



# Xintōpica®

Antipruritic.

Immunomodulator with Action on TH2 Lymphocytes - Selective Inhibitor of JAK1-Dependent Proinflammatory Cytokines

Control of Atopic Dermatitis and Pruritus Associated with Allergic Dermatitis in Dogs

Highly Palatable Soft Chews

Veterinary Use



## Composition

### Xintōpica® 1.5 mg

Each 1000 mg chewable tablet contains:  
Oclacitinib (as Oclacitinib maleate)..... 1.5 mg  
Excipients and flavorings.....q.s.ad..... 1 tablet

### Xintōpica® 3 mg

Each 2000 mg chewable tablet contains:  
Oclacitinib (as Oclacitinib maleate)..... 3 mg  
Excipients and flavorings.....q.s.ad..... 1 tablet

### Xintōpica® 6 mg

Each 1000 mg chewable tablet contains:  
Oclacitinib (as Oclacitinib maleate)..... 6 mg  
Excipients and flavorings.....q.s.ad..... 1 tablet

### Xintōpica® 12 mg

Each 2000 mg chewable tablet contains:  
Oclacitinib (as Oclacitinib maleate)..... 12 mg  
Excipients and flavorings.....q.s.ad..... 1 tablet

## Pharmaceutical form

**Xintōpica®** it is a soft, chewable tablet with a very pleasant flavor for dogs. It is brown (light to dark) in the shape of a truncated cone. It may have a marbled appearance, mottled, or both.

## Features

**Xintōpica®** contains oclacitinib maleate (CAS 1208319-26-9; ATC: QD11AH90), a synthetic sulfonamide-derived JAK inhibitor. Oclacitinib occurs as a white to off-white powder, insoluble in water but soluble in DMSO.

**Xintōpica®** is a fundamental drug for the treatment of canine atopic dermatitis, a novel systemic treatment related to the rapid, safe and adequate control of acute and chronic canine pruritus - and other symptoms - associated with allergic dermatitis. It can be used on dogs from 12 months and weighing 2.5 kg.

*Oclacitinib* was the first medication designed specifically to treat canine pruritus and inflammation due to allergic and atopic dermatitis. It works differently than steroids and cyclosporines. Compared to these and other existing therapies, *oclacitinib* has demonstrated overall superiority in both efficacy and speed of action: it offers an onset of itch relief within the first 4 hours after administration, thereby significantly reducing itch from the beginning, start of treatment

Due to the selective mechanism of the drug and its dosing interval, generalized immunosuppression is limited, making it a favorable option compared to other alternative therapy options such as glucocorticoids, modified cyclosporine, lokivetmab, antihistamines and essential grass acids.

Itching is the most common sign of allergies in dogs, and atopic dermatitis (environmental allergies) affects up to 15% of the canine population. Itching caused by allergic skin disease can be a short-term acute condition or can be recurrent, seasonal or chronic, impacting the quality of life of both the dog and the owner.

## Mechanism of Action, Pharmacokinetics and Pharmacodynamics

**Xintōpica®** contains *oclacitinib*, an active modern inhibitor of Janus kinases<sup>1</sup> (JAK or janikibs), thus interfering with the JAK-STAT signaling pathway. *Oclacitinib* selectively inhibits cytokines that are pro-inflammatory or have a role in the allergic response/pruritus/inflammation, thereby relieving the symptoms of allergic dermatitis with minimal impact on the immune system:  
- JAK1 inhibition: Inhibits the function of various pruritogenic and proinflammatory cytokines  
- Minimal effect on JAK2 and JAK3: With minimal effect on cytokines involved in hematopoiesis and innate immunity.

Specifically, *oclacitinib* inhibits IL-31, an important pruritogenic cytokine in atopic dogs, as well as proinflammatory cytokines such as IL-2, IL-4, IL-6 and IL-13 that also play an important role in canine atopic dermatitis. At approved doses, *oclacitinib* appears to have no effect on hematologic parameters, but at higher doses or frequencies, inhibition of hematopoiesis may occur in some dogs. *Oclacitinib* is not an antihistamine or glucocorticoid.

Under experimental conditions, *oclacitinib* delayed the development of dermatitis at the site of skin antigen exposure in atopic beagles. In a study of dogs (client-owned) with allergic dermatitis, pruritus scores were reduced by 31% within 4 hours of the first dose and by 67% at 14 days.

