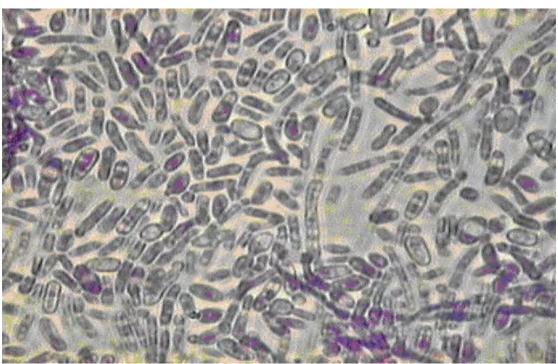


PROBIOTIC LACTIC YEAST®

NEW GENERATION PROBIOTIC

KLUYVEROMYCES B0399® (Turval B0399®)

Kluyveromyces marxianus fragilis B0399



"K. marxianus B0399® demonstrated a number of beneficial and strain specific properties desirable for application as a probiotic", research done by University of Bologna, Italy and University of Reading, UK and published by the American Society for Microbiology in the scientific journal Applied Environmental Microbiology, 2012 Feb; 78 (4)

APPROVALS AND RECOGNITIONS BY NATIONAL AND INTERNATIONAL AUTHORITIES:





for animal use:









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E-mail: info@turval.com



HUMAN NUTRITION



EUFYR [COOP, ITALY], THE FIRST COMMERCIALISED PROBIOTIC YOGURT CONTAINING KLUYVEROMYCES B0399®, WAS CHOSEN FOR THE UNIVERSAL EXHIBITION EXPO 2015 AS AN EXAMPLE OF LEADING INNOVATION IN FUNCTIONAL DAIRY PRODUCTS.

NEW GENERATION PROBIOTYC YOGURT WITH PROBIOTIC LACTIC YEAST® COOP ITALY





PROBIOTIC LACTIC YEAST® BROUGHT MULTIPLE AWARDS TO YOGURTS PRODUCERS FOR THE MOST INNOVATIVE PRODUCT

EUROPEAN AWARD

IN 2014 "EUFYR POMEGRANATE", PRODUCED BY ONE OF THE BIGGEST ITALIAN RETAILERS, COOP — ITALY, WINS PRESTIGIOUS PLMA'S INTERNATIONAL "SALUTE TO EXCELLENCE" AWARD IN AMSTERDAM; EUFYR IS THE WINNER AMONG 16 EUROPEAN COUNTRIES FOR THE BEST INNOVATION IN PRIVATE LABEL

Recognizing Innovation in Private Label

Welcome to PLMA's International Salute to Excellence Awards, honouring retailers for their commitment to their own brands and giving recognition to their innovative private label products. This year, more than 210 products were submitted by 45 retailers from 16 countries. These products covered 30 different categories of food, health and beauty and household products. Entries were evaluated by a panel of professional judges for taste, appearance, presentation, and value for money.

PLMA is proud to salute this year's winning retailers and their products, demonstrating once again the creativity and consumer responsiveness to private label today.

EASTERN EUROPEAN AWARD

IN 2015 KLUYVEROMYCES B0399® BRINGS THE SECOND INTERNATIONAL AWARD TO THE INNOVATIVE PROBIOTIC FERMENTED MILK BEVERAGE "JOGOFIR", PRODUCED BY THE AGRICULTURAL COMPANY "SAVA KOVACEVIC - DAIRY DANA" (SERBIA).

82nd INTERNATIONAL AGRICULTURAL FAIR OF NOVI SAD, SERBIA NOMINATED JOGOFIR THE "CHAMPION OF QUALITY AND NOVATION"





FOOD SUPPLEMENTS

NUMEROUS PROBIOTIC BRANDS BASED ON TURVAL B0399® DIFFERENT FORMULAS SUCCESSFULLY COLONISE WORLD MARKET

ITALIA



CAPSULES & DROPS
PAEDIATRICS & ADULTS

POWDER BAGS: K.MARXIANUS, VITAMINS, MINERALS, ENERGIZERS ADULTS ONLY



CAPSULES PAEDIATRICS & ADULTS



CAPSULES PAEDIATRICS & ADULTS



DUAL GIT KIT:

CAPSULES -LIOPHILIZED PAPAYA
CAPSULES -K.MARXIANUS B0399
PAEDIATRICS & ADULTS



CAPSULES - INTESTINAL FLORA BALANCE
OVULES - VAGINAL FLORA BALANCE
ADULTS



PROBIOTIC CHOCOLATE PRODUCTS
PAEDIATRICS & ADULTS

USA



INDIVIDUALLY WRAPPED SOFT CHEWS/CARAMELS PAEDIATRICS & ADULTS



CAPSULES PAEDIATRICS & ADULTS

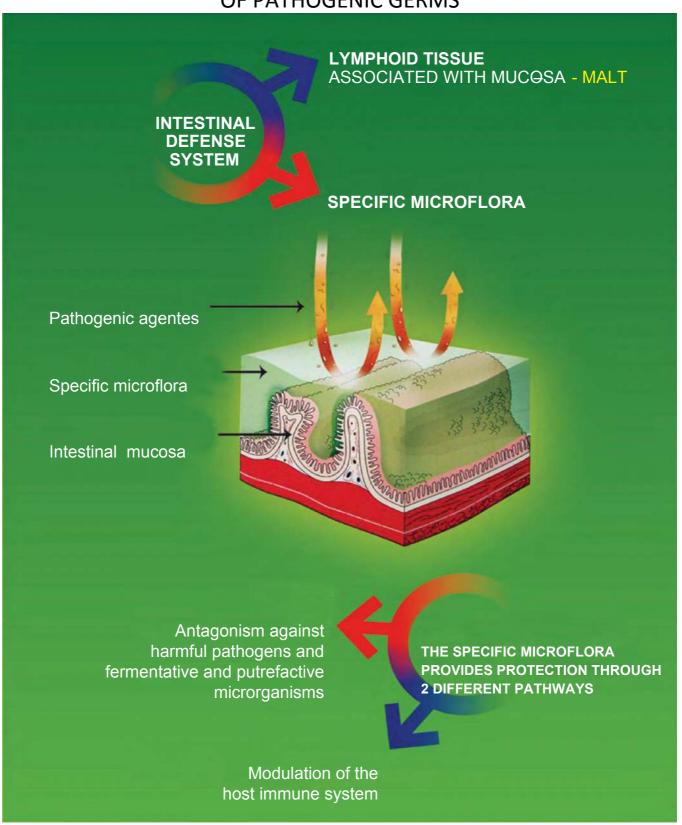
CANADA



CAPSULES PAEDIATRICS & ADULTS



GASTROINTESTINAL MUCOSA IS ONE OF THE MAIN SITES OF ENTRIES OF PATHOGENIC GERMS





PROBIOTIC LACTIC YEAST®, KLUYVEROMYCES B0399® IS DIFFERENT FROM COMMONLY USED LACTOBACILLUS, BIFIDOBACTERIUM & SACCHAROMYCES; IT IS CAPABLE OF PERFORMING BIOREGULATORY ACTION & REBALANCING OF THE INTESTINAL FLORA THROUGH:

- Unique biological properties such as: being natural & friendly, lactose degrading and insusceptible to antibiotics
- Natural resourse of prebiotics: Beta-glucans & oligosaccharides (GOS, MOS, FOS)
- Prevention & inhibition of pathogen development (clostridia, coliforms, candida etc.)
- Stimulation of development of the good endogenous flora
- >>> K. B0399[®] Is the only YEAST probiotic, totally "NATURAL" & "GUT FRIENDLY":
 - It efficiently stimulates development of the good gut flora (e.g. endogenous Bifidobacteria), even at low dosage (>100 times less then *S.boulardii* & *Bifidobacteria*)

(trial n.125, 132, 138, 143)

- It's naturally found in everyday food products and human gut flora
- "IMPROVE THE BALANCE OF THE GUT FLORA": health claim approved by the Italian Ministry of Health at 03.12 2009 conform at guideline about pre/probiotic (Dec. 2005)
- >>> SURPASSES THE GASTRIC BARRIER (thanks to the chitin constituent of the cell wall)
 AND ARRIVES IN THE INTESTINE ACTIVE AND ALIVE (even at low pH, such as pH3)

(trial n. 35, 130.4B, 79B, 130.1B, 143)

- >>> EFFICIENTLY COLONIZES INTESTINE adhering to enterocytes of the intestinal epithelium

 (trial n. 143)
- HAS STRONG ANTIMICOTIC ACTION (particularly against "Candida albicans") and EFFICIENTLY COMPETE AGAINST PATHOGENS through: a) direct adherence to epithelium, b) direct competition for nutrients, c) promotion of epithelial cell growth and reinforcement of the major gut barrier against infections, d) by decreasing pH it turns the local environment unsuitable for the growth of certain pathogens (eg. E.coli)

