



Pharmaceutical grade Benzalkonium Chloride

A cGMP manufactured antimicrobial
surfactant for use in multiple applications

enabling better

Novo Nordisk
Pharmatech A/S



By delivering excellence at every step, we help you do the same



Product attributes

- Proven record of efficacy against a broad spectrum of bacteria, fungi, and viruses
- Effective through a wide pH range
- Soluble in both aqueous and oily phases
- Surface active / adhesive cationic agent
- Very stable, proven under ICH Q1 conditions
- Five-year shelf life

Highest quality standards

Our quality system meets DS/EN ISO 9001 and the ICH Guide Q7 for Active Pharmaceutical Ingredients (ICH Q7).

We offer complete QA, QC and RA documentation and compliance with international pharmacopoeias: PhEur, USP/NF, JP and ChP

The best and safest ingredients...

If uniform high quality is the key to your products, you should begin with ours. As the world's leading supplier of cGMP Benzalkonium Chloride, a quaternary ammonium compound (Quat), we provide only the best and safest antimicrobial for the pharmaceutical, medical device and personal care industries.

Our Benzalkonium Chloride is produced according to the highest compliance standards and backed by complete regulatory documentation. This combination of high-purity product and regulatory services makes us an approved supplier to many of the world's leading pharmaceutical companies.

We are highly specialized in pharmaceutical grade Benzalkonium Chloride (BKC/BAK). The uniform quality of our finished product – and of yours – is ensured by our efficient quality control systems, fully validated processes, and rigorous laboratory quality control. In-process samples, as well as finished products, are carefully analyzed in our own modern, well-equipped laboratory.

... provide peace of mind

Novo Nordisk Pharmatech manufactures BKC/BAK in accordance with the cGMP Guide ICH Q7 for Active Pharmaceutical Ingredients (APIs), the highest quality standard in the industry.

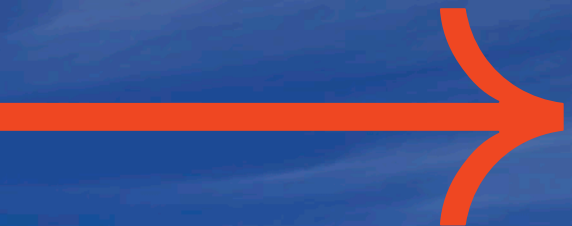
We are inspected and certified by the Danish Medicine Agency (DMA), which has mutual recognition agreement with the US FDA. A consistent, high level of product purity and our commitment as a true pharma manufacturer, help manufacturers reduce risks and achieve peace of mind.

BKC/BAK acts either as a broad-spectrum preservative or as a surface-active ingredient in a diverse range of formulations, including:

- Ophthalmic, Nasal, Oral & Respiratory, and Topical (including Wound Care).
- Whether as an excipient or an API, you can rely on our documentation, traceability, and monitoring.

Benzalkonium Chloride Products	Packaging Size	Item Number
FeF® Benzalkonium Chloride Ph.Eur., USP/NF	1 kg	7800014
	5kg	7800015
FeF® Benzalkonium Chloride Ph.Eur., USP/NF, JP	1 kg	7800012
	5 kg	7800013
FeF® Benzalkonium Chloride Solution 50% Ph.Eur., USP/NF	1 kg	7800004
	5 kg	7800005
	25 kg	7800006
	1000 kg	7800027
FeF® Benzalkonium Chloride Solution 50% Ph.Eur., USP/NF, JP	1 kg	7800009
	5 kg	7800010
	25 kg	7800011
FeF® Benzalkonium Chloride Solution 50% (45/55) Ph.Eur., USP/NF	1 kg	7800020
	25 kg	7800019
FeF® Benzalkonium Chloride Solution 50% (53/30/15/2) Ph.Eur., USP/NF	1 kg	7800008
FeF® Benzalkonium Chloride Solution 17% USP/NF	25 kg	7800003

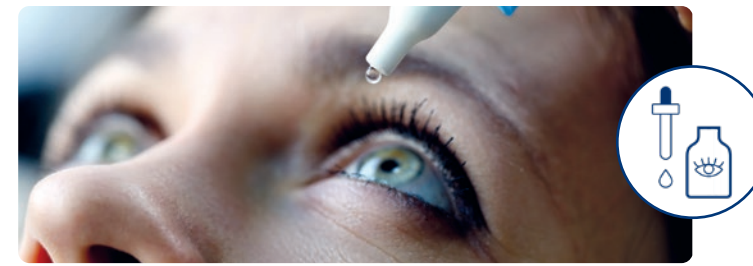
CAS No. 8001-54-5 REACH CAS No. 68424-85-1



Novo Nordisk Pharmatech helps pharmaceutical manufacturers minimize potential risks, providing peace of mind.

By supplying high quality, consistent and reliable cGMP manufactured Benzalkonium Chloride, we enable optimal processes, better medicines and better lives.