Following oral administration in dogs, *oclacitinib* had a bioavailability of 89%, with peak plasma concentrations occurring in less than 1 hour. Prandial status did not affect pharmacokinetics. *Oclacitinib* was not significantly bound to plasma proteins in dogs (66% to 69%). The apparent volume of distribution (at steady state) was 942 ml/kg, and total body plasma clearance was 5.3 ml/minute/kg. The terminal half-life was 3.5 hours (IV) and 4.1 hours (PO). *Oclacitinib* was metabolized into several compounds, with the oxidative form being the main metabolite (identified in plasma and urine). Less than 4% of the drug was excreted unchanged in the urine 24 hours after administration.

## Target Species

Dogs.

## Indications of use

Treatment of pruritus associated with allergic dermatitis in dogs, including flea allergies. Treatment of the clinical manifestations of atopic dermatitis in dogs. Temporary relief of pruritus associated with sarcoptic mange.

## Additional considerations regarding indications for use:

- *Oclacitinib* controls pruritus associated with allergic dermatitis, including flea allergies and atopic dermatitis.
- *Oclacitinib* is suitable for the treatment of both acute flares and long-term treatment of atopic dermatitis.
- Studies in dogs with atopic dermatitis indicate an efficacy rate comparable to that of glucocorticoids and cyclosporine, except that *oclacitinib* has a more rapid onset of action (within 24 hours) for the control of pruritus.

- *Oclacitinib* appears to reduce antimicrobial use in dogs with allergic dermatitis.  
- Based on case reports in dogs, *oclacitinib* has also been shown to be effective for the treatment of ischemic dermatopathy, hyperkeratotic erythema multiforme, autoimmune subepidermal bullous dermatosis, ulcerative dermatitis of the ear tip, cutaneous epitheliotropic T-cell lymphoma (partial remission) and as a temporary treatment to relieve itching associated with sarcoptic mange. Anecdotal reports also suggest that *oclacitinib* may be beneficial for the treatment of canine lupus and pemphigus.

## Route of Administration and Dosage, Considerations and Directives for Correct Administration

**Xintōpica®** It is administered orally, at 0.4 - 0.6 mg/kg PO every 12 hours for up to 14 days, then 0.4 - 0.6 mg/kg every 24 hours as maintenance therapy. The following table indicates the appropriate number and size of tablets to deliver 0.4-0.6mg of oclacitinib/kg body weight, depending on the dog's body weight:

Dog Weight (Kg)		Concentration and Number of Tablets to Administer - Xintōpica				Oclacitinib Dosage	
From	To	Xintōpica Tablets (mg) 1.5	Xintōpica Tablets (mg) 3	Xintōpica Tablets (mg) 6	Xintōpica Tablets (mg) 12	Maximum (mg/kg)	Minimum (mg/kg)
2.5	3.7	1				0.60	0.41
3.8	4.9	1.5				0.59	0.46
5	7.5		1			0.60	0.40
7.6	10.5		1.5			0.59	0.43
10.6	15			1		0.57	0.40
15.1	20			1.5		0.60	0.45
20.1	30			2	1	0.60	0.40
30.1	45				1.5	0.60	0.40
45.1	60				2	0.53	0.40

## Additional comments on dosage:

- Long-term maintenance therapy should be based on an individual risk-benefit assessment by the veterinarian.
- **Xintōpica®** can be administered without or with food (before or after eating). However, if your animal vomits or suspects that it is sick after a dose, try giving the medication with some food.
- The chewable tablets are divisible by the separation slot. To do this you can use the tablet cutter offered inside the **Xintōpica®** box.
- **Xintōpica®** is a highly palatable, soft and chewable tablet, which facilitates its administration due to its high acceptance. Alternatively, if applicable, it can be administered with food or by opening the animal's mouth and placing the tablet on the deep back of the tongue like any other medication.

