Advanced Formula

Thyro-Tabs® Canine The New Therapeutic Standard

Levothyroxine sodium tablets are inherently unstable. Light, humidity, and oxygen exposure can result in dose potency degradation and sub-optimal treatment. In 2009, the United States Pharmacopeia (USP) published new potency requirements for levothyroxine sodium tablets. The more stringent standards challenged manufacturers to improve their manufacturing and packaging procedures in order to meet these aggressive performance targets. To date, only LLOYD, Inc. has achieved the goal. Thyro-Tabs Canine, levothyroxine sodium tablets, USP is the only veterinary brand to retain the USP tablet designation by providing a minimum 95% dose potency throughout the indicated shelf life. As such, Thyro-Tabs has established a New Therapeutic Standard in the treatment of canine hypothyroidism.

The Trouble with Levothyroxine

Formulation Stability

Levothyroxine sodium [O-(4-hydroxy-3,5-diiodophenyl) -3,5-diiodo-L-tyrosine, monosodium salt, hydrate] medications are notoriously unstable. As reported in numerous scientific publications, levothyroxine sodium tablets are highly susceptible to degradation caused by environmental factors, including light, humidity, and oxygen. Moreover, the resultant drug degradation leads to potency erosion, dose variability, and sub-optimal clinical response.

Historically, levothyroxine tablets were manufactured with a broad potency tolerance, with a potential dose differential between newly manufactured tablets and those approaching expiration as great as 20%. Such dose variability clearly impedes achievement of therapeutically ideal T4 levels.

Canine Challenges

In addition to the inherent instability of levothyroxine sodium medications, canine patients are challenged with poor bioavailability (10%-22%[1]) and highly variable drug absorption. Although the reasons are not fully understood, studies have reported as much as a 4-fold difference in peak concentration values among dogs receiving the same dose.[2]

Within a dog population, the physiological characteristics of an individual dog are the most significant determinant of achievable serum T4 concentrations. Another primary factor influencing levothyroxine absorption is food. Giving levothyroxine with a meal decreases the absorption by 50%.[1] Because of the poor bioavailability and variable absorption, it is important to maintain a consistent dosing regimen for hypothyroid dogs. One key to achieving consistent serum T4 concentrations and more predictable clinical responses is reliable dose potency.

The United States Pharmacopeia (USP)

The USP is an independent, non-profit, scientific organization officially recognized by the Food and Drug Administration (FDA) as the accepted authority for defining pharmaceutical standards of purity, potency, and formulation characteristics.

A New Potency Standard

Prior to October 2009, the USP specification for levothyroxine sodium tablets required 90% - 110% dose potency throughout the indicated shelf life. In October 2009, in response to an FDA petition, the potency specification was tightened to a minimum of 95% and a maximum of 105% of the indicated dose. The source (October 2007) FDA petition[3] to improve dose reliability was based on the recommendation of the Joint Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Advisory Committee for Pharmaceutical Science held on 4 October 2006.

LLOYD™

Only manufacturers that adhere to this stringent new potency standard are permitted to use the USP designation for final dose form. Although manufacturers who fail to comply do commonly utilize a USP recognized active pharmaceutical ingredient, the final tablet form does not meet USP/FDA standards. As a result, many brands of levothyroxine sodium tablets were forced to remove the prominent “tablets, USP” from their labels.

Thyro-Tabs Canine, levothyroxine sodium tablets, USP (LLOYD, Inc., Shenandoah, Iowa) is the unique exception.

Advanced Formula
Thyro-Tabs® Canine

The only veterinary levothyroxine sodium tablet brand to adhere to the new USP/FDA tablet potency standards.

- ≥95% minimum per-tablet dose potency
- 30 month real-time tablet dose stability

The Sum of Its Parts

Achievement of the USP/FDA potency standard for levothyroxine sodium tablets is not based on the USP designated active ingredient alone, but rather the overall stability of the prescribed dose. Tablet potency is therefore a collective function of component ingredients, manufacturing technology, and the dispensed container closure system.

Achieving the New Standard

Controlling exposure and vulnerability to light, humidity, and oxygen are critical for maintaining stable, long-term levothyroxine sodium tablet potency. After more than eight years of extensive research and development work, LLOYD, Inc. has defined a highly specialized formulation and product containment system to achieve this goal. Through proprietary systems and techniques, advanced formula Thyro-Tabs is the only veterinary brand to guarantee a minimum 95% dose potency for a full 30 months from date of manufacture. In fact, Thyro-Tabs Canine is manufactured under identical conditions and standards as Thyro-Tabs® for humans.

Open Bottle Risks

New Best Practices for Sustainable Potency

Although the only way to assure absolute levothyroxine sodium tablet dose stability is to completely avoid exposure to light, humidity, and oxygen, ultimately, this is not possible. Therefore the best practice for dispensing levothyroxine sodium tablets requires minimized tablet degradation risk wherever possible. Toward that end, LLOYD, Inc. developed a dispense-ready 120-count bottle with an advanced closure system that specifically addresses long-term stability and potency control. This direct-dispense container system dramatically reduces in-clinic degradation risk by eliminating the need for repeated in-clinic open and count procedures. Additionally, the protective closure mechanism continues to provide added protection throughout the client use timeline.

The issue of levothyroxine sodium tablet instability, although long recognized, has only recently been addressed through tighter regulatory specifications. The new USP/FDA requirements challenged manufacturers to invest in finding solutions—for consistent dose potency and more reliable therapeutic outcomes.

