewardship

Background

Canine atopic dermatitis (AD) is a common, chronic, pruritic, inflammatory skin disease with a relapsing course that typically requires lifelong management (1,2,16). Affecting an estimated 10-15% of the global canine population, AD imposes substantial disease burden on both dogs and their caregivers through persistent pruritus, recurrent secondary infections, sleep disruption, frequent exacerbations, and erosion of quality of life (1,3). The disease characteristically begins in young adulthood and persists across the lifespan, necessitating sustained multimodal management rather than short-term interventions (1). Families must navigate a complex treatment landscape which may involve allergen avoidance strategies, skin-barrier repair regimens, infection management, long-term antipruritic, anti-inflammatory pharmacologic therapy, and allergen specific immunotherapy (1).

The economic and psychosocial impact of AD is substantial. Caregivers often incur substantial and ongoing cumulative costs, including veterinary consultations, diagnostic workups, medications, and ancillary therapies, sustained over years or decades (3). Indirect costs include caregiver stress, time invested in treatment administration, reduced household sleep quality, and diminished quality of life for both pet and family. Survey data consistently indicates that adherence to long-term dermatologic therapy can be inconsistent over extended periods, leading to inadequate disease control, clinical

This is a provisional file, not the final typeset article

flares, costly escalations to multimodal regimens, and deterioration of the veterinarian-client relationship (3,4). Thus, therapies that are easier to administer and more consistently accepted by dogs offer the potential to strengthen adherence and reduce both clinical and economic burdens (3).

Clinical outcomes depend not only on pharmacologic efficacy but also on the feasibility of day-to-day administration in home settings. Owners are more likely to sustain treatments that are easy, predictable, and rewarding, and struggle when dosing is aversive, time-consuming, or requires workarounds (4,5). This cumulative "treatment tax", even from small inefficiencies such as added time per dose or repeated administration challenges, can lead to missed doses, discontinuation, and reduced treatment control over time.

Home administration involves multiple friction points: dogs may refuse or detect tablets, while caregivers rely on strategies such as food concealment, crushing, or manual pilling (5). These approaches can increase time burden, introduce variability in dosing, and contribute to stress within the caregiver–dog relationship (3–5). Accordingly, administration ease represents a clinically relevant factor influencing real-world treatment execution (3).

Oclacitinib maleate (Apoquel®) is an oral Janus kinase inhibitor approved in multiple regions for the control of pruritus associated with allergic dermatitis and for the treatment of clinical manifestations of atopic dermatitis in dogs at least 12 months of age (1,6). It is available in two formulations: a conventional film-coated tablet (FCT) and a pork-flavored chewable tablet (CHEW). Under the labeled regimen, administered twice daily (BID) for up to 14 days during induction followed by once daily (QD) maintenance, regulatory pharmacokinetic studies indicate comparable overall systemic exposure (area under the plasma concentration–time curve) between FCT and CHEW formulations at steady state (7,12). The chewable formulation was developed to enhance palatability and voluntary acceptance. Regulatory guidance defines palatability as the likelihood that an animal voluntarily accepts an oral dosage form when offered, with voluntary acceptance studies typically quantifying acceptance proportions and time to consumption under standardized conditions (8)

The efficacy of oclacitinib for canine AD is well established in randomized controlled trials and prospective cohorts (1,6). Chewable oclacitinib was approved based on pharmacokinetic bridging demonstrating comparable systemic exposure to the film-coated tablet under labeled dosing. The key consideration, therefore, is whether formulation choice affects dosing ease, caregiver experience, adherence, and, ultimately, real-world disease control.

The research question addressed in this manuscript was whether chewable oclacitinib, compared with the film-coated tablet formulation, improves administration ease, owner experience, and adherence in dogs treated for allergic or atopic dermatitis in routine clinical practice. The objective was to report three complementary studies examining formulation-related differences in administration, owner experience, and treatment adherence. We hypothesized that the chewable formulation would reduce administration friction, improve adherence, and support more reliable real-world treatment execution during long-term disease management.

1 Methods

1.1 Study Oversight

This manuscript reports three complementary studies evaluating formulation-related differences between chewable oclacitinib (CHEW) and film-coated tablet oclacitinib (FCT) under routine clinical

conditions. Study 1 was a US pilot crossover study focused on immediate administration outcomes. Study 2 was an Italian owner-experience observational study focused on administration difficulty, time-to-dose, and owner-reported experience. Study 3 was a US randomized crossover study focused on treatment adherence and owner-reported administration experience. Supportive social media listening findings were included separately as contextual owner-voice data and were not treated as a fourth comparative study.

Study 1, a US pilot randomized two-period crossover (n = 11), evaluated proximal administration endpoints in a single general practice setting, including administration time, workaround frequency, and owner preference. Study 2, an Italian two-stage observational owner-experience study (n = 16 dogs; n = 15 owners), assessed voluntary acceptance, time-to-dose, dosing strategies, and owner-reported ease and preference in a dermatology practice setting in Italy, integrating quantitative and qualitative data with photographic and video documentation of the administration experience. Study 3, a larger US randomized crossover study (n = 64), evaluated treatment adherence defined as missing 2 or fewer doses during each 30-day treatment period and captured owner-reported administration experience, owner preference, PVAS, VetVAS, and adverse events. This manuscript reports the findings of these three studies together.

Table 1 summarizes each study's design, setting, sample size, endpoints, ethical oversight, and role in manuscript. For clarity and consistency throughout the manuscript, studies are referenced as follows: Study 1 (US pilot administration crossover; n = 11), Study 2 (Italian two-stage owner-experience study integrating administration acceptability and observational components; n = 16 dogs; n = 15 owners), and Study 3 (US multi-site adherence and outcomes crossover; n = 64).

1.2 Study Design, Population and Eligibility Criteria

1.2.1 Study 1: US Pilot Administration Crossover

Study 1 was a single-center pilot randomized crossover study conducted at a general veterinary practice in the United States from January to July 2024. The study evaluated proximal administration endpoints and owner experience over a 10-day observation period using a two-period, two-sequence (AB/BA) crossover design: five consecutive days of one formulation (CHEW or FCT) followed by five consecutive days of the alternative formulation, both administered twice daily (BID) at the labeled dose of 0.4–0.6 mg/kg body weight.

Study 1 enrolled client-owned dogs with veterinarian-diagnosed canine atopic dermatitis or allergic pruritus. Inclusion criteria were age 1 to 11 years, body weight 16 to 127 lbs. (7 to 58 kg), clinical presentation for pruritus or dermatitis, and owner willingness to administer study medication twice daily during the 10-day observation period. Dogs were excluded if they had contraindications to oclacitinib, recent changes in dermatologic medications within the preceding two weeks, or inability of the owner to comply with twice-daily dosing requirements.