## Tolerance and Safety

- It has been shown that in allergic dogs, chronic use of *oclacitinib* for up to 630 days was safe. In a prolonged twice-daily regimen in dogs with very severe cases of atopic dermatitis, *oclacitinib* maintained long-term efficacy and safety with only minor adverse events and clinically non-significant changes in blood tests. On the other hand, existing data show that the risk of malignancies due to long-term treatment with *oclacitinib* is not statistically different compared to the risk of alternative medications.
- *Oclacitinib* during pregnancy, lactation or in breeding animals has not been demonstrated. Use only in accordance with the benefit/ risk assessment carried out by the responsible veterinarian.
- **Overdose/Acute toxicity:** In rats, the oral LD 50 is 310 mg/kg. In safety margin studies, in beagles receiving doses of *oclacitinib* 5 times higher than indicated (3 mg/kg PO every 12 hours for 6 weeks, then every 24 hours for 20 weeks), clinically observed adverse effects attributable to the drug they included vomiting, diarrhea, interdigital furunculosis/dermatitis, papillomas, microscopic evidence of mild interstitial pneumonia and lymphoid hyperplasia, and chronic active inflammation in the lymph nodes draining feet affected by interdigital furunculosis. No deaths or serious effects were reported. For patients who have experienced or are suspected of having experienced an overdose, it is recommended that you consult your veterinarian immediately. There is not a specific antidote. In case of signs of overdose, treat the animal symptomatically.

## Adverse reactions

- *Oclacitinib* is well tolerated in dogs and does not usually present adverse effects. However, the following adverse effects have been observed infrequently up to day 16 of treatment: Diarrhea, vomiting, anorexia, lethargy, polydipsia (in most cases, transient effects and resolved spontaneously), cutaneous or subcutaneous lumps. After day 16: non-specific pododerma and dermal lumps; otitis, vomiting, diarrhea, histiocytoma, cystitis, skin yeast infections, pododermatitis, lipoma, polydipsia, lymphadenopathy, nausea, increased appetite and aggressiveness.
- *Oclacitinib* may increase susceptibility to infections (e.g., pneumonia, demodicosis, pododermatitis, pyoderma, otitis). Proteinuria, hematuria, hyposthenuria, and microalbuminemia have also been reported.
- The rate of UTI/cystitis was 11.3% in a long-term study, while a small prospective study in healthy dogs with no previous history of UTI concluded that *oclacitinib* did not increase the risk of bacterial UTI during a median of 6 months of the year study. Caution may be necessary when treating dogs with a prior history or predisposing factors of UTI, as the risk of UTI with administration of *oclacitinib* in this population has not been determined.
- New benign and malignant neoplastic diseases (or exacerbations of existing ones) have been observed in dogs treated with *oclacitinib*. Unspecified benign cutaneous and subcutaneous masses, histiocytomas and papillomas have also been described in dogs. A retrospective study (660 client-owned dogs followed for a mean of 36 months) indicated that long-term treatment with *oclacitinib* did not increase the risk of malignancy compared to an age- and breed-matched control group that was treated with other systemic medications for atopic dermatitis (eg, cyclosporine, glucocorticoids).
- Reductions in leukocyte counts (neutrophils, eosinophils, monocytes), transient increases in lymphocyte counts, and decreases in serum globulin have occurred, however, the mean values of the study population remained within normal ranges.
- A potential error when treating dogs that can cause overdose and therefore the administration - to small dogs - of tablets with higher doses, designed for larger dogs, should be avoided.
- If you observe or suspect any serious or other reactions not mentioned, contact your veterinarian immediately.

## Contraindications

- Do not use in case of known hypersensitivity to *oclacitinib* or any excipient.
- Do not use in dogs with evidence of serious infections, immunosuppression, such as hyperadrenocorticism, or with evident progressive malignancy.
- In dogs with severe liver disease or severe hypoproteinemia, the veterinarian must evaluate the risk/benefit ratio prior to treatment.

## Precautions

- This medication is approved for use in dogs only. It is not for human use.
- Do not use in dogs less than 12 months of age or less than 2.5 kg in weight. The treatment of dogs less than 12 months of age or less than 2.5 kg live weight should be carried out based on the benefit-risk assessment carried out by the responsible veterinarian.
- *Oclacitinib* is an immunomodulator so it could increase sensitivity to infections and exacerbate neoplastic conditions. If you suspect an infection or notice abnormal skin changes, new growths, or changes to pre-existing masses on your animal, contact your veterinarian immediately.
- When *oclacitinib* is administered to treat pruritus caused by allergic dermatitis, any underlying cause (e.g., flea allergy, contact dermatitis, food allergies) should be treated.
- In cases of allergic and atopic dermatitis, it is recommended to treat conditions that may complicate the condition (bacterial, fungal infections or parasitic infestations (e.g. fleas and acarosis).
- At label doses, there is an increased potential for susceptibility to infections, demodicosis, and

exacerbation or development of neoplastic diseases. Clinicians should avoid or carefully consider the use of *oclacitinib* in animals with pre-existing conditions, such as demodicosis, serious infections (e.g., pneumonia), and neoplastic diseases.

