SpecializedRx
3787 95th Ave. NE Suite 100
Circle Pines, MN 55014 USA

SubOral™ SL HMW *COOL MINT*

Anhydrous Sublingual Vehicle (Patent-Pending)

SubOral™ SL HMW is an anhydrous sublingual vehicle formulated to improve the solubility and sublingual penetration of oil and water-soluble actives of both large and small molecular weight. It is specifically designed to offer enhanced bioavailability potential for transcellular and paracellular transport. Uniquely formulated with its water-soluble properties, SubOral™ SL HMW incorporates a dual Natural Deep Eutectic Solvent (NADES) system and Nano PEGylated Transport System™ (NPTS)[10] that aids in forming and stabilizing micelles into nano emulsions to improve solubility of both hydrophobic and hydrophilic molecules for optimal solubilization and permeation enhancing properties.

SubOral™ SL HMW is formulated with Sodium Caprylate (C8), widely known as an intestinal permeation enhancer and biological stabilizer for oral delivery of fragile therapeutic peptide-based pharmaceuticals, preventing aggregation, denaturation, and promoting the unfolding of functional proteins and peptides.

This vehicle features an Oral Osmotic System (OROS) with a tonicity agent to adjust its osmotic pressure to match the isotonic conditions of human body fluids (300 mOsm/L). Iso-osmotic conditions prevent cell damage (lysis or crenation), decrease tissue irritation for repeated use, and optimize drug absorption and bioavailability.

Additionally, SubOral™ SL HMW is formulated with a unique cyclodextrin oligosaccharide with a hydrophilic exterior and a hydrophobic, non-polar interior cavity that can encapsulate parts of large peptides to assist in improving its overall solubility. This strategy is common in advanced formulations and is co-administered with GLP-1 agonists (such as semaglutide) for enhanced solubility in numerous drug formulations.

Highlights:

- ✓ Anhydrous, water-soluble formulation enabling extended BUDs for a wide spectrum of prescriptions
- ✓ Employs functional ingredients for large and small molecular weight compounds to be administered sublingually
- ✓ Rapidly forms an occlusive hydrogel emulsion when exposed to saliva for improved bioavailability
- ✓ Water based hydrogels vs. oil-based vehicles offer several advantages for sublingual delivery:
    - o Superior bioadhesion[8] and hydration potential for improved bioavailability via oral mucosal tissue delivery with a wide range of molecular weight actives
    - o Several oral delivery studies show water-soluble sublingual vehicles offer up to 5 times[9] more bioavailability than oil-soluble formulations
    - o Water-soluble properties allow for precise, uniform dosing without separation issues common in oil-based emulsions
    - o Ability to target a precise pH to maintain stability and solubility
    - o Taste, texture, and palatability are widely accepted
    - o Generally hypoallergenic and less likely to cause irritation than some oil sources
- ✓ Formulated with a unique dual NADES and NPTS system that potentially delivers greater solubilization and penetration, enhancing drug absorption and leading to improved bioavailability
- ✓ Promotes the unfolding of functional proteins and peptides, preventing aggregation more effectively than other systems for improved bioavailability
- ✓ Can be easily formulated with Salcaprozate Sodium (SNAC) due to its water-soluble properties
- ✓ Formulated to improve the solubility of poorly soluble drugs
- ✓ Ideally formulated for both HMW therapeutic biomolecules (peptides/proteins) as well as small molecular drugs (APIs)
- ✓ Can be homogenized without base degradation
- ✓ Ideal pH that mimics the natural oral mucosa pH
- ✓ Incorporates an Oral Osmotic System (OROS) with a widely used tonicity agent
- ✓ Stable suspension properties formed through a unique microgel network
- ✓ Improved protein stabilizing properties
- ✓ Sugar-free; utilizes only natural sweeteners
- ✓ For oil and water-soluble small and large molecules
- ✓ Occlusive bio-adhesive properties for prolonged absorption advantages
- ✓ Excellent suspension properties to improve drug loading capacity and increase the overall bioavailability of the medication
- ✓ Demonstrated great taste for prolonged sublingual absorption leading to improved patient compliance and satisfaction
- ✓ Allergen-free/gluten-free
- ✓ Water and oil miscible flavor ready
- ✓ Incorporates our proprietary Bitter-Bloc™ Technology for optimal palatability

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SKU	Size	NDC
B0257-80	500 mL	72467-0257-80
B0257-85	4 L	72467-0257-85

Natural Deep Eutectic Solvents (NADES) and Therapeutic Deep Eutectic Systems (THEDES):

Several studies[1234] have demonstrated that certain hydrated Deep Eutectic Solvents (DESs) can interact with intercellular lipids, creating wider water channels between lipid vesicles, enhancing the paracellular-like transport of hydrophilic compounds. This can be very effective through oral mucosa, a highly vascularized thin membrane. DESs and their specialized derivatives, Therapeutic Deep Eutectic Systems (THEDES), effectively increase the permeability of biological barriers[5] (such as the skin, intestinal wall) to various agents, including drugs, proteins, and nanoparticles. Their function leads to higher solubility and superior penetration through biological tissues. DESs enhance the systemic absorption[6] of subcutaneously injected therapeutic proteins (such as insulin) or larger proteins/peptides by reducing interactions with the subcutaneous matrix, a mechanism that can involve modulating the transport pathways. In essence, the unique properties of a DES can be leveraged in drug delivery systems to open or widen the paracellular route temporarily and reversibly[7], allowing for improved absorption of drugs that would otherwise struggle to cross epithelial barriers.