Applications overview by delivery route



Ophthalmic **6**



Nasal **8**



Topical **10**



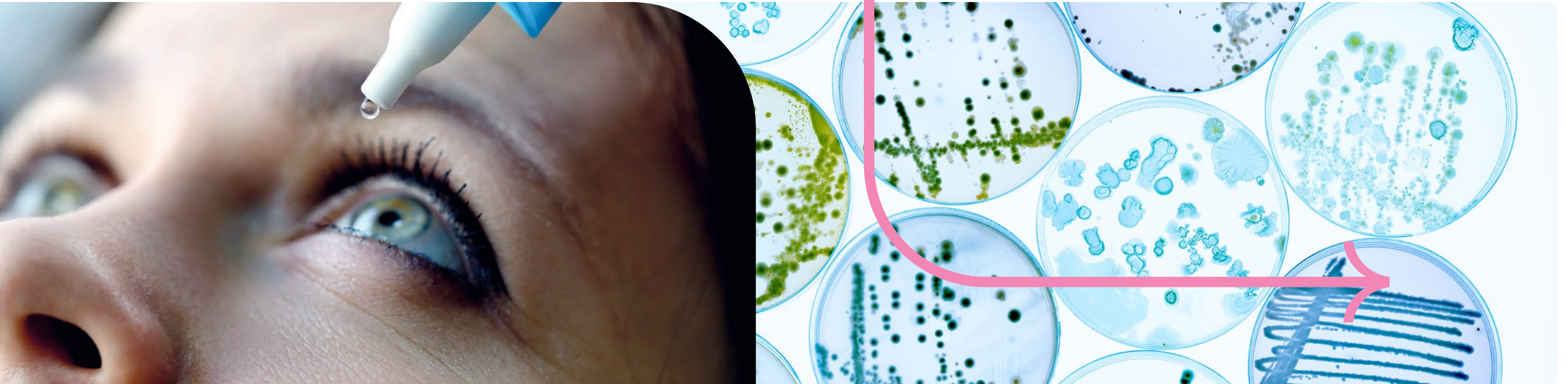
Wound Care **12**



Oral & Respiratory **14**



Ophthalmic



In human and veterinary formulations, it is essential to only utilize pure and safe ingredients to maintain patient safety.

Multidose products for ocular use are prone to contamination, both from environmental and corporeal flora. Microbial contamination presents a threat to the safety, the purity, and the efficacy of ophthalmic products, hence the importance of utilizing an effective preservative.

Formulations

Most formulators will opt for a robust and reliable, broad-spectrum preservative. One of the most common and effective preservatives is Benzalkonium Chloride (BKC/BAK).

It is widely used as an excipient in ophthalmic solutions, gels, and ointments, where very low concentrations are sufficient to obtain the desired preservative effect. Its concentration typically varies from 0.001% to 0.01%.

Properties

The alkyl chain length distribution in BKC/BAK often plays a major role for ophthalmic formulators. Our production and process know-how allows us to offer BKC/BAK with a completely well-defined alkyl chain length distribution, whether it is with our standard chain length with C12 and C14, or in combination with C16 and C18.

BKC/BAK is effective against all relevant microorganisms part of standard AET (Antimicrobial Efficacy Testing), including gram + and gram- bacteria, MRSA and *P. aeruginosa*, either alone or as part of a preservative system.

Because of its strong surfactant properties, BKC/BAK can help active substances to better adhere to the cornea or help transport an active ingredient through it. It also has emulsifying properties in oil/water formulations.

BKC/BAK is non-volatile and extremely stable at various temperatures. It is effective at very low concentrations and through a very wide pH range (4-11).

Safety

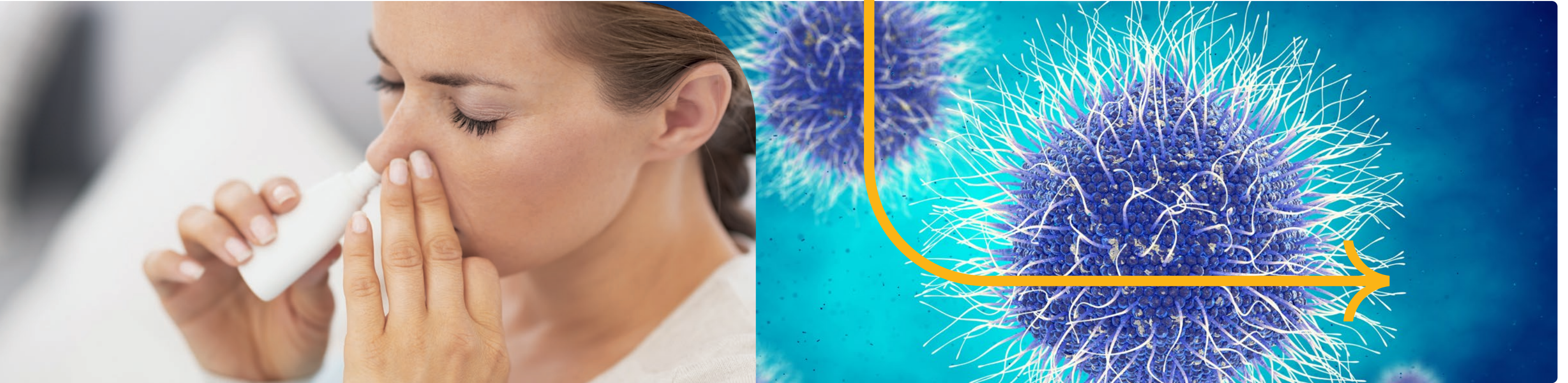
BAK/BKC is considered by authorities as being safe for use as a preservative for ocular use. Several preservatives including BKC/BAK are known to cause local irritation, specially under prolonged or chronic use. A guiding principle is to minimize preservative levels in the formulation, proportional with adequate preservative efficacy at the end of shelf-life.