LLOYD, Inc. has taken the lead in this effort. Through dedicated research, we have optimized the Thyro-Tabs formulation and packaging so veterinary practitioners and pet owners alike can feel confident that every tablet is providing the correct dose, and the proper endocrinologic support.

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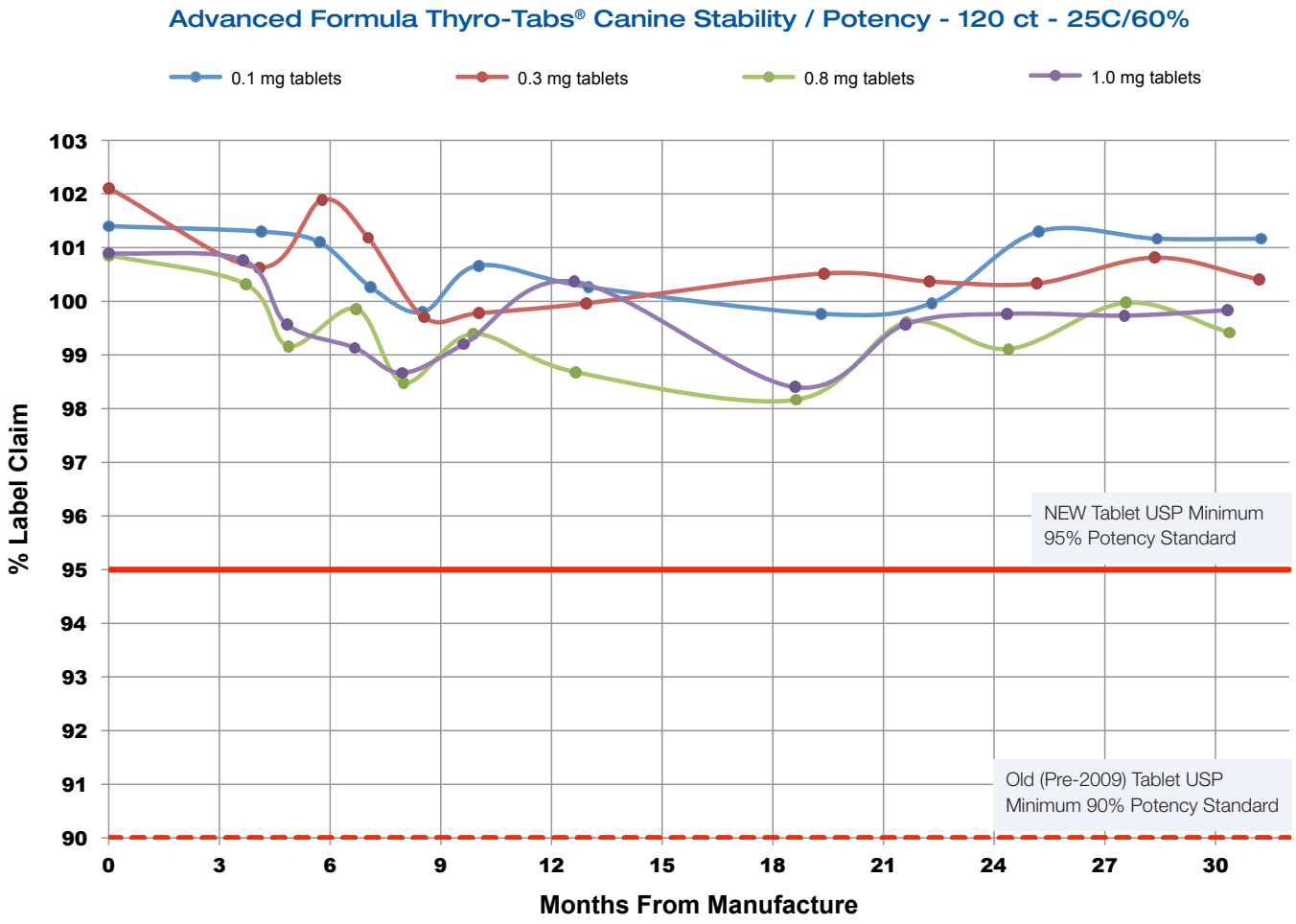
References

1. Le Traon G, Burgaud S, Horspool LJ. Pharmacokinetics of total thyroxine in dogs after administration of an oral solution of levothyroxine sodium. *J Vet Pharmacol Ther* 2008;31:95-101.
2. Nachreiner RF, Refsal K, Ravis WR, et al. Pharmacokinetics of L-thyroxine after its oral administration in dogs. *Am J Vet Res* 1993;54:2091-2098.
3. http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM161274.pdf



Thyro-Tabs® Canine (levothyroxine sodium tablets, USP) potency at 30 months

Pre- 2009 USP/FDA standards mandated a minimum 90% potency standard for levothyroxine sodium medications. Such a wide tolerance risks a significant level of sub-optimal therapy for hypothyroid dogs. Only Thyro-Tabs guarantees ≥ 95% dose potency per tablet. Plus only Thyro-Tabs provides 30 months real-time tablet dose stability.

The New Therapeutic Standard

In light of low canine bioavailability and high absorption variability among individual dogs, reliable dose potency becomes an essential tool toward successful therapy. Advanced Formula Thyro-Tabs is the only levothyroxine sodium tablet to provide a 30-month minimum 95% tablet dose potency guarantee, as recognized by the USP. As such, Thyro-Tabs sets a new therapeutic standard in the treatment of canine hypothyroidism.

Thyro-Tabs® Canine (levothyroxine sodium **tablets, USP**): Available in degradation-resistant 120-count, direct-dispense containers and economical (1,080 tablet), 9-container, bulk packs.

LLOYD, Inc.
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