Eleven dogs were enrolled. Mean age was 4.85 years (range 2 to 11 years). Mean body weight was 52.8 lbs. (range 16 to 127 lbs.). Breed distribution included mixed breeds (n = 2), Golden Retrievers (n = 2), and single representatives of Bichon Frise, Brittany Spaniel, Miniature Schnauzer, Cairn Terrier, Mastiff, and French Bulldog. Six dogs received CHEW first and five received FCT first. All dogs completed both crossover periods.

Endpoints included administration time, measured to the nearest second from presentation to ingestion and censored at 5 minutes; voluntary acceptance status, defined as ingestion without

This is a provisional file, not the final typeset article

resistance versus requiring a workaround; types and frequencies of workarounds employed, including pill pockets, food wrapping, crushing, and manual pilling; and owner-rated ease and formulation preference assessed using categorical scales and visual analog ratings. Owners were instructed to first offer each formulation for voluntary consumption (hand or empty bowl) for up to 5 minutes before employing any workaround; subsequent administration methods were at owner discretion but required to be consistent across study periods.

1.2.2 Study 2: Italian Owner Preference Study (Two-Stage Observational Design)

Study 2 enrolled client-owned dogs with dermatologist-confirmed canine atopic dermatitis evaluated by a board-certified veterinary dermatologist in Italy, with patient assessments conducted during routine veterinary visits. Inclusion criteria were age 1 to 10 years, body weight 8 to 36 kg, confirmation of atopic dermatitis using standardized diagnostic criteria, and owner provision of informed consent. Dogs were excluded if they had received systemic corticosteroids or other immunosuppressive therapy within four weeks of study entry, or if they had comorbid conditions that could confound dermatologic assessment.

Sixteen dogs were enrolled. Median age was 4.8 years (range 2 to 9 years). Median body weight was 21.4 kg (range 8.5 to 36.0 kg). Eight dogs were male and eight were female. All dogs completed both sequential study stages, Stage 1 film-coated tablet and Stage 2 chewable tablet, under routine home administration conditions.

Owners of enrolled dogs participated in structured survey assessments during each stage. Inclusion criteria for the owner component were active oclacitinib prescription and willingness to document medication administration using photo and video recordings captured during home dosing. Fifteen owners completed both Stage 1 (film-coated tablet) and Stage 2 (chewable tablet), each following approximately two weeks of routine use. Survey responses were supplemented with photo and video documentation of administration events. The survey instrument included both closed-ended and open-ended items assessing administration method, voluntary acceptance, time to administration, perceived ease, and overall experience, with full survey materials provided in the Supplementary Methods.

1.2.3 Study 3: US Adherence and Outcomes Crossover

Study 3 was a randomized crossover study conducted in five US general veterinary practices. Dogs received CHEW and FCT across two 30-day treatment periods in a randomized crossover design. The primary endpoint was treatment adherence, defined as missing 2 or fewer doses during each 30-day treatment period. Secondary measures included owner-reported ease and difficulty of administration, owner preference, owner-assessed pruritus using the Pruritus Visual Analog Scale (PVAS), veterinarian-assessed outcomes using the Veterinarian Visual Analog Scale (VetVAS), and adverse events. Secondary clinical variables were summarized descriptively in the study report.

Study 3 enrolled client-owned dogs with veterinarian-diagnosed allergic dermatitis or chronic allergic skin disease receiving oclacitinib in routine practice. Sixty-four dogs were enrolled, and 60 completed both treatment periods and were included in the per-protocol analysis. Owner survey responses were collected at Days 30 and 60 to assess administration difficulty, future formulation preference, and related treatment experience.

1.3 Study Randomization and Crossover and Control

Across the three studies, formulation comparisons were conducted using within-subject designs. Studies 1 and 3 employed randomized crossover designs, and Study 2 used a two-stage observational before–after design incorporating formulation switching. These approaches allowed each dog-owner unit to serve as its own control, minimizing confounding from stable individual characteristics such as temperament, caregiver behavior, household logistics, and baseline disease severity.

Studies 1 and 3 used two-period, two-sequence (AB/BA) crossover designs so that each dog received both formulations. In sequence AB, dogs received CHEW first, followed by FCT after the washout period, while sequence BA received the reverse order. Randomization lists were computer generated using SAS PROC PLAN with permuted blocks of four and were stratified by site where applicable. Allocation was concealed using sequentially numbered opaque envelopes opened at the time of enrollment. Oclacitinib has a plasma half-life of approximately four hours; therefore, a 7 ± 1 day washout period in Study 3, or predefined inter-period intervals in Studies 1 and 2, was considered sufficient to minimize pharmacologic carryover. Sequence-by-period interaction testing was performed to assess potential behavioral carryover effects, and no significant carryover was detected in any study. Investigators assessing clinical outcomes were blinded to treatment sequence where feasible.

Study 2 did not involve randomization. Owners sequentially completed surveys after their dog had been prescribed each formulation by the attending veterinarian during routine clinical care, reflecting the observational and non-interventional nature of this study.

1.4 Dosing and Administration

All dogs received oclacitinib in both film-coated and chewable formulations at the labeled dose of 0.4 to 0.6 mg/kg twice daily for up to 14 days during induction, followed by once-daily maintenance dosing (7,8).

In Studies 1 and 3, owners were instructed to administer medication as they would in routine home practice and to maintain a consistent feeding status, either with or without food, across treatment periods. In the US pilot study (Study 1), owners offered each tablet openly on the palm or in a bowl and were instructed to record the administration process, including time to ingestion and acceptance or resistance behaviors, using smartphone video from presentation to ingestion for subsequent review. If the tablet was not consumed within five minutes, owners were permitted to use their usual workaround, which was recorded using predefined categories.

In the Italian two-stage observational study (Study 2), owners administered both formulations sequentially during prescribed therapy, following standardized offering instructions. Owners first attempted administration in an empty food bowl for three minutes, followed by offering the tablet by hand for three to five minutes. If the tablet was not accepted within this observation window, owners were allowed to use their usual workaround methods, including food concealment, pill pockets, or manual pilling, which were recorded. Owners captured photo and video recordings at baseline, mid-period, and end-of-period to document administration experience and dog behavior.

1.5 Adherence Monitoring

In Studies 1 and 2, adherence-related endpoints were assessed using owner-reported measures including ease of administration, time-to-dose, need for workarounds, and voluntary acceptance. Study 1 additionally incorporated video documentation to enable objective review of administration speed and dog behavior during dosing.

This is a provisional file, not the final typeset article

In Study 3, adherence was assessed using the study-defined treatment criterion of missing 2 or fewer doses during each 30-day treatment period. Adherence outcomes were summarized from study completion data and owner survey responses collected at follow-up visits.