Utilizing BKC/BAK of true cGMP quality and from a reliable source, can help minimize preservative-associated risks.

Microbial contamination presents a threat to the safety, the purity, and the efficacy of ophthalmic products, hence the importance of utilizing an effective preservative.



Nasal



Like ophthalmic products, multidose nasal products are prone to contamination from environmental and corporeal flora. Microbial contamination presents a threat to the safety, the purity, and the efficacy of nasal products, hence the importance of utilizing an effective preservative

This goes for both human and veterinary formulations coming into contact with mucosal tissue, where only the purest and safest ingredients must be used.

Formulations

One of the most common broad-spectrum preservatives is Benzalkonium Chloride (BKC/BAK). BKC/BAK is widely used as an excipient in nasal sprays, nebulizers, drops, and ointments where its concentration typically varies from 0.005% up to 0.2%.

Very low concentrations of BKC/BAK are required to achieve the desired preservative effect. The table (right) reports effectivity in nasal sprays with as little as 0.002% (0.02 mg/ml). In this comparison, BKC/BAK is effective at the lowest concentrations.

Properties

Many preservatives are volatile to greater or lesser extents and susceptible to losses by sublimation or evaporation. BKC/BAK is non-volatile, stable, has a broad-spectrum activity and is active throughout a wide pH range (4-11).

BKC/BAK is also highly effective against enveloped viruses such as SARS-CoV, adenoviruses, rhinoviruses, influenza, etc. While standard preservative AET (Antimicrobial Efficacy Tests) do not require to include viruses, BKC/BAK can be used as an anti-viral active through nasal delivery to prevent infections.

Safety

BAK/BKC is considered by authorities as being safe for use as a preservative for nasal use. Several preservatives including BKC/BAK are known to cause local irritation, specially under prolonged or chronic use. A guiding principle is to minimize preservative levels in the formulation, proportional with adequate preservative efficacy at the end of shelf-life.

Utilizing BKC/BAK of true cGMP quality and from a reliable source, can help minimize preservative-associated risks.

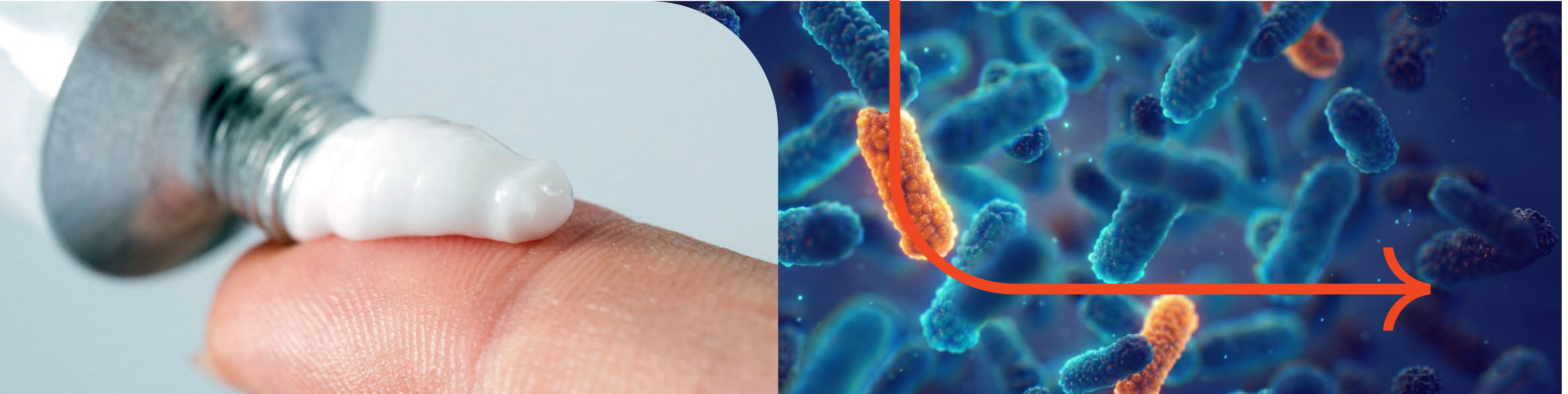
Name	Concentration for Efficacy mg/ml
Benzalkonium Chloride	0.02-0.33 (US 0.2-0.7)
Benzethonium Chloride	0.2
Benzyl alcohol	2.4-9.0
Sodium benzoate	1-2
Potassium sorbate	1-2
Chlorobutanol	0.5
Sodium edetate (EDTA)	0.1-2.0
Chlorhexidine (cream)	Not known
Methylparaben	0.1-0.25
Propylparaben	0.17
Phenylethyl alcohol	0.025
Thimerosal	0.003-0.01 (discontinued)
Phenylmercuric acetate	0.02

Source: D. Ward, Intertek UK, 2021

Like ophthalmic products, multidose nasal products are prone to contamination from environmental and corporeal flora.



