

Carbomer 974

Brand Name: BufferGel

Drug Class: Microbicides

Drug Description

Carbomer 974 is a water-based, detergent-free, buffering agent that contributes to the acidic buffering action of BufferGel, an investigational microbicide and spermicide gel. [1] Carbomer 974, a cross-linked polyacrylic acid, is highly negatively charged, containing thousands of ionizable carboxyl groups per molecule, and has a molecular weight of several billion. These carboxyl groups can release hydrogen ions, the active agents that provide the acid-buffering action of BufferGel. [2] In addition, these carboxyl groups, with the polymer's high molecular weight, prevent transmucosal absorption of the buffer agent. Moreover, as a polymeric buffer, the product will not become hypertonic when high concentrations of buffer material are used and will not cause the cytotoxicity that is seen with use of small, absorbable buffers such as acetic or lactic acid. [3] [4]

HIV/AIDS-Related Uses

Carbomer 974, as the source of acid-buffering action in BufferGel, maintains vaginal acidity, impairing or preventing the transmission of HIV. BufferGel is being investigated in Phase I and II trials for the prevention of sexual transmission of HIV. [5] [6]

Non-HIV/AIDS-Related Uses

Carbomer 974, formulated as BufferGel, is being studied for use as a contraceptive. As a microbicial spermicide, carbomer 974 provides buffering activity to maintain vaginal acidity in the presence of alkaline semen. BufferGel has been proven safe and effective as a contraceptive in Phase III trials. [7] Two contraceptive trials of more than 1,200 women showed BufferGel combined with a diaphragm to be non-inferior to Gynol II (a nonoxynol-9 based spermicide) used with a diaphragm. [8]

In addition, carbomer 974 blocks the alkalizing action of semen that enables acid-sensitive pathogens that cause sexually transmitted diseases (STDs) to transmit infection. [9] Carbomer 974 is

effective in vitro against herpes simplex viruses, Chlamydia trachomatis, Neisseria gonorrhoea, and other STD pathogens. [10]

In a pilot study of 10 women, BufferGel was moderately effective as a treatment for bacterial vaginosis. [11] An international, Phase I study of BufferGel as a contraceptive reported an 80% decrease in prevalence of bacterial vaginosis in women using the drug once daily for 1 week. [12]

Carbomer 974 polymer also is used as a gelling or tableting agent in many pharmaceuticals. [13]

Pharmacology

Carbomer 974 is a negatively charged, high-molecular-weight polymer that provides active, ionizable carboxyl groups for acid-buffering activity. Carbomer 974 is not absorbed and can neutralize twice its volume of base buffers, such as semen. [14] [15] Carbomer 974 is formulated to buffer the concentration of free hydrogen ions at 0.1 mM, the level normally found in the vaginal lumen (pH 3.8 to 4.0). Hydrogen ions are buffered by the carboxyl groups that occur in large quantities on the carbomer 974 polymer. Carbomer 974 acidifies semen to a pH less than or equal to 5. [16] In vitro, sperm and many STD pathogens are inactivated at a pH less than 5. HIV specifically is inactivated in the acidic environment below pH 4 to 5.8. [17]

BufferGel is being compared with another investigational microbicide agent, PRO 2000 gel, in a Phase II/IIb, four-arm, randomized, single-blind, placebo-controlled trial. Unlike BufferGel, PRO 2000 inhibits viral entry into cells. Participants will be given single-dose, prefilled applicators of gel containing BufferGel, PRO 2000, placebo gel, or no treatment to use intravaginally up to 60 minutes before each act of intercourse. [18] [19]

Adverse Events/Toxicity

In a Phase I clinical trial, BufferGel showed minimal toxicity and was well tolerated, although two-thirds of participants reported at least one mild or moderate adverse event. The most common

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Adverse Events/Toxicity (cont.)

adverse events were vaginal itching and irritation. Some symptoms disappeared within 1 hour after application of the product. Vaginal candidiasis and hyperkeratotic lesions required discontinuation of the product in a small percentage of trial participants. Three colposcopic abnormalities were observed, but no cases of epithelial disruption occurred.[20]

An international Phase I clinical trial had similar results. Adverse events were categorized as mild to moderate and included presence of *Candida* on wet mount, vaginal and vulvar itching or burning after gel insertion or when passing urine, labial rash, lower abdominal pain, and vaginal discharge. Irritation was reported in approximately 25% of women in the study and was generally mild and of short duration. Epithelial abnormalities detected by pelvic exam or colposcopy were uncommon.[21] In both trials, adverse effects of BufferGel were generally self limiting and readily resolved. Both trials reported a high degree of compliance and acceptability.[22] [23]

In a Phase I clinical trial of penile application of BufferGel, no serious adverse events or urethral inflammation were reported, and adverse event rates were not significantly different from placebo.[24]

In two Phase I trials of BufferGel conducted in 125 women, a significant decrease in bacterial vaginosis was noted, along with some self-limiting, local genitourinary signs and symptoms, including erythema, pruritis, and dysuria.[25]

Clinical Trials

For information on clinical trials that involve Carbomer 974, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Carbomer 974 AND HIV Infections.

Dosing Information

Mode of Delivery: Intravaginal.[26]

Dosage Form: Topical gel.[27]

BufferGel contains 5% carbomer 974.[28] In Phase II studies, BufferGel is packaged as a single-use, prefilled applicator to be administered up to 60 minutes prior to sexual intercourse.[29]

Storage: Store at room temperature.[30]

Chemistry

CAS Name: Carbomer 974P[31]

CAS Number: 151687-96-6[32]

Physical Description: Colorless, tasteless, odorless, and aqueous gel, formulated at pH 3.9 to 4.0, with sufficient buffer capacity to acidify (to pH less than 5) approximately twice its own volume of human semen.[33] [34]

Stability: Carbomer 974 as formulated in BufferGel contains no oils and so is compatible with condoms and diaphragms. It is osmotically balanced with the following physiological salt constituents: dibasic potassium phosphate, magnesium sulfate, dibasic sodium phosphate, sorbic acid, monobasic sodium phosphate, and disodium EDTA.[35] [36]

Other Names

Carbopol 974P[37]

Carbopol polymer[38]

Carbomer 974P[39]

Further Reading

ClinicalTrials.gov -BufferGel and PRO 2000/5: Vaginal Gels to Prevent HIV Infection in Women. Available at:

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Further Reading (cont.)

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Manufacturer Information

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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