1.6 Measurement Procedures and Quality Assurance

Administration time, voluntary acceptance, workaround use, pruritus severity, adherence, and owner-reported experience were assessed using standardized procedures across studies. Time-to-dose was measured by stopwatch or verified video timestamp and censored at five minutes if ingestion did not occur. Administration events were documented by video or photography where applicable. In Study 3, adherence was assessed according to the predefined study criterion of missing 2 or fewer doses during each 30-day treatment period, together with owner-reported administration experience and clinical assessments. Pruritus was assessed using validated visual analog scales, and owner satisfaction was captured using structured Likert-scale instruments; qualitative data in Study 2 were analyzed using reflexive thematic analysis (1,5).

All quantitative data were recorded in electronic case report forms or secure survey platforms with predefined verification and audit procedures. Detailed operational protocols and quality assurance procedures are provided in the Supplementary Methods.

1.7 Outcome Definitions

Primary and secondary outcomes were prespecified for each study in alignment with its design and objectives. Across studies, endpoints captured proximal administration metrics, owner experience, and, where applicable, adherence and clinical outcomes. Primary outcomes focused on formulation-related administration performance or adherence, while secondary outcomes included workaround use, behavioral responses, satisfaction measures, and clinical assessments. A structured summary of all primary and secondary endpoints by study is provided in Table 2.

1.8 Statistical Analysis

Descriptive statistics were used to summarize administration, owner-experience, adherence, and clinical variables across the three studies. For Study 1, outcomes were reported descriptively because of the pilot design and small sample size. For Study 2, quantitative survey responses were summarized using frequency counts, proportions, and mean administration times, and qualitative owner narratives were analyzed using Braun and Clarke's six-stage reflexive thematic analysis framework with NVivo software (13).

For Study 3, the primary adherence endpoint, defined as missing 2 or fewer doses during each 30-day treatment period, was analyzed using a generalized linear mixed model with treatment, sequence, and treatment-by-sequence interaction as fixed effects, as specified in the study report. Secondary variables, including owner-reported administration difficulty, owner preference, PVAS, VetVAS, and adverse events, were summarized descriptively.

Quantitative analyses were performed using SAS version 9.4. Survey-based summaries were generated using Qualtrics analytics where applicable, and qualitative data management and coding were performed using NVivo version 14. Statistical tests are reported only for analyses specified in the individual study reports.

1.9 Social Media Listening for Owner Voice Analytics

Supportive social media listening analyses were conducted on publicly available posts from major pet-owner discussion platforms over a defined multi-year period, building on prior work examining changes in online discussion of canine pruritus and treatment topics (5,11,15). Posts were filtered using predefined relevance criteria and analyzed using a combination of rule-based classification and large language model-assisted thematic coding to identify administration-related experiences, barriers, and facilitators (5). The social media listening and thematic coding workflow is summarized in Figure 4.

Results

1.10 Study 1: US Pilot Administration Crossover Study

1.10.1 Administration Time and Voluntary Acceptance

Study 1 included 11 dogs completing both crossover periods. Apoquel Chewable (CHEW) was administered in less than 1 minute in 10/11 dogs (91%), whereas Apoquel film-coated tablet (FCT) was administered in less than 1 minute in 5/11 dogs (45%). CHEW administration required 1 to 2 minutes in 1/11 dogs (9%). FCT administration required 1 to 2 minutes in 4/11 dogs (36%), 2 to 5 minutes in 1/11 dogs (9%), and more than 5 minutes in 1/11 dogs (9%).

1.10.2 Food Requirements and Workarounds

Nine of 11 dogs (82%) required at least one type of food to facilitate FCT administration, including peanut butter in 4/11 dogs (36%), cheese in 4/11 (36%), pill pockets in 1/11 (9%), hot dogs in 1/11 (9%), pepperoni in 1/11 (9%), and bacon in 1/11 (9%). In contrast, 2/11 dogs (18%) required food for CHEW administration, including peanut butter in 1/11 (9%) and mixed vegetables in 1/11 (9%). Multiple administration methods were required in 7/11 dogs (64%) during FCT administration compared with 1/11 dogs (9%) during CHEW administration.

1.10.3 Dog Behaviors with Film-coated Tablet

Observed behaviors during FCT administration included turning the head away or running in 3/11 dogs (27%), spitting out or gagging in 5/11 (45%), reluctance or selective behavior in 3/11 (27%), complete ignoring of the tablet in 2/11 (18%), and general difficulty with administration in 3/11 (27%). Seven of 11 dogs (64%) accepted FCT only when food was provided.

1.10.4 Ease Ratings and Owner Preference

Ten of 11 owners (91%) rated CHEW administration as very easy or easy. For FCT, 1/11 owners (9%) rated administration as very easy or easy, 6/11 (55%) rated it as difficult or very difficult, and 4/11 (36%) rated it as neutral. Overall, 10/11 owners (91%) expressed a preference for CHEW (Figure 1).

1.10.5 Adverse Events

There were no reported adverse events in Study 1.

1.11 Study 2: Italian Owner Preference Study

1.11.1 Voluntary Acceptance

Study 2 included 16 dogs and 15 owner participants. Owners frequently reported that dogs accepted the chewable formulation readily during routine administration. Qualitative responses described dogs

This is a provisional file, not the final typeset article

willingly taking the chewable tablet when offered, often treating it as a reward, whereas the film-coated tablet more often required additional effort or workaround strategies.

1.11.2 Time-to-dose

Owners reported shorter administration times with the chewable formulation than with the film-coated tablet. Mean administration time was 1.6 minutes for CHEW and 4.0 minutes for FCT.

1.11.3 Workarounds

Owners commonly reported relying on food concealment or other workaround strategies when administering FCT, whereas CHEW was typically accepted without additional aids.

1.11.4 Owner Ratings

Owners consistently described administration of CHEW as easier and more positive than administration of FCT.

1.11.5 Owner-reported Difficulty with Film-coated Tablets

Eleven of 15 owners (73%) reported difficulties or additional effort when administering FCT. Of the 15 owners, 30% reported difficulty despite the use of food aids, and 3% reported force-administering the medication. Two of 15 owners (16%) reported no difficulty with FCT administration.

1.11.6 Positive Experience with Chewable Formulation

Twelve of 15 owners (80%) reported that CHEW administration was an enjoyable experience for both owner and dog. Of the 15 owners, 30% specifically cited shorter administration time, 30% described immediate and willing acceptance, and 12% reported feeling happy and relieved during CHEW administration. One owner reported no additional benefit associated with the chewable formulation.

1.11.7 Methods of Administration

Most owners reported administering CHEW directly by hand without food aids. In contrast, FCT administration more often involved food wrapping or force pilling because of reluctance when the tablet was offered freely.

