Helsinn publishes new data evaluating chlormethine gel's mode of action in *Dermatology and Therapy*

Lugano, Switzerland, October 18, 2022 - Helsinn Group ("Helsinn"), a fully integrated global biopharma company with a diversified pipeline of innovative oncology assets, announces that research from an *in vitro* study of chlormethine gel has been published in the journal *Dermatology and Therapy*.

This article, "Chlormethine Gel for the treatment of Mycosis Fungoides Cutaneous T-Cell Lymphoma: In Vitro Release and Permeation Testing", evaluated part of the mode of action of chlormethine (CL) gel once applied to the skin. In a preliminary, proof-of-concept, *in vitro* study, the release profile of 0.016% chlormethine gel was evaluated compared to an ointment-based formulation of CL. The absorption profile of the CL gel was also evaluated in *ex vivo* healthy human skin using *in vitro* permeation testing (IVPT).

Results from the study indicate that the rate of chlormethine release from the CL gel formulation was statistically higher in comparison to the ointment formulation. In addition, data indicate that only a minimal amount of the CL can pass through the epidermis reaching the dermis, suggesting that most of the applied CL reacted within the epidermal layer. This finding is consistent with the lack of evidence of systemic absorption seen with CL gel[1,2] and further supports the notion that drug-drug interactions are very unlikely.

Details of the publication:

- **Title:** "Chlormethine Gel for the treatment of Mycosis Fungoides Cutaneous T-Cell Lymphoma: In Vitro Release and Permeation Testing."
- **Authors:** Claudio Giuliano, Stefano Frizzarin, Alessandro Alonzi, Virginia Stimamiglio and Pablo L. Ortiz-Romero
- **Link:** https://pubmed.ncbi.nlm.nih.gov/36229764/.

Chlormethine gel 0.016%, also known as mechlorethamine gel, is approved in multiple countries, including the EU and US, and is marketed under the trade names LEDAGA® and VALCHLOR®.

The authorized use for each country varies based on the design of the registrational trial and the individual health authority requirements. For more details, please refer to the approved product information for each respective jurisdiction.

Dr. Silvia Sebastiani, Group Head of Medical Affairs, commented: *"Chlormethine is a well-established and effective topical therapy for treating lesions in patients with MF-CTCL and is available in a variety of formulations. Understanding CL gel's mode of action and how it permeates through the skin is extremely important for its use in clinical practice."*

About LEDAGA®

LEDAGA® gel is an alkylating drug indicated for the topical treatment of MF-CTCL in adult patients. LEDAGA® is a gel which is applied topically once a day. The drug has been approved by the European Commission (for the treatment of MF-CTCL in adult patients). Since June 2019, LEDAGA® is commercialized in almost 30 countries including Europe, Canada, Latin America.

For additional information please see the EU Summary of Product Characteristics.

About VALCHLOR® in the US

VALCHLOR® (mechlorethamine) gel 0.016% is indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL) in patients who have received prior skin-directed therapy.

IMPORTANT SAFETY INFORMATION FOR VALCHLOR®

Contraindications:

VALCHLOR® is contraindicated in patients with known severe hypersensitivity to mechlorethamine. Hypersensitivity reactions, including anaphylaxis, have occurred with topical formulations of mechlorethamine.

HELSINN
Building quality cancer care together

WARNINGS AND PRECAUTIONS

Mucosal or eye injury: Exposure of mucous membranes to mechlorethamine such as the oral mucosa or nasal mucosa causes pain, redness, and ulceration, which may be severe. Exposure of the eyes causes pain, burns, inflammation, photophobia, and blurred vision. Blindness and severe irreversible anterior eye injury may occur. Should eye exposure or mucosal contact occur, immediately irrigate for at least 15 minutes with copious amounts of water, followed by immediate medical consultation.

Secondary exposure: Avoid direct skin contact with VALCHLOR® in individuals other than the patients due to risk of dermatitis, mucosal injury, and secondary cancers.

