Anestop contains Dexpanthenol 8%, Amethocaine, Propitocaine and Lignocaine.
The three local anaesthetics are present at a low concentration and their main role in this formulation of Dexpanthenol is linked to their antimicrobial/antimycotic effect.

Indeed, amethocaine, propitocaine and lignocaine have a well-established anti-mycotic, bacteriostatic and, in certain cases, bactericidal effect (1)**.** Propitocaine has proved to be able to trongly limit the growth of Staphylococcus aureus at all tested concentrations (0.5%, 0.25%, 0.125%). It also limited the growth of Pseudomonas aeruginosa at the concentrations of 0.5% and 0.25%, but not of 0.125%. Amethocaine inhibited the growth of Staphylococcus aureus at the concentration of 0.5%, and of Pseudomonas aeruginosa at the concentrations of 0.5% and 0.25%[(1)].
Aydin et al.(2,3) have investigated the antimicrobial effects of different concentrations of Ropivacaine, Bupivacaine, Lidocaine (Lignocaine) and Prilocaine (Propitocaine) on strains of Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa and Candida albicans. The inoculums taken from diluted suspensions were re-inoculated in blood agar and incubated for 18–24 h at 35 °C **;** then the colonies were counted. Ropivacaine did not inhibit the growth of any of the micro-organisms tested. On the other hand, Bupivacaine reduced the number of viable cells of Pseudomonas aeruginosa at the concentrations of 0.5% and 0.25%, and Lidocaine and Prilocaine reduced the number of viable cells of all micro-organisms tested at the concentration of 2%. Prilocaine**,** at the concentration of 1% reduced the number of viable cells of Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa. Lidocaine, at the concentration of 1% reduced only the viable cells of Pseudomonas aeruginosa, and Prilocaine, at the concentration of 0.5% reduced only the growth of Escherichia coli. In conclusion, Lidocaine and Prilocaine have shown the most powerful antimicrobial effects (2,3).
Fazly et al. have demonstrated the antibacterial activity of four local anaesthetics: Amethocaine, Procaine, Lignocaine and Cinchocaine. All these anaesthetics inhibited the growth of several bacterial strains (Escherichia coli) (4).
So, the three local anaesthetics contained in Anestop (Amethocaine, Lignocaine and Propitocaine) have an antimicrobial activity, associated with poor or absent penetration, and thus a very poor anaesthetic effect at these concentrations.

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Dexpanthenol is the main ingredient of Anestop. The concentration of this ingredient in our product is 8 %. Dexpanthenol is topically used in creams, lotions, solutions or ointments for the treatment of minor skin disorders, such as itching, mild eczema, stings, bites, poison ivy, poison oak and diaper rash, as well as to improve wound healing (5-7).

Topical administration of dexpanthenol may have beneficial effects on healing skin and mucous membrane lesions (8).

Recently, it has been provided in vivo evidence for a stabilizing effect of dexpanthenol on the skin barrier function (9).

The main function of dexpanthenol, when topically used, is to act as a protective barrier against water loss and in order to prevent harmful substances and micro-organisms from entering the body. Thus dexpanthenol provides an **indirect anti-inflammatory effect.**

When topically used**,** dexpanthenol is not considered to have a systemic pharmacological effect (see European Pharmacopoeia), so the largest use of this compound can be found in most skin care and beauty products; even the most popular dexpanthenol- based products, like PENATEN (Johnson & Johnson, A.T.C. class: 7AF6X - puericulture and infancy) and BE-PANTEN (Roche, A.T.C. class: 6AD8X – hygiene and cosmetics) are nor classified as medicinal products, neither as medical devices. So, Anestop could satisfy the point A.2 of the 93/42/CEE for a medical device classification: *"any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used on human beings for the purpose of: […] treatment or alleviation of disease […] alleviation or compensation for any injury […] replacement of a physiological process and wich does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but wich may be assisted in its functions by such means;"*

Concerning the criteria so far analysed, in order to decide if a MDD or a MPD regime could be applied we must take into account the way and the method used for the purpose the product is intended for (*minimization of discomfort, moisturisation by preventing transepidermal water loss, preparation of the skin for treatment*). According to the current scientific data, it is not obtained by metabolic, immunological or pharmacological means, since dexpanthenol is considered to have a pharmacological effect exclusively by oral or systemic assumption, but never by a topical usage at the common concentrations present in topical products. Thus, there is not a dose-response

correlation, neither a direct interaction between the molecules of the substance and a cellular constituent, in absence of whatever direct response or block to another agent response.

Usually, the topical administration of dexpanthenol preparations is well tolerated, with minimal risk of skin irritancy or sensitization. Particularly valuable is the excellent skin compatibility of dexpanthenol. This substance has been granted the GRAS status (Generally Regarded As Safe) by the strict regulatory American authorities. The dexpanthenol contained in Anestop topically used and at the amount of concentration present in the above mentioned formulation, cannot be considered to have a pharmaceutical effect on the human body (art.1 directive 65/65 CEE , directive 2001/83/CE).

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