1.11.8 Thematic Analysis Findings

Qualitative thematic analysis using Braun and Clarke's reflexive methodology identified four recurring themes (13). First, owners described a preference for the chewable formulation, citing ease of administration, shorter administration time, and higher acceptance. Second, owners described challenges with film-coated tablet administration, including reluctance, resistance behaviors, and repeated failed attempts. Third, owners frequently reported reliance on food-based masking strategies, including peanut butter and cheese, to facilitate FCT administration. Fourth, owners described positive dog behavior with CHEW, including eager and voluntary acceptance, often with treat-like perception.

1.11.9 Adverse Events

There were no reported adverse events in Study 2.

1.12 Study 3: US Adherence and Outcomes Crossover Study

1.12.1 Study Population and Primary Adherence Outcome

Study 3 enrolled 64 dogs from five US general veterinary practices, of which 60 completed both treatment periods and were included in the per-protocol analysis. The primary endpoint was treatment adherence, defined as missing two or fewer doses during each 30-day treatment period, corresponding to approximately ≥96% of scheduled doses administered under a twice-daily regimen. During CHEW administration, 57/60 dogs met the adherence criterion (95.00%), compared with 49/60 dogs during FCT administration (81.67%) (Figure 2). In practical terms, dogs meeting the adherence threshold missed no more than two doses over approximately 60 scheduled administrations, whereas dogs not meeting the threshold missed three or more doses during the treatment period.

1.12.2 Statistical Analysis of Adherence

In the primary generalized linear mixed model, treatment adherence was analyzed with treatment, sequence, and treatment-by-sequence interaction as fixed effects. The main treatment effect was not significant in this primary model ($p = 0.0920$) but trended toward significance. Additional exploratory analyses showed significant differences between formulations after model simplification; however, these were not the primary prespecified analysis.

1.12.3 Owner-reported Administration Experience

Fifty-six owners completed both satisfaction surveys at Days 30 and 60. Owner-reported ease of administration favored CHEW. On a 1 to 10 scale, where 1 indicated easy and 10 indicated difficult, mean difficulty scores were 1.4 for CHEW and 3.7 for FCT. Most owners reported concealing FCT in food, with 52/54 owners (96%) reporting that the film-coated tablet had to be hidden in food, compared with 16/56 owners (29%) for CHEW. Dogs receiving FCT had a higher chance of missing treatments than dogs receiving CHEW (P=0.003).

1.12.4 Owner Preference and Recommendation

After use of both formulations, 42/55 owners (76%) reported a future preference for chewable tablets, 10/55 (18%) preferred film-coated tablets, and 3/55 (5%) reported no preference. Most owners (52/55 (95%)) also reported that flavored tablets were easier to administer, and 49/55 (89%) indicating that they would prefer flavored tablets when the option was available. Detailed Study 3 adherence and owner-reported administration outcomes by formulation are summarized in Table 4.

1.12.5 Owner-reported Itch Control and Secondary Clinical Variables

Secondary variables, including PVAS, VetVAS, and owner satisfaction, were summarized descriptively without formal statistical testing (Figure 3). Owner-perceived itch control, measured on a 1 to 10 scale where 1 indicated very well controlled and 10 indicated not well controlled, had mean scores of 3.0 for CHEW and 3.3 for FCT. Given the established relationship between treatment adherence and therapeutic outcomes, missed doses may plausibly influence the consistency of clinical response; however, no formal analysis of adherence–outcome relationships was performed in this study.

1.12.6 Study Completion and Adverse Events

Four dogs did not complete the study and were excluded from the final analysis. Reported reasons were development of a skin infection requiring antibiotics, toe injury requiring antibiotics and

This is a provisional file, not the final typeset article

NSAIDs, failure to return for the Day 60 examination, and vomiting and diarrhea before Day 60. No additional formulation-specific adverse event rates were reported. Key administration, adherence, owner experience, and clinical outcome findings across the three studies are summarized in Table 3.

1.13 Supportive Social Media Listening Analysis

A supportive social media listening analysis examined 4,787 posts describing oral medication administration in dogs, including a coded subset of 613 posts referencing chewable or treat-like administration. Within this coded subset, the most frequently identified themes were interest from other household animals during dosing (e.g., other pets approaching or competing for treat-like medication) (19.2%), child and family involvement in dosing rituals (15.3%), ingredient and protein sensitivity (13.2%), training-as-reinforcer (12.9%), calorie accounting and treat substitution (12.7%), and on-the-go or travel dosing (10.9%). Additional themes included habit-stacking routines (6.5%), multi-pet management during administration (6.5%), and puzzle or enrichment-based delivery (4.6%) (Table 5) (5).

2 Discussion

Across three complementary studies conducted in routine clinical settings, the chewable oclacitinib formulation was consistently associated with easier administration than the film-coated tablet. Although the studies differed in design and endpoints, all three showed the same directional pattern: the chewable formulation was accepted more readily, required fewer administration aids or workaround strategies, and was preferred by owners. Taken together, these findings indicate that formulation influences not only the mechanics of drug delivery but also the day-to-day feasibility of long-term treatment in canine atopic dermatitis.

Study 1 provides the clearest evidence that the chewable formulation reduced immediate administration friction. In this pilot crossover study, chewable doses were administered more quickly, rarely required food aids, and were strongly preferred by owners. The main contribution of this study is not statistical precision, given the small sample size, but demonstration of a clear behavioral difference at the point of dosing. These findings indicate that the chewable formulation changed the administration event itself, reducing delay, resistance, and reliance on concealment strategies.

Study 2 extends these findings by showing that owner experience was not only easier but also more positive with the chewable formulation. Owners reported shorter administration times, fewer difficulties, and a more enjoyable interaction for both owner and dog. This is important because long-term treatment success in canine atopic dermatitis depends not only on whether a dose can be given, but whether it can be given repeatedly without generating frustration or stress. The Italian observational data therefore add an experiential dimension to the quantitative findings, showing that formulation may influence the emotional burden of repeated medication administration.

Study 3 builds on the first two studies by showing that these administration advantages were accompanied by higher adherence to the study-defined treatment criterion and more favorable owner-reported administration experience. More dogs met the adherence criterion during chewable administration than during film-coated tablet administration, and owners reported lower difficulty scores, less need to hide the formulation in food, and stronger future preference for chewable tablets. Because the primary treatment effect in the main statistical model trended toward, but was not significant, these findings should be interpreted cautiously. Nevertheless, the overall pattern

remained directionally consistent with Studies 1 and 2, indicating that reduced administration burden may support more reliable treatment delivery in the home setting. Given the established relationship between treatment adherence and therapeutic outcomes, even modest deviations from prescribed dosing, such as missed doses, may plausibly contribute to less consistent clinical control, although this relationship was not formally tested in the present study.