 (trial n. 57, 143, 96A, 129)
- >>> IT MODULATES IMMUNE RESPONSE through: a) fine modulation of the level of anti- and proinflammatory cytokines, possibly attenuating the proinflammatory effect in inflammatory disorders such as irritable bowel syndrome (IBS) and Celiac Disease, among others; b) as a rich source of PREBIOTICS, it gives rise to immunostimulating beta-glucans and oligosaccharides (GOS, MOS, FOS)

 (trial n. 96A B, 129)
- **IT IS NATURALY INSUSCEPTIBLE TO ANTIBIOTICS AND PREVENTS THE MOST COMMON SIDE EFFECTS OF ANTIBIOTIC THERAPY**: being yeast, not a bacterium, K. B0399® has such molecular and subcellular structures that are not damaged by commonly used antibiotics, this enables to prevent or restore intestinal imbalances caused by antibiotic therapy and associated diarrhea.

 (trial n. 84.01; 84.02)
- >>> DIGESTS LACTOSE, thanks to the elevated production of B-galactosidase (the enzyme for lactose digestion); it is particularly recommended for lactose intolerant individuals

 (trial n. 35)
- >>> SUPPORTS REDUCTION OF GASTRO-INTESTINAL (GI) DISCOMFORT AND IMPROVES THE CHARACTERISTICS OF EVACUATION AND THE GLOBAL ASSESSMENT OF RELIEF OF IBS SYMPTOMS: various human studies substantiate a causal relationship between the consumption of Kluyveromyces B0399 and the improvement of GI symptoms of discomfort.

(trial n. 16, 125, 130, 132, 138)



COMPARISON OF THE **PROPERTIES AND INDICATIONS** OF *KLUYVEROMYCES* B0399® AND *LACTOBACILLUS P.& BIFIDOBACTERIUM SPP.*

ROPERTIES AND INDICATIONS	KLUYVEROMYCES B0399®	LACTOBACILLUS SPP. BIFIDOBACTERIUM SPP.
Cell type	THE YEAST (Eukaryotic)	BACTERIA (Prokaryotic)
Passing gastric barrier alive and active	CHITIN BASED CELL WALL	NOT DECLARED
Production of useful substances for the body	 Oligosaccharides, oligopeptides, such as: ß GALACTOSIDASE (LACTASE). Enzyme responsible for breaking down lactose B-glucans and oligosaccharides: GOS, FOS, MOS other functional enzymes such as: B GLUCANASE, INULINASE; enzymes for oligosach. production 	Example for Lactobacillus reuteri: REUTERIN (antimicrobic substance of the broad spectrum)
Resistance to infectious agents (Bacteriophages)	HIGH	LOW
Mandatory conservation in fridge	NO	YES
Storage temperature	3-25 ° C	3-8 ° C
Administration for those who are lactose intolerant	SPECIFICALLY INDICATED	ALLOWED
Antibiotic susceptibility	NONE (due to its "yeast" nature)	Susceptible to most commonly used antibiotics
Dioxide (CO2) production in the gut	Insignificant level	YES
Production of ATP (energy available to the organism)	HIGH (2 ATP / 1 C6H12O6)	LOW (1 ATP / 1 C6H12O6)
Digestion of lactose	HIGH (the production of ß-GALACTOSIDASE)	HIGH (the production of ß-GALACTOSIDASE)
Dosage - Therapeutic minimum and its effect upon gut flora	LOW ~ "natural"; efficiently colonise intestine even when taken at low dosage such as: 10 million CFU / day., respecting the natural microflora of the patient's bowel	HIGH drastic impact on the natural microflora due to the high dosage suggested (10 billion CFU / day)
Anti-micotic action (anticandidiasis)	SPECIFIC: Against - Candida albicans proposed mechanism: by contact inhibition	GENERAL: proposed mechanism: produce microbicidal molecules (example reuterin)