Topical



Topical antiseptics are extensively used both in hospitals, health care settings and households. A robust, safe and effective broad-spectrum antimicrobial can be used as a preventive antiseptic, to treat or prevent wound sepsis or treat skin conditions.

Benzalkonium Chloride (BKC/BAK) is a well-known active and has a long history of use in topical products such as antiseptic liquids, foams, creams, and gels.

No matter the formulation, a product coming into contact with healthy or damaged epithelial tissue must only contain pure and safe ingredients.

Properties

BKC/BAK acts on a wide range of microorganisms, from gram+ to gram- bacteria, mold, yeast, and enveloped viruses such as SARS-CoV, HIV, herpes, and influenza. It also has a spermicidal effect.

BKC/BAK is odorless and colorless, and its effectiveness ranges from pH 4 to 11. As a strong surfactant, it offers residual activity on the skin and the ability to mix well in both aqueous and oily phases, making it an ideal antimicrobial ingredient. It is non-volatile, non-flammable and extremely resistant to various temperature conditions.

BKC/BAK is active at very low concentrations, making it a cost-effective choice.

Formulations

BKC/BAK is used in both human and veterinary topical products. Here are examples of topical formulations together with typical concentrations:

- Skin cleansing solutions or wipes - 0.01 to 0.1%
- Hand sanitizers - 0.1% to 1.5%
- Antiseptic creams to treat nappy rash, eczema, psoriasis, acne, and other dermatoses - 0.1 to 1%
- Antiviral gels and creams to treat herpes and cold sore infections - 0.01 to 0.1%
- Scalp/Hair products to treat seborrheic dermatitis - 0.1 to 1%
- Wound care products including wound wash or irrigation - 0.01 to 0.1%
- Spermicide in the form of foams, creams, and ampoules - 0.1 to 1%

Safety

In recent years, several actives have been removed from the market due to safety and efficacy concerns. BKC/BAK is one of the few compounds still considered safe and effective by e.g., the US FDA for use in topical antiseptics. Moreover, it is recommended by several national agencies to prevent the spread of COVID.

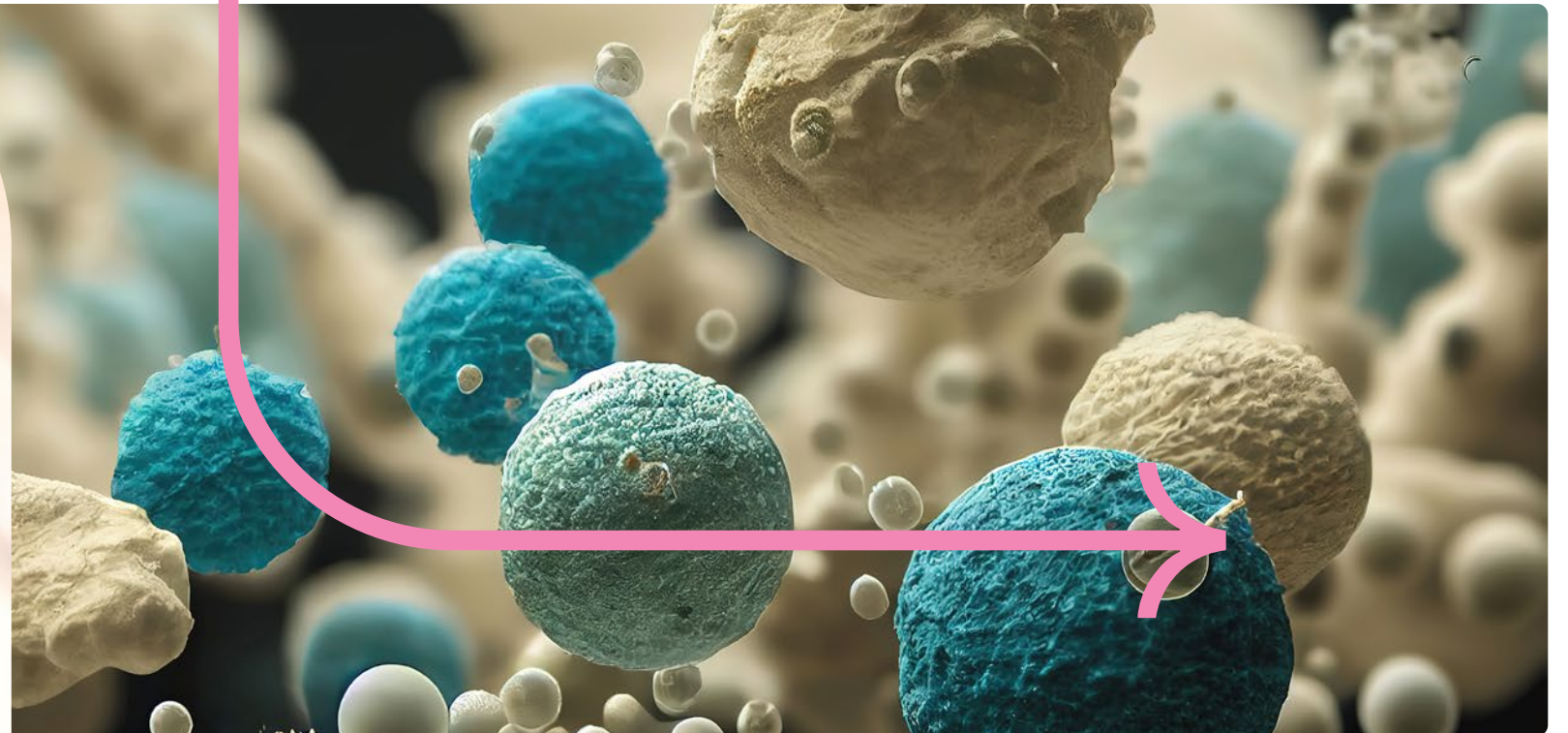
BKC/BAK can be classified as a skin irritant under chronic use. Nevertheless, BKC/BAK is more friendly to the skin than alcohol, which only offers momentary disinfection by contact and evaporation. Tertiary amines are used in the manufacture of BKC/BAK, where free amine is a possible impurity and can be responsible for skin irritation.