Viewed together, the three studies suggest a coherent pattern: the chewable formulation was easier to give, more positively experienced by owners, and associated with better treatment execution under routine conditions. The studies were not designed to formally test whether administration ease and owner experience explain the relationship between formulation and adherence using a predefined statistical mediation analysis; however, the results are consistent with a pathway in which formulation affects administration ease and owner experience, which in turn may influence adherence. This interpretation is biologically and behaviorally plausible in a disease that requires sustained owner involvement and repeated oral dosing.

This interpretation is consistent with published external evidence. Field acceptance work has shown high repeated voluntary acceptance of chewable oclacitinib in client-owned dogs, and multinational owner-preference research has shown that owners favor chewable over film-coated formulations in both short- and long-term treatment scenarios (9,12). In addition, caregiver-burden research in veterinary dermatology indicates that treatment complexity is linked to owner stress and to deterioration in the veterinarian-client relationship, supporting the clinical relevance of reducing administration burden (14). Observational evidence further suggests that improved control with consistent oclacitinib use may reduce concomitant dermatologic therapy and systemic antimicrobial use while improving owner-reported quality of life (10).

Social media listening findings should be interpreted as supportive rather than primary evidence in this manuscript. They do not constitute a fourth study of formulation performance, but they do provide real-world context showing that dog owners frequently describe oral medication administration as effortful, emotionally negative, and dependent on workarounds such as food concealment or manual pilling. Within that broader owner-voice dataset, chewable or treat-like formulations were more often discussed positively and were associated with fewer practical barriers to administration. These observations are directionally consistent with the three reported studies and help contextualize why formulation differences may matter in routine home use.

From a clinical perspective, these findings suggest that formulation choice should be considered part of treatment planning rather than a secondary product characteristic. In a condition that often requires long-term daily therapy, a formulation that is easier for owners to administer may support more reliable treatment execution, reduce dosing-related stress, and lessen dependence on additional administration strategies. This may be particularly relevant in households already managing multimodal therapy or in dogs with established resistance to oral medication.

Several limitations should be considered. Sample sizes in Studies 1 and 2 were modest, and the observational design of Study 2 introduces the possibility of reporting and selection bias. Owner blinding was not feasible because the formulations are visibly and functionally different. Study 3 provided the strongest adherence data within the present manuscript, but its observation window was still relatively short for a lifelong disease, and the primary modeled treatment effect was not significant. In addition, all three studies were conducted in dogs already receiving oclacitinib in routine practice, which may limit generalizability to treatment-naive populations.

This is a provisional file, not the final typeset article

The evidence base also has important strengths. This manuscript reports three distinct but complementary studies rather than relying on a single endpoint or design. The studies were conducted in different practice environments and populations and produced a highly consistent directional signal across administration time, workaround use, ease of administration, and owner preference for chewable tablet. Study 3 strengthens the overall interpretation by extending these findings into a comparative adherence framework under routine practice conditions.

Future studies should examine whether the adherence differences observed here persist over longer follow-up periods and whether they translate into improved treatment outcomes, including reductions in relapse frequency, adjunctive therapy use, and healthcare utilization. Given the established relationship between adherence and therapeutic response, improved treatment execution associated with chewable formulations may plausibly support more consistent clinical control in routine care, although this was not directly tested in the present studies. It would also be useful to evaluate whether structured owner counseling further amplifies the benefits of improved adherence and administration ease with chewable formulations in real-world settings.

3 Conclusion

Across three complementary studies, chewable oclacitinib was consistently associated with easier administration than the film-coated tablet, with faster dosing, fewer workaround strategies, higher owner-reported ease and preference, and, in the adherence crossover study, higher adherence to the study-defined treatment criterion and more favorable owner-reported administration experience. These findings indicate that formulation is a clinically relevant factor influencing whether treatment can be delivered reliably in the home setting. In canine atopic dermatitis, where long-term disease control depends on sustained owner execution of daily therapy, selecting a formulation that reduces administration burden may support more consistent treatment and better real-world management outcomes.

Abbreviations

- **AD**: Atopic dermatitis
- **ARRIVE**: Animal Research: Reporting of In Vivo Experiments
- **AUC**: Area under the plasma concentration-time curve
- **BID**: Twice daily
- **CHEW**: Chewable tablet formulation of oclacitinib
- **CI**: Confidence interval
- **Cmax**: Peak plasma concentration
- **DVM**: Doctor of Veterinary Medicine
- **FCT**: Film-coated tablet formulation of oclacitinib
- **ICADA**: International Committee on Allergic Diseases of Animals
- **NADA**: New Animal Drug Application
- **NVivo**: Qualitative data analysis software
- **PK**: Pharmacokinetic
- **PVAS**: Pruritus Visual Analog Scale
- **QD**: Once daily
- **SAS**: Statistical analysis software
- **SML**: Social media listening
- **US**: United States

- **VetVAS**: Veterinarian-assessed Visual Analog Scale
- **WCVD**: World Congress of Veterinary Dermatology

Declarations

Ethics approval and consent to participate

All studies involved client-owned dogs and/or owner-reported outcomes and were conducted with appropriate informed consent and institutional oversight. Studies 1–3 were reviewed and approved by the Zoetis Ethical Review Board (ERB). The social media listening components were reviewed and approved by the University of Surrey Ethics Committee (reference FHMS 21-22/026 EGA, Amendment 3). All procedures were conducted in accordance with applicable Good Clinical Practice principles for veterinary clinical investigations and relevant institutional requirements. Where reporting checklists were applicable, ARRIVE 2.0 guidance was used to support transparent reporting, and the completed checklist is provided in the Supplementary Materials.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because they include proprietary study data and owner-reported research materials, but de-identified aggregate data from Studies 1 to 3 may be made available from the corresponding author on reasonable request and with permission from the study sponsor.

Competing Interest

MG and AW are employees of Zoetis Inc. TS, GT, TR, and KW are affiliated with the University of Surrey. CN was compensated to conduct study 2. Zoetis funded the studies reported in this manuscript and contributed to study design, data collection, analysis, interpretation, and manuscript review. The final decision on manuscript content remained with the authors.

Funding

This work was supported by Zoetis Inc. through a research collaboration with the University of Surrey DataHub (vHive).

Author Contributions

TS, GT, KW, and TR contributed to study conceptualization and methodology. TS and KW led the analysis of the three reported studies. TS, KW and GT drafted the manuscript. GT supported data curation and interpretation of owner-experience and owner-voice components. TR supported

This is a provisional file, not the final typeset article

analytical methods and review of results. All authors critically revised the manuscript and approved the final version.

Acknowledgments

The authors thank the participating veterinary practices and dog owners who contributed to Studies 1 to 3. The authors also acknowledge the study teams and survey support personnel involved in data collection, management, and study coordination.