COMPARISON OF THE **PROPERTIES AND INDICATIONS** OF

KLUYVEROMYCES B0399® AND SACCHAROMYCES BOULARDII

PROPERTIES AND INDICATIONS	KLUYVEROMYCES B0399®	SACCHAROMYCES BOULARDII
β-galactosidase activity	Yes +++	NO
Ability to produce lactic acid and positively reduce the intestinal pH	Yes +++	NO
Side effects	NOT DETECTED	YES (not recommended for fragile patients) *
Increase the number of good bacteria of the gut natural flora (bifidobacteria)	Demonstrated	NO
Dosage - Therapeutic minimum and its effect upon gut flora	LOW ~ "natural" 10 million CFU / day	HIGH - 10 billion CFU / day drastic impact on the natural microflora
Is it frequently encountered in every-day food	YES (is in many cheeses and naturally fermented kefyr)	NO (comes from lichens)
Anti-micotic action (anti-candidiasis)	SPECIFIC: Against - Candida albicans proposed mechanism: contact inhibition	SPECIFIC: Against Candida albicans; by antimycotic effect of capric acid

^{*}Pag 24 of EFSA QPS2013 update – EFSA Journal;

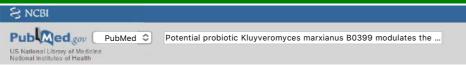
TABLE SHOWING THE COMPARISION BETWEEN ANTIBIOTIC RESISTANCES

ANTIBODY TYPE	KLUYVEROMYCES B0399®	LACTOBASCILLUS REUTERI	
Bacitracin	R	U	
Colistin	R	U	
Penicillin	R	R	
AMP(Ampicillin)	R	R	
Oxytetracycline	R	U	
AMX(Amoxicillin)	R	R	
GM (Gentamicin)	R	I .	
CMP (Chloramphenicol)	R	U	
Erythromycin	R	S	
Tetracycline	R	S	
Clorotetracycline.HCL	R	U	
Tartared Tilosin	R	U	
Nalidixic Acid (Chinolons)	R	R	
Lincomicin (Lincomicins)	R	U	
Rifampicin (Rifamycins)	R	S	
Quinupristin/Dalfopristin	R	U	
Linezolid (Oxazolidinones)	R	U	
Teicoplanin (Glycopepetides)	R	U	
Trimethoprim	R	U	
Sulfadiazine	R	U	
Legend: R=Resistant; I= Intermediate; S=Sensible; U=Undeclared			



Trial n. 143

Maccaferri S1, Klinder A et al.; University of Bologna, Italy & University of Reading, United Kingdom

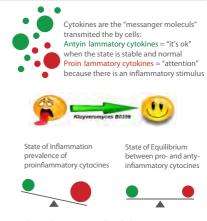


Appl Environ Microbiol. 2012 Feb;78(4):956-64. doi: 10.1128/AEM.06385-11. Epub 2011 Dec 9

Potential probiotic Kluyveromyces marxianus B0399 modulates the immune response in Caco-2 cells and peripheral blood mononuclear cells and impacts the human gut microbiota in an in vitro colonic model system.

Abstract

the aim of this study was to broadly investigate the beneficial properties of the lactic yeast Kluyveromyces marxianus (formerly Kluyveromyces fragilis) B0399. Potential probiotic traits of K. marxianus B0399 were investigated: adhesion and immune modulation, and the effect of the administration of 10(7) CFU/day of K. marxianus B0399 on the composition and metabolic activity of the human intestinal microbiota in a 3 stage continuous culture system simulating the human colon. We demonstrated that this strain was highly adhesive to human enterocyte like Caco 2 cells and modulated the immune response, inducing proinflammatory cytokines in peripheral blood mononuclear cells (PBMCs). In the presence of inflammatory stimulation with lipopolysaccharide (LPS), K. marxianus B0399 provoked decreases in the levels of production of proinflammatory cytokines in PBMCs and Caco 2 cells, thus ameliorating the inflammatory response. Furthermore, K. marxianus B0399 induced increase in the bifidobacterial concentration ... The effects of K. marxianus B0399 on adhesion, immune function, and colonic microbiota demonstrate that this strain possesses a number of beneficial and strain specific properties desirable for a microorganism considered for application as a probiotic.



•The cytokines are normally in balance. •When an inflammatory stimulus Intervenes, pro-inflammatory cytokines prevail (red) Kluyveromyces B0399 induces the pro-inflammatory cytokines' concentration drop, restoring the balance

Prof G. Mustacchi, Cancer Center health services n 1 Triestina, Univerity of Trieste, Italy

EVALUATION OF THE COLONIZATION CAPACITY OF THE GASTROINTESTINAL TRACT IN HEALTHY SUBJECTS, AFTER THE UTILIZATION OF KLUYVEROMYCES B0399, THROUGH EXAMINATION OF FAECES.