By carefully controlling manufacturing under validated GMP conditions, and using synthetic raw materials from qualified suppliers, it is possible to reduce the content of impurities to a minimum.

No matter the formulation, a product coming into contact epithelial tissue must only contain pure and safe ingredients.



Wound Care



Antiseptics play a central role in wound care where they are used for both prevention and treatment. To treat a wound and promote its healing, or to prevent infections during e.g. catheter use, the antiseptic can come in direct contact with both natural orifices and damaged tissue, often well beyond the skin derma. Therefore the importance of using of safe and pure ingredients.

Wound care antiseptics can be found in the form of topical products, medical devices or combination products. A robust, broad-spectrum antimicrobial in pharmaceutical grade can be a good choice for any of these product forms.

Properties

BKC/BAK acts on a wide range of microorganisms, from gram+ to gram- bacteria, mold, yeast, and enveloped viruses such as SARS-CoV, HIV, herpes, and influenza.

BKC/BAK is odorless and colorless, and its effectiveness ranges from pH 4 to 11. As a strong surfactant, it offers residual activity on the skin and the ability to mix well in both aqueous and oily phases, making it an ideal antimicrobial ingredient. It is non-volatile, non-flammable and extremely resistant to various temperature conditions.

BKC/BAK is active at very low concentrations, making it a cost-effective choice.

Formulations

Here are examples of wound care where BKC/BAK can be used and its typical concentrations:

- Wound dressing such as antiseptic bandages/ plasters/ patches - 0.01 to 0.1%.
- Wound wash, cleansing solutions or foams, cleansing wipes: 0.01 to 0.1%
- Irrigation solutions for the bladder and urethra: 0.005 to 0.02%
- Retention lavage of the bladder - 0.0025 to 0.005%
- Coated sutures and catheters: BKC/BAK can be coated or impregnated to reduce catheter-induced sepsis.
- Surgical glues (adhesives) and haemostatic pastes can be preserved with BKC/BAK where it can also act in preventing sepsis.

Safety

In recent years, several antiseptic actives have been removed from the market due to safety and efficacy concerns. BKC/BAK is one of the few compounds still considered safe and effective by e.g., the US FDA.

