PRESCRIPTION MONOGRAPH

Compounded Active Ingredients: Niacinamide/ GHK-Cu/Estriol in Hyaluronic Acid
Form: Topical Cream

Drug Class:

- GHK-Cu: Peptide complex (endogenous tripeptide); Copper-binding growth factor analog
- Niacinamide: Vitamin B3 derivative
- Estriol (E3): Estrogen; agonist at estrogen receptors
- Hyaluronic Acid (HA): Naturally occurring glycosaminoglycan; humectant and hydrating skin-support ingredient

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Mechanism of Action[1,2,3,4]: When compounded together, Niacinamide/ GHK-Cu/Estriol in Hyaluronic Acid is designed to provide hydration, barrier support, and structural skin support, with particular relevance to skin experiencing age- or hormone-associated changes. It is intended to:

- Encourage the skin's natural production and remodeling of collagen and elastin, proteins that help maintain firmness and elasticity. These supportive effects may help soften the appearance of fine lines and improve overall skin texture over time.
- Support fibroblasts and keratinocytes, important cells involved in maintaining and renewing the skin. By supporting these natural repair processes, it may help improve the appearance and quality of aging or environmentally stressed skin.
- Support the skin's natural barrier and help it retain moisture more effectively. A healthier barrier can leave skin feeling smoother, more hydrated, and less susceptible to dryness and irritation.
- Reduce the transfer of pigment into surface skin cells, which may gradually improve the appearance of dark spots and uneven tone.
- Attract and retain water at the skin's surface, helping improve hydration and softness. Better-hydrated skin can also temporarily make fine lines appear less noticeable and give the skin a smoother, fuller appearance.
- Support the structural proteins that give skin collagen, moisture, firmness, and elasticity in estrogen-deficient skin.

Indications Commonly Prescribed For:

- Fine lines and wrinkles
- Dry or dehydrated skin
- Thinner or more fragile-looking skin
- Loss of firmness and elasticity
- Changes in skin quality associated with menopause
- Rough or uneven texture
- Dull or tired-looking skin
- Uneven skin tone and visible discoloration
- Decreased skin plumpness
- Red or blotchy-looking skin
- Supporting healthier-looking, more resilient skin
- Overall improvement in the appearance of mature or aging skin

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Before Use: Let your healthcare provider know if you

- Have any medication allergies before you take this compounded preparation.
- Have any liver or kidney problems.
- Are taking any supplements of medications
- Are using any other topical treatments

Contraindications:

- Known hypersensitivity to GHK-Cu, niacinamide, estriol, copper-containing ingredients, or formulation components
- Copper metabolism disorders (e.g., Wilson's disease hemochromatosis)
- Application to actively infected or severely damaged skin without clinical evaluation
- Use immediately following aggressive dermatologic procedures unless directed by the treating clinician
- Known or suspected estrogen-dependent malignancy
- History or significant risk of estrogen-sensitive disease
- Unexplained abnormal genital bleeding

Cautions: Let your Healthcare provider know if you experience any adverse side effects. Apply sunscreen daily during the duration of treatment. Do not apply directly to eyes and mucous membranes.

Warnings and Precautions

- Monitor for signs of copper overload with prolonged systemic use.
- Monitor for new or unexplained vaginal bleeding during treatment.
- Copper peptides can oxidize in low-pH formulas; avoid mixing with strong acids or pure vitamin C serums.
- Use daily broad-spectrum sunscreen due to increases in UV sensitivity to prevent photoaging, discoloration, or additional visible skin damage.
- Compromised skin may absorb topical ingredients differently and may be more prone to irritation. Timing after lasers, chemical peels, microneedling, or other procedures should be determined by the treating clinician.
- Hormone-Sensitive Conditions: patients with a personal history of estrogen-sensitive breast, uterine, ovarian, or other hormone-responsive disease require individualized clinical assessment.
- Concurrent Hormone Therapy: Patients using systemic or vaginal estrogen, compounded hormone replacement therapy, or other estrogen-containing medications should disclose these therapies.