Category	Anhydrous Water-Soluble Sublingual Suspension Vehicle
Appearance	White to off-white opaque viscous liquid
Description	SubOral™ SL HMW is an ideally formulated water-soluble sublingual vehicle designed to improve solubility for hydrophilic/hydrophobic, small/large molecular weight molecules with enhanced bioavailability potential for transcellular and paracellular transport.
Ingredients	Glycerol, Polysorbate, Polyethylene Glycol, Betaine Anhydrous, Sodium Caprylate, Poloxamer, Hydroxypropyl Cyclodextrin, Bitter-Bloc™(Natural Flavor Enhancer), Stevia (TruClear Stevia Plus™), natural mint flavor, and other inert proprietary ingredients.
Allergy	Per the 2004 Food Allergen Labeling and Consumer Protection Act, no allergen declarations are required for this product as relating to corn, milk, egg, tree nuts, fish, crustacean shellfish, wheat, peanuts, gluten, and soybeans.
Technical Data	Shelf Life: At time of revision R01, 12 months from date of manufacture when stored in original, unopened container in a cool, dry place. Density approx. 1.23 g/mL. pH 6-7. Viscosity @ 25°C 8000-9000 cP. Water Activity (Aw) ≤ 0.6. Total Plate Count, Aerobic $\leq 10^3$ CFU/g. Temperature may slightly affect viscosity with cooler temperatures increasing viscosity and warmer temperatures reducing viscosity.
Safety Data	All ingredients classified as “Generally Recognized As Safe” (GRAS) and inactive excipient ingredients by the US FDA.
Handling & Storage	Comment: Shake well prior to use. Storage Conditions: Product can be stored at room temperature. Product should be kept in a tightly sealed container and protected from humidity.
Comments	Formulation and variants are currently patent pending. MSDS is available upon request. Contact a SpecializedRx Representative for questions and further use guidance. Email: sales@specializedrx.com

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[1]National Library of Medicine, Penetration Process of a Hydrated Deep Eutectic Solvent Through the Stratum Corneum and its Application as a Protein Penetration Enhancer. https://pmc.ncbi.nlm.nih.gov/articles/PMC7493194/

[2]MDPI Journal, Advancements in Therapeutic Deep Eutectic Solvents as Multifunctional Transdermal Delivery Systems. https://www.mdpi.com/1999-4923/18/3/360

[3]International Journal of Pharmaceutical Sciences, Deep Eutectic Solvents as Solubility Enhancers: A Systematic Review. Volume 03 | Issue 10 | Article Id IJPS/250310415

[4]International Journal of Pharmaceutical Sciences, Development and In Vitro Evaluation of a Deep Eutectic System to Improve Cefuroxime Axetil Solubility by Enhancing the Dissolution. Volume 03 | Issue 12 | Article Id IJPS/250312253

[5]MDPI Journal, Deep Eutectic Systems as Novel Vehicles for Assisting Drug Transdermal Delivery. https://www.mdpi.com/1999-4923/14/11/2265

[6]Wiley Advanced Science, Deep Eutectic Solvents for Subcutaneous Delivery of Protein Therapeutics. https://advanced.onlinelibrary.wiley.com/doi/10.1002/advs.202205389

[7]ScienceDirect, Deep eutectic solvents@enteric technology for orally delivering anticoagulant macromolecule drug. https://www.sciencedirect.com/science/article/pii/S2211383525007178?via%3Dihub

[8]ScienceDirect, Mucoadhesion, hydration and rheological properties of non-aqueous delivery systems (NADS) for the oral cavity. https://www.sciencedirect.com/science/article/abs/pii/S0300571208000274?via%3Dihub

[9]True North Labs, April 24, 2024, Water-soluble or Oil-Soluble Cannabinoids: Exploring mechanisms of absorption, bioavailability, and fat solubility of cannabis products. https://www.truenorthlabs.ch/news/water-soluble-vs-oil-soluble-cannabis-products-key-differences-and-why-they-matter#:~:text=Water%2Dsoluble%20powder%20has%20been,with%20a%20high%2Dfat%20meal

[10]National Library of Medicine / International Journal of Nanomedicine. 2007 Dec;2(4):735–741. PEGylation of nanoparticles improves their cytoplasmic transport. https://pmc.ncbi.nlm.nih.gov/articles/PMC2676827/