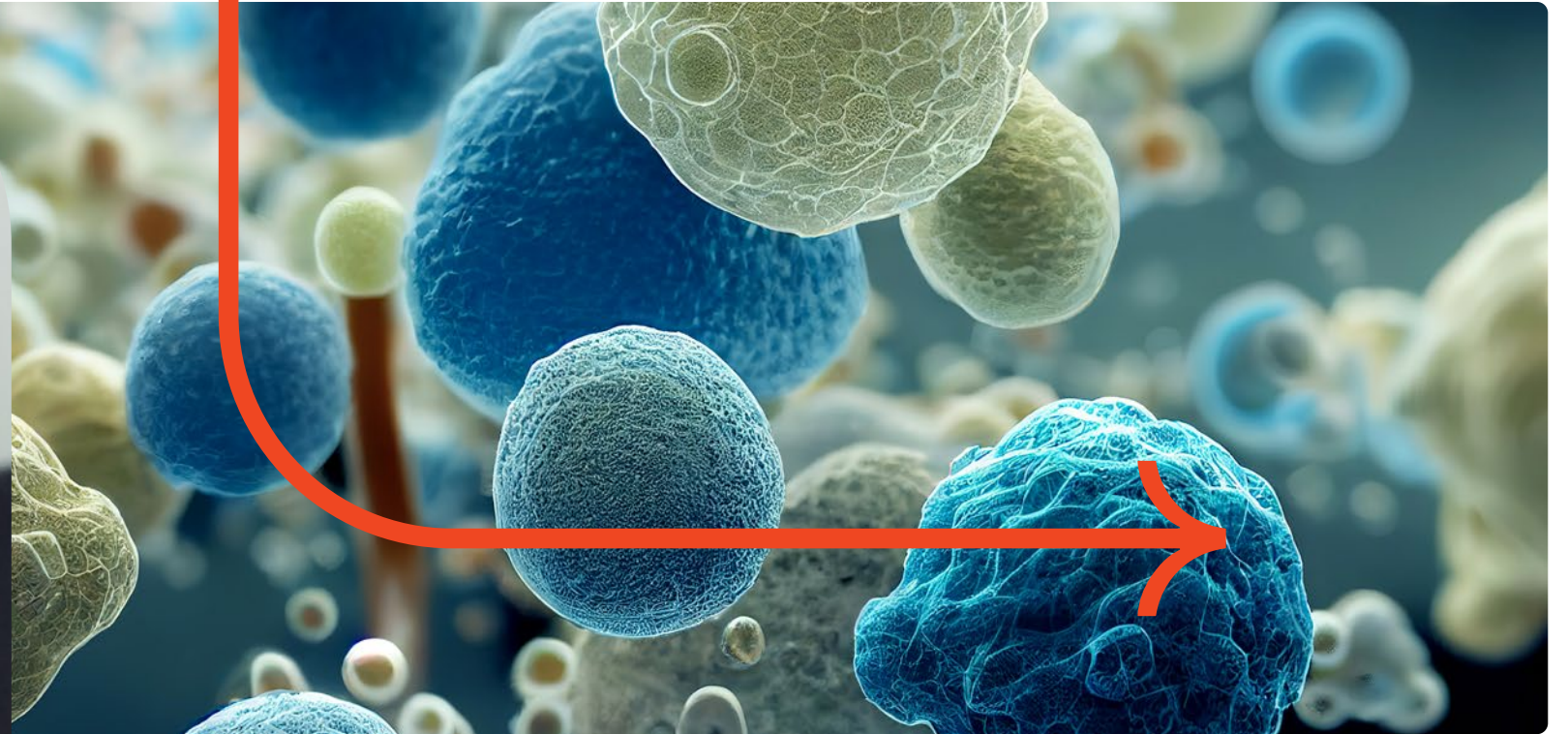
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By carefully controlling manufacturing under validated GMP conditions, and using synthetic raw materials from qualified suppliers, it is possible to reduce the content of impurities to a minimum.

Antiseptics play a central role in wound care where they are used for both prevention and treatment.



Oral & Respiratory



Antimicrobial actives are often found in oral health products, as antiseptics or preservatives. They are used to help prevent the buildup of plaque and gingivitis, and they can also help control bad breath and reduce the risk of tooth decay.

They are also found in throat lozenges and cough syrups, often in combination with a pain-relieving agent such as benzocaine, where they can be beneficial in the treatment of minor throat infections caused by bacteria or fungi.

Gum gels are designed to relieve pain from teething or sore gums, and often contain antiseptics in addition to pain-relieving ingredients like lidocaine. Antimicrobial agents may be added to help prevent infection and reduce inflammation in the affected area. This is particularly important for teething gels, as teething can create small openings in the gums where bacteria can enter and cause infection. In multi-dose respiratory formulations, an antimicrobial preservative can be added to maintain product efficacy and safety.

Properties

BKC/BAK acts on a wide range of microorganisms, from gram+ to gram- bacteria, mold, yeast, and enveloped viruses such as SARS-CoV, HIV, herpes, and influenza. BKC/BAK is active at very low concentrations, making it a cost-effective choice. BKC/BAK is odorless and colorless, and its effectiveness ranges from pH 4 to 11. It is non-volatile and extremely resistant to various temperature conditions, making it an ideal antimicrobial ingredient.

With its hydrophilic and hydrophobic characteristics, BKC/BAK impacts both the antibacterial and cleansing (oil-dissolving) effects of oral products through surface actions. It reduces the surface tension of the fluid situation in the mouth, to make other ingredients in the product contact the teeth better. It actively mixes with, and dissolves plaque to make the cleaning process more effective. It also produces foaming effects to enhance the cleaning process and remove debris. Another use is to distribute the flavors in the product.

Formulations

BKC/BAK can be used either as an excipient or an active pharmaceutical ingredient (API) for oral and dental formulations. Below are some examples, together with typical concentrations:

- Lozenges: antiseptic to treat superficial infections in the mouth and throat - 1.0 to 2.0 mg/lozenge
- Gels and creams: pain-relieving gum gels, often combined with lidocaine - 0.01 to 0.1%
- Antiseptic mouth sprays: - 0.05 to 0.1%
- Dentistry products: rinsing fluids, antiseptic fills - 0.05 to 0.1%
- Denture adhesive: - 0.1 to 0.15%
- Respiratory tract products nebulizers and inhalators: - 0.01 to 0.1%

Safety

BKC/BAK is considered by health authorities as being safe and is approved by regulatory agencies such as the US Food and Drug Administration (FDA) and the EMEA for use in oral care products.