References

[1] Olivry T, DeBoer DJ, Favrot C, Jackson HA, Mueller RS, Nuttall T, Prélaud P. Treatment of canine atopic dermatitis: 2015 updated guidelines from the International Committee on Allergic Diseases of Animals (ICADA). BMC Vet Res. 2015;11:210. doi:10.1186/s12917-015-0514-6.

[2] Eisenschenk MC, Hensel P, Saridomichelakis MN, Tamamoto-Mochizuki C, Pucheu-Haston CM, Santoro D. Introduction to the ICADA 2023 canine atopic dermatitis pathogenesis review articles and updated definition. Vet Dermatol. 2024;35(1):3-4.

[3] Spitznagel MB, Hillier A, Gober M, Carlson MD. Treatment complexity and caregiver burden are linked in owners of dogs with allergic/atopic dermatitis. Vet Dermatol. 2021;32:192-e50. doi:10.1111/vde.12938.

[4] Lavan R, Armstrong R, Tunceli K, Normile D. Dog owner flea/tick medication purchases in the USA. Parasit Vectors. 2018;11:581. doi:10.1186/s13071-018-3142-8.

[5] Tarrant G, Rai T, Wright A, Street T, Wells K. Using social media listening to identify the real-world challenges faced by dog owners globally when administering oral medications. Front Vet Sci. 2025;12:1502236. doi:10.3389/fvets.2025.1502236.

[6] Cosgrove SB, Cleaver DM, King VL, Gilmer AR, Daniels AE, Wren JA, Stegemann MR. Long-term compassionate use of oclacitinib in dogs with atopic and allergic skin disease: safety, efficacy and quality of life. Vet Dermatol. 2015;26:171-179, e35. doi:10.1111/vde.12194.

[7] U.S. Food and Drug Administration Center for Veterinary Medicine. Corrected Freedom of Information Summary, NADA 141-555: Apoquel chewable (oclacitinib maleate chewable tablets) [Internet]. 2023 [cited 2026 Jan 21]. Available from: https://animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFoi/14146

[8] Committee for Medicinal Products for Veterinary Use (CVMP). Guideline on the demonstration of palatability of veterinary medicinal products [Internet]. London: European Medicines Agency; 2014 [cited 2026 Jan 21]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-demonstration-palatability-veterinary-medicinal-products_en.pdf

[9] Wright A, Hillier A, Lambert J, Mwacalimba K, Lloyd N, Kagiwada T, Hashiguchi Y, Hours C, Riley D, Enstone A, et al. Dog owners' perceptions of the convenience and value of chewable oclacitinib: quantitative survey data from an international survey. Animals. 2024;14:952. doi:10.3390/ani14060952.

[10] Mwacalimba K, Hillier A, Rosenbaum M, Brennan C, Amodie D. Diminished antimicrobial drug use in dogs with allergic dermatitis treated with oclacitinib. Front Vet Sci. 2023;10:1207582. doi:10.3389/fvets.2023.1207582.

[11] Boyden L, Cherry G, Rai T, Wright A, Wells K. Global changes in pet owner awareness of pruritus and online discussion of treatments in dogs: a retrospective Twitter/X-based study spanning 2009-2022. In: Proceedings of the 10th World Congress of Veterinary Dermatology (WCVD10); 2024 Jul 25-29; Boston, MA, USA [Internet]. 2024 [cited 2025 Jul 10]. Available from: https://wavd.org/world-congress/boston-2024/

[12] Visser M, Walsh K, King V, Sture G, Caneva L. Acceptance of oclacitinib maleate (Apoquel®) chewable tablets in client-owned dogs with allergic and atopic dermatitis. BMC Vet Res. 2022;18:103. doi:10.1186/s12917-022-03210-x.

[13] Braun V, Clarke V. One size fits all? What counts as quality practice in (reflexive) thematic analysis? Qual Res Psychol. 2021;18:328-352. doi:10.1080/14780887.2020.1769238.

[14] Spitznagel MB, Patrick K, Hillier A, Gober M, Carlson MD. Caregiver burden, treatment complexity, and the veterinarian-client relationship in owners of dog with skin disease. Vet Dermatol. 2022;33:208-213, e59. doi:10.1111/vde.13065.

[15] Lavan R, Normile D, Husain I, Singh A, Armstrong R, Heaney K. An assessment of canine ectoparasiticide administration compliance in the USA. Parasit Vectors. 2022;15:32. doi:10.1186/s13071-021-05134-1.

[16] Miller J, Simpson A, Bloom P, Diesel A, Friedeck A, Paterson T, Wisecup M, Yu CM. 2023 AAHA management of allergic skin diseases in dogs and cats guidelines. J Am Anim Hosp Assoc. 2023;59(6). doi:10.5326/JAAHA-MS-7396.

4 Supplementary Material

Supplementary material includes detailed eligibility criteria for each study, complete randomization and washout protocols, administration procedures and video documentation requirements, detailed statistical methods, and thematic analysis methodology.

5 Tables

Table 1. Overview of studies included in this manuscript

Study	Study Name	Design	Location	Sample Size	Primary Focus	Ethics Status	Role in Manuscript
1	US Pilot Administration Crossover (23SORDER-01-04)	Randomized crossover	US general practice	n = 11	Administration ease, time-to-dose, workarounds, owner preference	Zoetis ERB (approved)	Primary (proof-of-concept)

This is a provisional file, not the final typeset article

2	Italian Owner Preference Study (Two-Stage Observational Design) (INTLORDER M-02-22)	Two-stage, non-randomized observational survey (Stage 1: FCT; Stage 2: CHEW; sequential within-dog exposure)	Italy (dermatology practice center)	n = 16 dogs; n = 15 owners	Voluntary acceptance; time-to-dose; workaround strategies; owner-rated ease and enjoyment	Zoetis Ethical Review Board; written informed owner consent obtained	Real-world owner-experience and acceptability dataset integrating quantitative and qualitative outcomes
3	US Adherence and Outcomes Crossover (23SORDER-01-03)	Randomized crossover	US multi-site (5 practices)	n = 64	Treatment adherence defined as missing 2 or fewer doses during each 30-day treatment period; owner-reported administration experience	Zoetis ERB (approved)	Primary (comparative adherence and owner-reported administration experience)

Abbreviations: FCT, film-coated tablet; CHEW, chewable tablet; PVAS, Pruritus Visual Analog Scale; VetVAS, Veterinarian Visual Analog Scale.