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Adverse Reactions: If you experience any side effects or adverse reactions, including those not listed, please contact your healthcare provider. Seek emergency care if symptoms are severe.

Common:

- Mild skin irritation
- Mild redness
- UV sensitivity
- Temporary burning or stinging
- Itching
- Dryness
- Mild irritation
- Application-site sensitivity
- Breast tenderness
- Breast fullness
- Headache
- Menstrual Spotting
- Changes in vaginal symptoms
- Hormone-related skin changes

Serious, but Rare:

- Contact dermatitis
- Copper toxicity
- Allergic Reactions (hives, swelling)
- Persistent inflammatory reactions
- Unexplained vaginal bleeding
- Clinically meaningful systemic estrogen exposure
- Potential effects on estrogen-sensitive tissues

Interactions:

- Retinoids: Tretinoin, retinol, and related products may increase dryness or irritation when introduced simultaneously. Stagger use.
- AHAs/BHAs: Glycolic, lactic, salicylic, and other exfoliating acids may increase sensitivity and barrier irritation. Stagger use.
- Chemical peels or resurfacing treatments: Recently treated skin may be more reactive, so application timing should be individualized.
- Other copper-containing products: Additional exposure may be unnecessary and could complicate assessment of irritation or treatment response.
- Systemic or vaginal estrogen: May increase overall estrogen exposure; concurrent therapy should be reviewed by the prescriber.
- Other compounded hormone creams: May contribute additional estrogen or other hormone exposure.

Use in Specific Populations:

- Pregnancy: Avoid due to estriol
- Pediatrics: Avoid use
- Geriatrics: Frequently used for anti-aging benefit
- Post-procedure: Excellent for healing and redness reduction
- Men: Safe and non-feminizing at topical estriol doses <0.05%.

Storage:

- Store in original container at room temperature (up to 30°C or 86°F)
- Store in a cool dry place away from heat, sunlight, and moisture

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How to Use: This compounded preparation is in the form of a topical cream. The cream is a special container that will administer 0.6ml dose. Clean desired area prior to use. To administer remove the protective covering on the top of the dispenser. Place the jar on a flat surface. Using clean, dry hands, gently press down on the top of the pump. This will dispense a measured amount of cream through the center opening. Confirm the cream has exited the holes at the top of the dispenser. Apply the cream onto the desired area. Continue to rub the area until the cream is evenly dispersed over the desired area. Replace the protective cover and store the device until next dose. If you miss a dose apply as soon as you remember, but not at the time for the next dose. The desired results may take up to several weeks.

Monitoring Parameters:

- Skin response over 8–12 weeks
- Copper and ceruloplasmin levels in extended systemic protocols
- Estrogen specific monitoring considerations:
    - Breast tenderness or other possible estrogenic symptoms
    - Unexpected vaginal spotting or bleeding
    - Changes in concurrent hormone therapy

Citations:

1. Maquart FX, Pickart L, Laurent M, Gillery P, Monboisse JC, Borel JP. Stimulation of collagen synthesis in fibroblast cultures by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu2+. FEBS Lett. 1988;238(2):343-346. doi:10.1016/0014-5793(88)80509-x
2. Bissett DL, Miyamoto K, Sun P, Li J, Berge CA. Topical niacinamide reduces yellowing, wrinkling, red blotchiness, and hyperpigmented spots in aging facial skin. *Int J Cosmet Sci*. 2004;26(5):231-238. doi:10.1111/j.1467-2494.2004.00228.x
3. Bravo B, Correia P, Gonçalves Junior JE, Sant'Anna B, Kerob D. Benefits of topical hyaluronic acid for skin quality and signs of skin aging: From literature review to clinical evidence. Dermatol Ther. 2022;35(12):e15903. doi:10.1111/dth.15903
4. Schmidt JB, Binder M, Demschik G, Bieglmayer C, Reiner A. Treatment of skin aging with topical estrogens. Int J Dermatol. 1996;35(9):669-674. doi:10.1111/j.1365-4362.1996.tb03701.x

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