Impurities from non-pharmaceutical ingredient sources can pose a risk. Utilizing BKC/BAK of true cGMP quality and from a reliable source, can help minimize risks.

By carefully controlling manufacturing under validated GMP conditions, and using synthetic raw materials from qualified suppliers, it is possible to reduce the content of impurities to a minimum.

With its hydrophilic and hydrophobic characteristics, BKC/BAK impacts both the antibacterial and cleansing effects of oral products through surface actions.

Product characteristics



Benzalkonium Chloride (BKC/BAK) is a Quaternary Ammonium Compound, and as such is a strong cationic surfactant. In addition to its broad-spectrum antimicrobial properties, it can act as an emulsifier and as a “supporting” compound to help carry APIs through e.g., mucous membranes or the cornea of the eye. Its strong attraction to surfaces provides residual activity when used as an antiseptic, where it remains active on the skin after contact.

BKC/BAK is non-volatile and can withstand an impressive range of temperature conditions, as supported by ICH Q1A stability studies. It is effective at pH levels between 4 and 11. Its effectiveness increases while pH increases; the higher the pH, the lower the concentration needed to obtain an antimicrobial effect. As opposed to bacteriostatic/fungistatic compounds which only prevent micro-organisms from dividing (growing), BKC/BAK is bactericidal/fungicidal, meaning it kills micro-organisms, whether they are in a growth phase or not.

BKC/BAK is odorless, colorless, easy to formulate, surface active/adhesive, non-volatile and very stable. Its robustness and broad-spectrum activity at low concentrations make it a cost-effective antimicrobial solution.

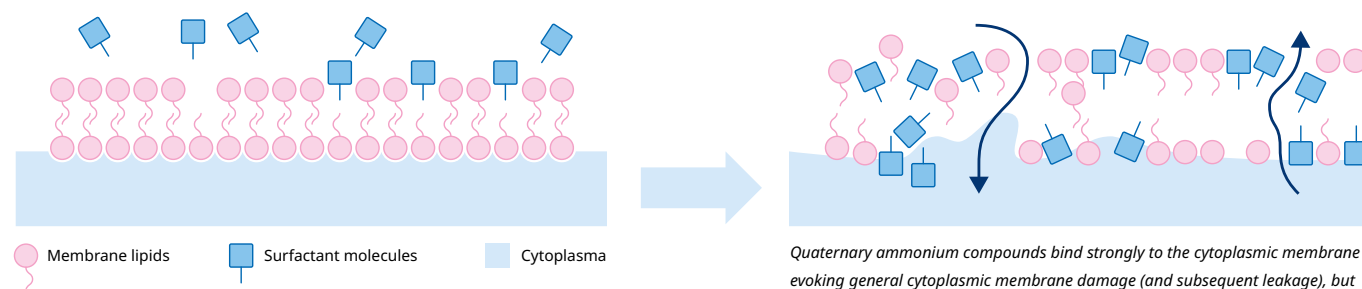
Mode of action

As a strong surfactant, BKC/BAK is attracted to negatively charged surfaces, such as microbial membranes. BKC/BAK is made of a hydrophilic and a hydrophobic part. Its hydrophobic alkyl (fatty) chains have a good affinity for bacterial membranes, where they disrupt the membrane's structure and provoke leaking of the cytoplasm.

Broad-spectrum antimicrobial activity

Our BKC/BAK has been tested against several AET-relevant microbial strains and confirmed to be effective against a wide range of micro-organisms at low concentrations. In the following table, BKC/BAK is compared to ethanol and a positive control containing Meropenem, a broad-spectrum antibiotic.

The MICs were determined by micro broth dilution method according to CLSI guidelines. Fresh overnight colonies from agar plates were suspended to a turbidity of 0.5 McFarland and further diluted in the required broth to 1x10⁶ CFU/ml. A total of 50 µl diluted bacterial suspension was added to wells containing 50 µl of test solutions. All compounds were tested in triplicate and the plates were incubated between 16 and 72 hours, depending on the strain.



Quaternary ammonium compounds bind strongly to the cytoplasmic membrane evoking general cytoplasmic membrane damage (and subsequent leakage), but particularly targeting the phospholipid bi-layer.

Minimal Inhibitory Concentrations. Mean results in % or ug/ml.