The present study evaluates the colonization capacity of Kluyveromyces marxianus B0399. The product was administered to 17 healthy volunteers for 14---day period. The feces of the healthy individuals were analyzed to evaluate the presence of Kluyveromyces B0399, at time TO, (before the start of the administration) and at the end, at time T14 (after 14 days). The healthy subjects' consumption of K. B0399 at the dosage of 20 million CFU/die for 2 weeks resulted fully sufficient for gut colonization, with no collateral effects.

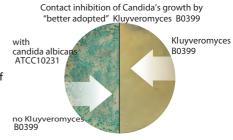
Results: 16/17 of enlisted subjects gave assessable results (94.12%) At T14, 100% sample results positive for the yeast colonisation, with a significant statistical increment with respect to T0. Similarly, the quantitative assessment between T0 and T14 highlight a statistically significant difference in number of yeast colonies, with the average increment ≈ 3 logarithms (range from 1 to 6).

Detected colonization demonstrates the resistance towards the gastric barrier and hypothesizes that Kluyveromyces B0399 will efficiently colonize intestine even if administered with sensibly lower dosages than those examined (for example 5-10 million CFU/day).

Dr. T. Cettolo, Dr. L. Riul - Laboratory Specialized in Microbiology of the ASA CCIAA of Udine, Italy

IN VITRO TEST ON THE INFLUENCE OF LACTIC YEAST TYPE (KLUYVEROMYCES MARXIANUS FRAGILIS B0399) ON THE DEVELOPMENT OF CANDIDA ALBICANS ATCC10231. **SUMMARY**

The test demonstrated that Candida does not and colonizes the plate in the presence of Kluyveromyces B0399; similarly if Kluyveromyces is added (administered) before Candida, the growth of Candida will be prevented (inhibited) by previously populated Kluyveromyces B0399, The results imply that K. marxianus has better adhesiveness and develop on the majority of the surface while inhibiting the growth of the pathogenic yeast.



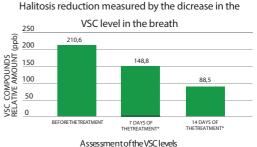
Dr. P. Nobili, Dr. A. R. Zanvit - Biological Dentistry Department, Italian Dental Institute - Milan, Italy

HALITOSIS TREATMENT WITH KLUYVEROMYCES Results: 3 cycles of B0399

SUMMARY

A population of patients of both sexes affected by halitosis, with and 14 days after the ages 18 65, were subjected to the halitosis treatment through the administration of antibiotic resistant lactic yeasts, Kluyveromyces B0399 at the dosage 10/20 million CFU/capsule/die and the evaluation of the VSC (Volatile Sulphur superior, halitosis is Compounds) levels in the breath with a digital halimeter.

measurements during the trial: before the treatment, 7 days after treatment; 100ppb is taken for the threshold level; if VSC count is considered.





Trial n.125

Pr. Roda – Clinical medicine department, Bologna University, Italy

EFFECTS OF A YOGURT CONTAINING KLUYVEROMYCES B0399® ON PATIENTS WITH IRRITABLE BOWEL SYNDROME—A DOUBLE" BLIND, RANDOMIZED, PLACEBO CONTROLLED CLINICAL STUDY SUMMARY

This study evaluates the effects of a yogurt formulated with addition of Kluyveromyces B0399 10/20 million CFU/packaging, n atients suffering from IBS. A double blind, monocentric study, controlled against a yogurt containing *Streptococcus t, Lattobacillus b* and *Bifidobacterium lactis BB12*, in parallel groups of patients affected by IBS. Total patients 92; active treated group 46; control group 46. The study comprises a daily collection of data for every patient during 8 weeks trial period divided in 3 phases: 2 weeks pre treatment or "basal", 4 weeks

"treatment" and 2 weeks post treatment or "washout".