- Due to its potential effect on certain clinicopathological parameters, periodic monitoring with complete blood counts and serum biochemistry is recommended in long-term treatments.
- If there is no improvement, stop the medication and contact your veterinarian.
- Keep the product in the aluminum blister until use.
- Do not eat, drink or smoke while handling the tablets.
- Wash your hands after handling the tablets.
- In case of accidental contact with the eyes, wash them immediately with water or saline solution for at least 15 minutes and seek medical advice.
- In case of accidental ingestion by a person, seek medical advice immediately and show this insert or the box.
- The remaining tablets should be stored in the blister and administered at the next dose.
- Agrovet Market S.A. is not responsible for the consequences derived from the use (of the product) other than that indicated in this leaflet.

## Interactions with other medications and other forms of interaction

- *Oclacitinib* causes minimal canine cytochrome P450 inhibition, and no significant drug interactions have been reported to date.
- It has been reported to be safe for use with other common medications, including vaccines, NSAIDs, antibiotics, parasitocides, anticonvulsants, and allergen immunotherapy.
- *Oclacitinib* at the indicated doses was shown to be well tolerated when administered in combination with carboplatin or doxorubicin in a small pilot study.
- Cyclosporine: Although the simultaneous administration of *oclacitinib* and cyclosporine appears safe when administered for up to 3 weeks, the combination of cyclosporine and *oclacitinib* is theoretically contraindicated for long-term use, especially in cases where infection is present, due to the increased theoretical risk of immunosuppression.
- Immunosuppressive agents (azathioprine, glucocorticoids, mycophenolate): The use of *oclacitinib* in combination with systemic glucocorticoids or other systemic immunosuppressive agents has not been evaluated, especially with long-term administration. Concomitant use may lead to additive immunosuppression and increase the risk of infection.
- Vaccines: a decrease in the serological response to vaccination with Canine Parainfluenza and Canine Rabies has been detected in puppies that were treated with *oclacitinib* compared to untreated controls. The clinical relevance of these effects observed for animals vaccinated while administered *oclacitinib* (according to the recommended dosage) is unclear.
- Tigilano Tiglato: Use together with caution.
- After 30 days of treatment at the indicated dose, *oclacitinib* did not interfere with the reactivity results of serum and intradermal allergic tests.

## Storage

Store in a cool, dry place, in its original packaging, protected from light between 15°C and 30°C. Keep out of the reach of children and pets. The remaining tablets should be stored in the blister and administered at the next dose.

## Commercial Presentation

**Xintōpica®** is presented in 4 concentrations of the active ingredient, containing: 1.5, 3, 6 and 12 mg of oclacitinib per soft tablet, and are presented in:

### Xintōpica® 1.5 mg

Box x 32 soft chewable tablets (8 sealed aluminized blisters x 4 tablets) x 1000 mg

### Xintōpica® 3 mg

Box x 32 soft chewable tablets (8 sealed aluminized blisters x 4 tablets) x 2000 mg

### Xintōpica® 6 mg

Box x 32 soft chewable tablets (8 sealed aluminized blisters x 4 tablets) x 1000 mg

### Xintōpica® 12 mg

Box x 32 soft chewable tablets (8 sealed aluminized blisters x 4 tablets) x 2000 mg

**Xintōpica® 1.5 mg:** Reg. SENASA Peru: F.115.031.N.00012.

**Xintōpica® 3 mg:** Reg. SENASA Peru: F.115.031.N.00011.

**Xintōpica® 6 mg:** Reg. SENASA Peru: F.115.031.N.00009.

**Xintōpica® 12 mg:** Reg. SENASA Peru: F.115.031.N.00010.

**Xintōpica®** is a registered trademark of **Agrovet Market S.A.**  
**Petmedica®** is a division of **Agrovet Market Health**

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**Agrovet**  
MARKET

<sup>1</sup> Janus kinases or Janus kinases are a family of proteins belonging to enzymes associated with cytokine receptors.