Species	ATCC	BKC %	Ethanol %	Meropenem	Control strain/ Meropenem ug/ml
<i>Candida albicans</i>	2091	<0.001	>1	<16	-
<i>Corynebacteria amycolatum</i>	33685	0.002	>1	0.006	0.06-0.25
<i>Streptococcus dysgalactiae</i>	12394	<0.001	>1	<0.015	0.06-0.25
<i>Enterococcus faecalis</i>	29212	<0.001	>1	0.125-8	-
<i>Staphylococcus aureus MRSA</i>	33591	<0.001	>1	16	2-8
<i>Staphylococcus aureus</i>	29213	<0.001	>1	0.06	-
<i>Pseudomonas aeruginosa</i>	27853	0.008	>1	0.5	0.03-0.12
<i>Mycobacterium abscessus</i> NFM32	-	<0.001	>1	<0.001	0.25-1
<i>Acinetobacter Baumani</i>	19606	0.002	>1	1	-
<i>Staphylococcus epidermidis</i>	12228	<0.001	>1	0.06	-
<i>Staphylococcus lugdunensis</i>	70328	<0.001	>1	0.25	-

Source: Danish Serum Institute, 2016

Compatibility and ingredient interactions

It is useful to be aware of compatibilities and incompatibilities for BKC/BAK (please see illustration).

Most formulators will opt for a robust and reliable, broad-spectrum antimicrobial. If specific, problematic microorganisms are targeted, a combination of different compounds might be the solution. To enhance activity, you can for example:

- Add synergistic ingredients
- Adjust the pH of the formulation
- Adjust (increase) the concentration of the antimicrobial.

Ingredient compatibilities and interactions are important features that can affect your formulation's efficacy and stability, either negatively or positively. Multiphase products such as creams, gels or ointments can include aqueous and oily phases needing to be maintained in equilibrium. Some compounds will distribute between oil and aqueous phases, which can reduce their efficacy.

BKC/BAK is a positively charged surfactant, comprising both a hydrophilic and a hydrophobic part and making it suitable for multiphase products such as creams and ointments, while still acting as an antimicrobial.

Solubility: BKC/BAK is miscible with water or lower alcohols, such as methanol, ethanol, and propanol in all ratios. It is not miscible with benzene or ether.

Stability: 5 years shelf life.

Following can decrease activity:

- Mixing with ordinary soaps and/or **anionic compounds** such as carboxymethyl cellulose **may decrease the activity**
- Can be inhibited by Tween® and by lecithin
- Avoid mixing with citrates, iodides, nitrates, permanganates, salicylates, silver salts and tartrates.
- Incompatibilities also reported with aluminium, fluorescein sodium, hydrogen peroxide, kaolin, some sulfonamides and hyaluronic acid.

Following can increase activity:

- Chelators such as EDTA acts synergistically by increasing the permeability of BKC into cells and therefore the efficacy of the preservative.
- BKC can be combined with **EDTA, benzyl alcohol, 2-phenylethanol or 3-phenylpropanol to enhance e.g. anti-pseudomonal activity.**
- Synergy is also observed with Cetrimide, 3-cresol, chlorhexidine and organo mercurials.



About us

Enabling better medicines, Enabling better lives

More than 30 years of cGMP experience

Novo Nordisk Pharmatech specializes in supplying ingredients for the biopharmaceutical and pharmaceutical industries. We were established in 1949, acquired by Novo Nordisk in 1986 and obtained our first GMP certificate in 1991.

Our highly qualified personal work continuously on product development and improving documentation to suit your needs. We are highly specialized in what we do, and all our customers are important to us.

Reduce your risks with pharma grade antimicrobials

Risk management is an integrated part of our daily routine and every planned change undergoes a rigorous assessment, thereby minimizing variations that could affect product and process specifications.

This combined with our know-how, ensures we can deliver high batch-to-batch consistency, thereby reducing the risk of variation for your processes. We offer full ingredient traceability, change notifications, quality agreements and a range of statements kept up-to-date by our QA department.

Ease registration with extensive documentation

We offer an extensive range of documents to help you meet registration and regulatory requirements. This includes multicompendial analyses and access to regulatory documentation. We ensure preparation of Active Substance Master Files in accordance with the latest authority requirements.

To further facilitate your drug registrations, we offer access to our Certificates of Suitability (CEP/COS) according to the European Pharmacopoeia Monographs.

Secure supply chain

Our proven record of reliable delivery assures you of continuous availability to keep development on track and production flowing. Our products can be shipped according to your requirements, in a variety of packing solutions, meeting demands for small- and large-size packaging.

Sustainability and Triple Bottom Line

As an environmentally responsible manufacturer, our concern for the surrounding environment takes a very high priority.

We continuously aim to reduce our environmental impact by developing safe processes, optimizing effective resource utilization and minimizing discharge and waste. Our environmental management system is certified according to ISO 14001 and ISO 450001.

Novo Nordisk is a member of the UN Global Compact and World Business Council for Sustainable Development (WBCSD).

As a fully owned Novo Nordisk subsidiary, we follow the same general policies for sustainability, business ethics and code of conduct.

We believe that a healthy economy, environment, and society are fundamental to long-term business success. This is why we manage our business in accordance with the Triple Bottom Line (TBL) business principle, conducting activities in a Financially, Environmentally and Socially responsible way.

As a token of our commitment to sustainability, Novo Nordisk Pharmatech is certified Platinum by EcoVadis.





By delivering quality at every step, we provide peace of mind to manufacturers and patients worldwide, enabling superior medicines and improving lives.