Acts on addominal pain, in patients with IBS

of each between the study phases:

bloating and/or meteriorism,

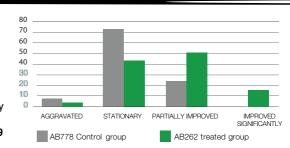
abdominal pain or discomfort

number of daily evacuations

characteristics of the evacuation (sense of difficulty, incomplete evacuation, urgency to evacuate)

the consistency of the feces according to validated Bristol Stool Scale (every two weeks)

Results can be summarized in general representation of Kluyveromyces B0399 efficacy in reducing personal discomforts, controlling symptoms of IBS and improving the sense of subjective well being:



Trial n. 132

Dr. S. Andreoli – medical director dep. Gastroenterology at Hospital of Udine, Italy

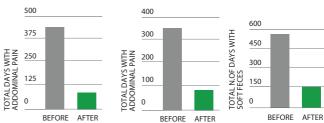
EFFECTS OF KLUYVEROMYCES B0399 ON PATIENTS WITH IRRITABLE BOWEL SYNDROME

SUMMARY

Clinical results of the treatment with the lactic yeast Kluyveromyces B0399 for Irritable Bowel Syndrome. This study, based on the gathering of symtomatological data before and after the treatment, demonstrates that the prolonged use of Kluyveromyces marxianus fragilis B0399, the dosage of 10/20 million CFU/capsule/day, significantly improves the clinical picture and above all improves the quality of life of these patients. The product was administered to 50 patients: 15 men with ages of 20 62 and 35 women with ages of 22 55 in the following way: one capsule every 12h for a month and a maintenance period with one capsule before breakfast for two months.

Results relevant symtomatological data of the patients were compared "before" and at the end ("after") the treatment:





Trial n. 16

Dr. S. Andreoli – medical director dep. Gastroenterology at Hospital of Udine, Italy

TRIAL WITH KLUYVEROMYCES B0399 ON PATIENTS WITH IRRITABLE BOWEL SYNDROME SUMMARY

45 patients were treated, predominantly female, from the ages of 20 to 70 years (average age 38). All the patients were excluded of organic pathologies with rectoscopy and/or opaque clisma, or colonoscopy. Research was done on occult blood, parasites, total IgE, blood count, serum iron. Cea and alpha - fetoprotein were also researched in elderly. Relevant symptoms present in the patients at least three months before the trial and followed along the trial period:

- pain or abdominal distension attenuated after discharge
- bowel movement pattern change or change in feces consistency
- alteration of clarification that becomes difficult, urgent with the sensation of incomplete discharge myxorrhea.

Results: Group A (1 capsule every 8 h for 20 days): a considerable improvement in abdominal distension with an accelerated rate of discharge and emission of soft feces; Group B (1 capsule every 12 h for 30 days): an improvement in abdominal distension, fecal consistency with regular bowel movement and regular clarification; Group C (1 capsule per day for 60 days): improvements of the symptoms present, but not consistent.

Trial n. 75

Dr. A.Tuli- irector of the Clinic of Dermatology, University of Studies "G. di Annunzio" Chietti, Italy

PRELIMINARY STUDY ON THE EFFECTS OF KLUYVEROMYCES B0399 ON PATIENTS WITH ATOPIC DERMATITIS SUMMARY

The study involved 10 patients (age: 6 10) with atopic dermatitis and high total IgE. Subject were subjected to the treatment with Kluyveromyces B0399 at the dosage 10/20 million CFU /day for 30 days. At the end of the trial the total serum IgE reduced to normal level.



APPLICATIONS

>>> PEDIATRICS

- CONSTIPATION
- DIARRHEA
- IRRITABLE BOWEL
- ATOPIC DERMATITIS
- LACTOSE INTOLERANCE
- LACK OF BREAST MILK IN BREASTFEEDING

>>> GASTROENTEROLOGY

- IRRITABLE BOWEL
- NONSPECIFIC ENTERITIS
- COLITIS
- CONSTIPATION
- DIARRHEA
- LACTOSE INTOLERANCE

>>> GYNECOLOGY

- CANDIDA ALBICANS MYCOSIS
- LACK OF BREAST MILK IN BREASTFEEDING (TO ADMINISTER TO MOTHER)

>>> GERIATRICS and UROLOGY

- URINARY TRACT INFECTION
- CONSTIPATION
- DIARRHEA
- LACTOSE INTOLERANCE

>> ONCOLOGY

• IN PATIENTS UNDERGOING RADIATION AND CHEMOTHERAPY

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Web site: www.turval.com

I Laboratori Turval affiancano la ChildCare WorldWide (CCWW) ONLUS nel progetto di

formazione di medici pediatri ed infermieri nelle patologie specifiche dell'Africa sub-sahariana

l'urval - il primo del suo genere ad avi

ottenuto l'autorizzazione delle autorità