Dermatitis: Dermatitis may be moderately severe or severe. Monitor patients for redness, swelling, inflammation, itchiness, blisters, ulceration, and secondary skin infections. Stop treatment with VALCHLOR® or reduce dose frequency.

Non-melanoma skin cancer: Monitor patients during and after treatment with VALCHLOR®.

Embryo-fetal toxicity: May cause fetal harm. Women should avoid becoming pregnant while using VALCHLOR® due to the potential hazard to the fetus. For nursing mothers, do not breastfeed during treatment with VALCHLOR®.

Flammable gel: VALCHLOR® is an alcohol-based gel. Avoid fire, flame, and smoking until the gel has dried.

ADVERSE REACTIONS

The most common adverse reactions (≥5%) were dermatitis (56%), pruritus (20%), bacterial skin infection (11%), skin ulceration or blistering (6%), and hyperpigmentation (5%). These reactions may be moderately severe or severe. Elderly patients aged 65 and older may be more susceptible. Depending on severity, treatment reduction, suspension, or discontinuation may be required.

USE IN SPECIFIC POPULATIONS

Contraception: Females who are able to become pregnant, and males with female partners who are able to become pregnant, should use a barrier method of contraception to avoid direct exposure of reproductive organs to VALCHLOR®.

Infertility: The reproductive effects of VALCHLOR® have not been studied: however systemically administered mechlorethamine may impair fertility. The reversibility of the effect on fertility is unknown.

DOSING AND APPLICATION

VALCHLOR® is for topical dermatologic use only. Apply a thin film of gel once daily to affected areas of the skin. VALCHLOR® is a cytotoxic drug and special handling and disposal procedures should be followed during use. Caregivers must wear disposable nitrile gloves when applying VALCHLOR®. Patients and caregivers must thoroughly wash hands after handling or applying VALCHLOR®.

To report SUSPECTED ADVERSE REACTIONS, contact Helsinn Therapeutics (U.S.), Inc. at 1-855-482-5245 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

Please see the US full Prescribing Information and Medication Guide for VALCHLOR®

About Helsinn

Helsinn is a fully integrated global biopharma company headquartered in Lugano, Switzerland. It is focused on improving the lives of cancer patients all over the world with a leading position in cancer supportive care and an innovative pipeline of cancer therapeutics.

Helsinn is a third-generation family-owned company, that since 1976 has been focused on improving the lives of patients, guided by core values of respect, integrity and quality. It operates a unique licensing business model with integrated drug development and manufacturing capabilities. Helsinn has a commercial presence in 190 countries either directly, with operating subsidiaries in the U.S. and China, or via its network of long-standing trusted partners. Helsinn

also has a fully integrated supply chain and product development through its subsidiary in Ireland, Helsinn Birex Pharmaceuticals Ltd.

Helsinn plays an active and central role in promoting social transformation in favor of people and the environment. Corporate social responsibility is at the heart of everything we do, which is reinforced in the company's strategic plan by a commitment to sustainable growth.
To learn more about Helsinn please visit www.helsinn.com

References:

1. Querfeld C, Geskin LJ, Kim EJ, et al. Lack of systemic absorption of topical mechlorethamine gel in patients with mycosis fungoides cutaneous T-cell lymphoma. Journal of Investigative Dermatology. 2021;141(6):1601-4 e2.
2. Lessin SR, Duvic M, Guitart J, et al. Topical chemotherapy in cutaneous T-cell lymphoma: positive results of a randomized, controlled, multicenter trial testing the efficacy and safety of a novel mechlorethamine, 0.02%, gel in mycosis fungoides. JAMA Dermatology. 2013;149(1):25-32.

For more information:

Helsinn Media Contact:
Paola Bonvicini, Group Head of Communication
Lugano, Switzerland
Tel: +41 (0) 91 985 21 21
Email: Info-hhc@helsinn.com

For more information, please visit www.helsinn.com and follow us on Twitter and LinkedIn