Table 2. Summary of Primary and Secondary Outcomes by Study

Study Number / Title	Primary Outcome(s)	Secondary Outcome(s)
Study 1: US Pilot Administration Crossover	Administration time; voluntary acceptance; owner-rated ease of administration	Food requirements: administration methods used; owner preference; dog behavioral response categories including turning away, gagging, reluctance, and ignoring the tablet
Study 2: Italian Owner Preference Study (Two-Stage Observational Design)	Owner-reported administration experience, including perceived difficulty administering film-coated tablets and reported enjoyment of chewable administration	Mean administration time: methods used to administer medication (e.g., food concealment, manual administration); owner-rated ease and enjoyment of administration; qualitative owner feedback on the administration experience
Study 3: US Adherence and Outcomes Crossover	Treatment adherence, defined as missing 2 or fewer doses during each 30-day treatment period	Owner survey responses on ease/difficulty of administration; owner preference; owner-assessed pruritus (PVAS); veterinarian-assessed outcomes (VetVAS); adverse events

Abbreviations: PVAS, Pruritus Visual Analog Scale; VetVAS, Veterinarian Visual Analog Scale.

619 **Table 3. Administration and Adherence Outcomes: Formulation Comparison Across Studies**

Outcome	CHEW	FCT	Effect size	Statistical test
Study 1: US Pilot Administration Crossover (n = 11)				
Administration in <1 minute	91% (10/11)	45% (5/11)	+46 percentage points	Descriptive; pilot not powered for formal comparison
Required food aids	18% (2/11)	82% (9/11)	−64 percentage points	Descriptive; pilot not powered for formal comparison
Multiple methods required	9% (1/11)	64% (7/11)	−55 percentage points	Descriptive; pilot not powered for formal comparison
Rated “easy” or “very easy”	91% (10/11)	9% (1/11)	+82 percentage points	Descriptive; pilot not powered for formal comparison
Overall owner preference	91% (10/11) preferred CHEW	9% (1/11) preferred FCT	—	Descriptive; pilot not powered for formal comparison
Study 2: Italian Owner Preference Study (n = 15 owners)				
Mean administration time (minutes)	1.6	4.0	−2.4 minutes	Descriptive
Owners reporting difficulty with FCT administration	—	73% (11/15)	—	Descriptive
Owners reporting no difficulty with FCT administration	—	16% (2/15)	—	Descriptive
CHEW administration reported as enjoyable for owner and dog	80% (12/15)	—	—	Descriptive
Owners reporting no additional benefit with CHEW	9% (1/15)	—	—	Descriptive
Study 3: US Adherence and Outcomes Crossover (n = 60 completers)				
Dogs meeting adherence criterion (missing ≤2 doses)	95.00% (57/60)	81.67% (49/60)	+13.33 percentage points	Primary model p = 0.0920
Owner-reported administration difficulty score (1 = easy; 10 = difficult)	1.4	3.7	−2.3 points	Descriptive

This is a provisional file, not the final typeset article

Owners reporting formulation had to be hidden in food	29% (16/56)	96% (52/54)	−67 percentage points	Descriptive
Future owner preference after using both formulations	76% (42/55) preferred CHEW	18% (10/55) preferred FCT; 5% (3/55) no preference	—	Descriptive

620

621 Abbreviations used: chewable tablet (CHEW); film-coated tablet (FCT); percentage points (pp).

622 **Table 4. Study 3 Adherence and Owner-Reported Administration Outcomes by Formulation**

Outcome	CHEW	FCT
Dogs enrolled	64	64
Dogs completing both periods (per-protocol analysis)	60	60
Dogs meeting adherence criterion (missing ≤2 doses)	57/60 (95.00%)	49/60 (81.67%)
Dogs not meeting adherence criterion (missing >2 doses)	3/60 (5.00%)	11/60 (18.33%)
Mean owner-reported administration difficulty score (1 = easy; 10 = difficult)	1.4	3.7
Owners reporting formulation had to be hidden in food	16/56 (29%)	52/54 (96%)
Future owner preference after using both formulations	42/55 (76%) preferred CHEW	10/55 (18%) preferred FCT; 3/55 (5%) no preference

623 Table note: Adherence in Study 3 was defined as missing 2 or fewer doses during each 30-day
624 treatment period. Owner survey denominators vary because not all owners completed every survey
625 item.

626 **Table 5. Owner-Voice Themes Identified Through Social Media Listening (n = 613 Posts)**

Theme	Proportion of coded posts (%)
Cross-species attraction	19.2
Child and family involvement	15.3
Ingredient and protein sensitivity	13.2
Training-as-reinforcer	12.9
Calorie accounting and treat substitution	12.7
On-the-go and travel dosing	10.9
Habit-stacking with routines	6.5
Multi-pet choreography	6.5
Puzzle and enrichment delivery	4.6

627 **6 Figures**

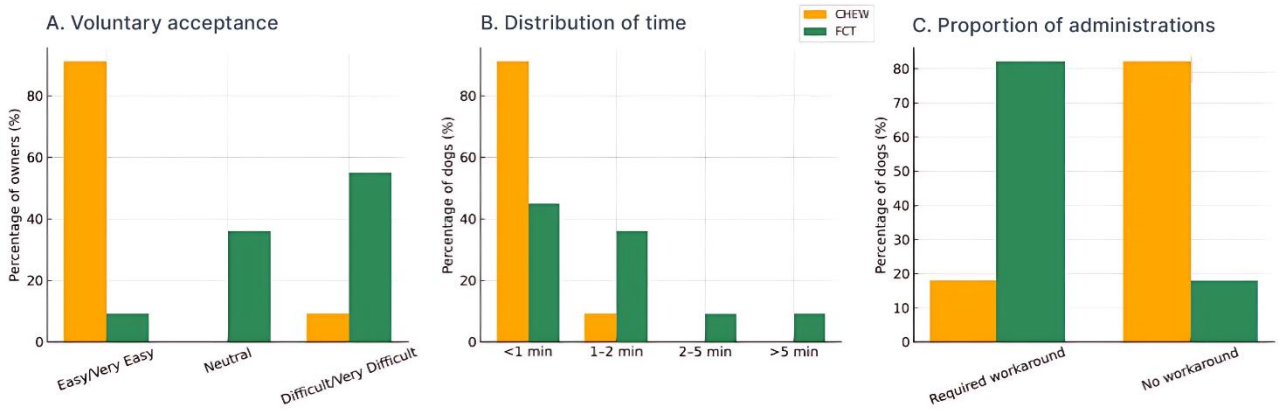


Figure 1. Study 1 pilot crossover outcomes. Administration outcomes in Study 1 (US pilot administration crossover; n = 11). (A) Voluntary acceptance of CHEW versus FCT within 5 minutes. (B) Distribution of time to dose. (C) Proportion of administrations requiring a workaround, including concealment in food, pill pocket use, or manual pilling.

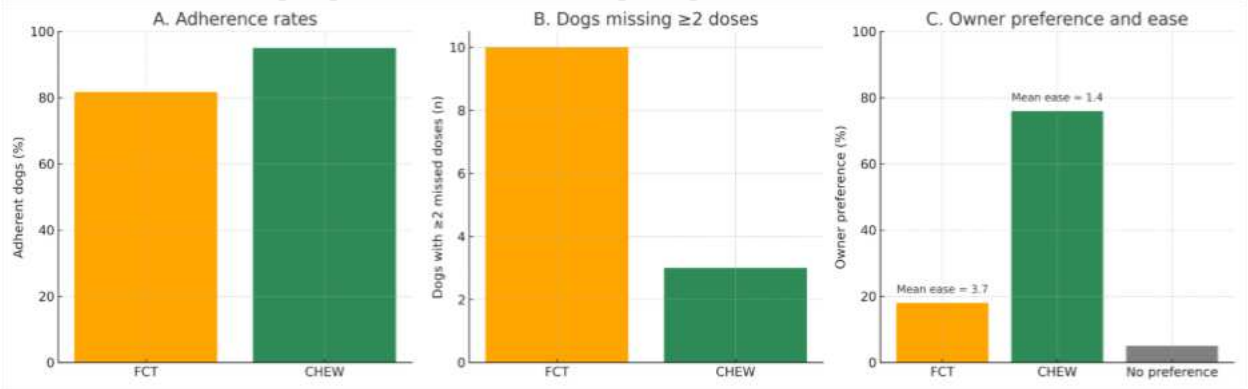


Figure 2. Study 3 adherence outcomes. Adherence outcomes from Study 3 (US adherence and outcomes crossover; n = 60 completers). The proportion of dogs meeting the study-defined adherence criterion of missing 2 or fewer doses during each 30-day treatment period is shown for CHEW and FCT.

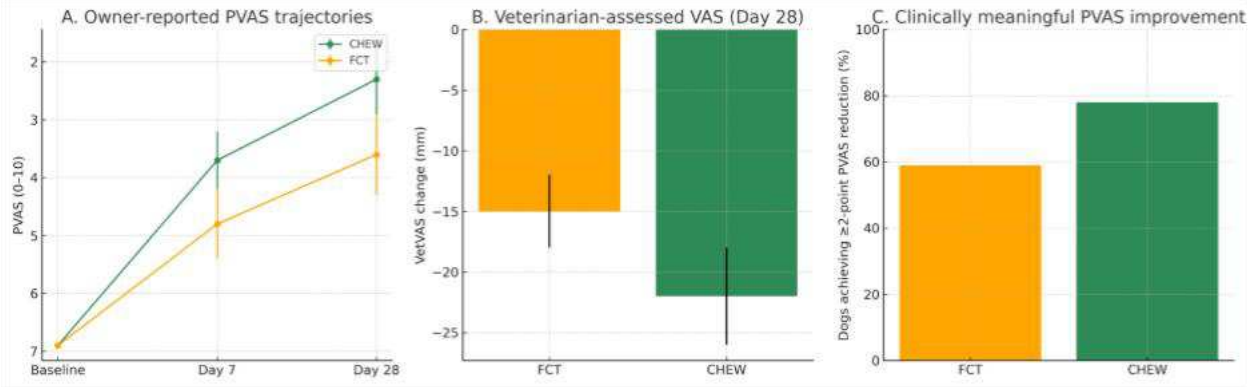


Figure 3. Study 3 secondary clinical variables. Descriptive summaries of owner-reported itch control and veterinarian-assessed outcomes from Study 3. Secondary clinical variables were summarized descriptively in the final study report and were not subjected to formal statistical comparison.

This is a provisional file, not the final typeset article

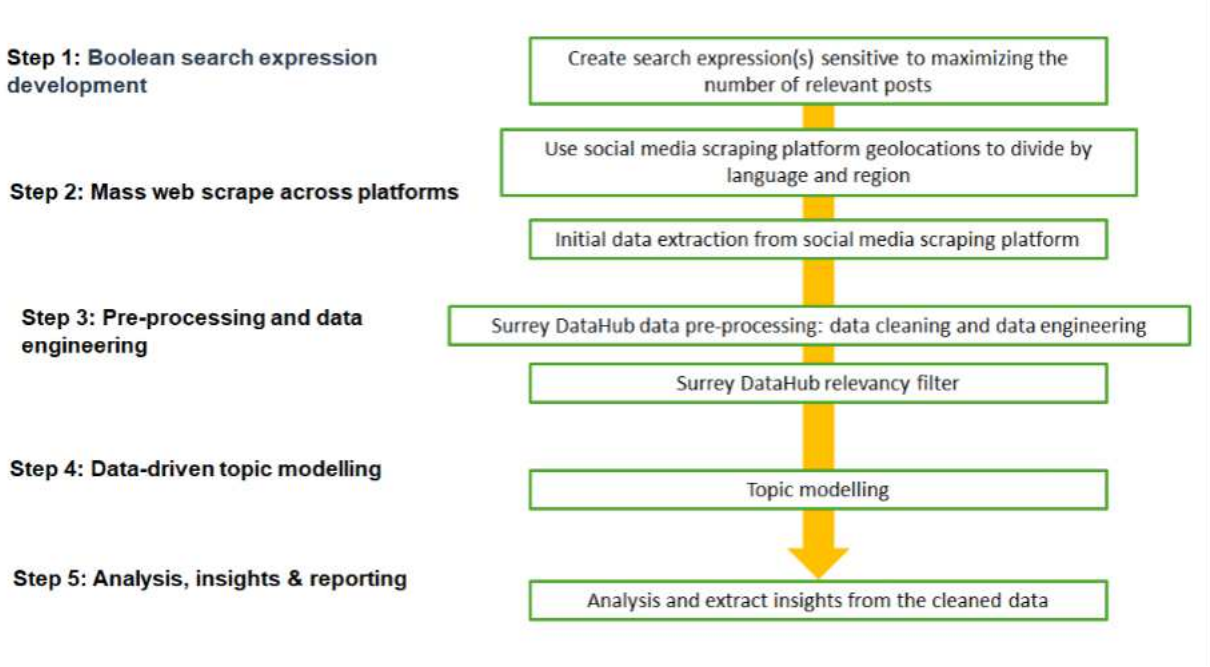


Figure 4. Social media listening (SML) workflow for owner-voice analytics. Workflow for SML applied to owner-voice analytics. Public posts are collected across platforms (Reddit, X, blogs, forums, Facebook), filtered for relevance to oral dosing, and processed via natural language processing (NLP)-assisted classification followed by thematic coding. A filtered, hand-coded sample (n=613 of 4,787 posts) was used to estimate topic prevalence, highlighting reward-based dosing, on-the-go dosing, daily routine anchoring, multi-pet choreography to avoid resource guarding, flavor/ingredient sensitivity, and less frequent puzzle/enrichment delivery.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMethodsv9.1.docx