To be sold by retail on the prescription of a Registered Medical Practitioner or oncologist only

PRESCRIBING INFORMATION

LEVISCD2™

Lozenges

[*Levilactobacillus brevis* CD2 Lozenges]

GENERIC NAME

Levilactobacillus brevis CD2 Lozenges

COMPOSITION

Each lozenge contains:

Live, lyophilized lactic acid bacteria *Levilactobacillus brevis* CD2 Not less than 2 Billion CFU.

Excipients: Fructose, Pearlitol (mannitol), Aspartame, Talc, Colloidal Silicon Dioxide, Magnesium Stearate, Vanilla Cream flavour, Strawberry flavour

DOSAGE FORM

Oral Lozenges

DESCRIPTION

LEVISCD2 lozenges contain *Levilactobacillus brevis* CD2 strain, which has been proven to attenuate the inflammatory processes through activities of its unique enzymes (in particular, Arginine Deiminase).

Arginine Deiminase from *Levilactobacillus brevis* CD2 competes for Arginine with inducible Nitric Oxide Synthase (INOS) to revert the metabolism of arginine into ammonia and citrulline resulting in downregulation of Nitric Oxide (NO) and polyamine synthesis.

By downregulating NO and Polyamine levels,LEVISCD2 has shown strong anti-inflammatory effects in conditions such as radiotherapy and/or chemotherapy induced oral mucositis in cancer patients and in patients undergoing Hematopoietic Stem Cell Transplant. (HSCT)

INDICATIONS[3-4]

LEVISCD2 is indicated for the prevention of radiotherapy and chemotherapy induced oral mucositis in cancer patients.

DOSE AND METHOD OF ADMINISTRATION

CTRT : for Adults- One LEVISCD2 lozenge to be taken 4-6 times a day from the first day of therapy until 1 week after the last CRT administration (for the management of the oral mucositis)[3].

HSCT (Above 10 years) One LEVISCD2 lozenge to be taken 3-6 times a day 4 to 7 days before initiation of chemotherapy and to be continued until resolution of mucositis or till day +24 post stem cell infusion, whichever occurs early (for the Prevention of the oral mucositis).[4]

Mode of Administration: Oral Administration.

LEVISCD2 lozenges are intended to be dissolved slowly in the mouth. For best results, LEVISCD2 lozenges must dissolve naturally in the mouth like a lozenge. Do not chew, crush, or swallow the whole lozenge. Move the lozenge around the mouth till it dissolves completely by itself.

USE IN SPECIAL POPULATIONS

Pregnancy and Lactation

Safety and efficacy in pregnant or lactating women have not been studied yet.

Pediatrics

Caution should be exercised while administering LEVISCD2 in kids for the choking hazard.

Geriatrics

Caution should be exercised while administering LEVISCD2 in elderly patients for the choking hazard.

CONTRAINDICATIONS

LEVISCD2 is contraindicated in the following conditions:

1. Known Hypersensitivity to any of the ingredients mentioned above.
2. Known neuromuscular dysfunction with impaired swallowing and cough reflex.
3. Known cases of phenylketonuria.

WARNINGS and PRECAUTIONS

Please refer to use in special population.

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Do not consume anything 30 minutes before and after intake of LEVISCD2.

LEVISCD2 lozenges contain aspartame and fructose.

1. Aspartame is a source of phenylalanine. May be harmful for people with phenylketonuria.
2. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

DRUG INTERACTIONS

No drug interactions have been reported so far with LEVISCD2.

OVERDOSE

Do not exceed the instructed doses without the advice of the healthcare professional.

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

Pharmacodynamics

LEVISCD2 produces high levels of arginine deiminase and sphingomyelinase[1]. Eukaryotic human cells can convert arginine into nitric oxide and polyamines by the actions of nitric oxide synthase and arginase, respectively.

Arginine deiminase of bacterial origin competes with nitric oxide synthase and converts arginine to ammonia and citrulline; downregulating its conversion to nitric oxide, leading to a reduction in the levels of some of the known inflammatory parameters (cytokines IL-1a, IL-6, IL-8, TNF-a, IFN-y, PGE2 and matrix metalloproteinases)[2].Bacterial sphingomyelinase can hydrolyse the platelet activating factor (PAF), a potent inflammatory cytokine, known to be associated with oral mucositis[3].

Pharmacokinetics

Levilactobacillus brevis CD2 is administered *via* lozenges designed for topical action within the oral cavity. Clinical studies in patients receiving chemotherapy and radiotherapy have demonstrated beneficial effects on oral mucosal inflammation, suggesting a local mechanism of action. While some material may be swallowed after dissolution, the therapeutic benefit of *Levilactobacillus brevis* CD2 lozenges is attributed to their local activity in the oral cavity.

SHELF LIFE

Please see Mfg. Date/Expiry Date printed on pack. Do not use the product after the expiry date which is stated on the packaging.

PACKAGING INFORMATION

Bottle containing 20 lozenges.

STORAGE AND HANDLING INSTRUCTIONS

To be stored between 2-8 °C (in refrigerator) protected from light and moisture. Do not freeze.

Keep out of reach of children.

LEVISCD2™ is a trademark of Wembrace Biopharma Pvt. Ltd., India.

REFERENCES

1. Di Marzio L, Russo FP, D'Alò S, Biordi L, Ulisse S, Amicosante G, De Simone C, Cifone MG. Apoptotic effects of selected strains of lactic acid bacteria on a human T leukernia cell line are associated with bacterial arginine deiminase and/or sphingomyelinase activities. Nutrition and Cancer 2001;40(2):185-96.

2. Riccia DN, Bizzini F, Perilli MG, Polimeni A, Amicosante G, Cifone MG. Anti-inflammatory effects of Lactobacillus brevis (CD2) on periodontal disease. Oral Dis. 2007 Jul; 13(4):376-85.

3. Sharma A, Rath GK, Chaudhary SP, Thakar A, Mohanti BK, Bahadur S. Lactobacillus brevis CD2 lozenges reduce radiation- and chemotherapy-induced mucositis in patients with head and neck cancer: A randomized double-blind placebo-controlled study. Eur J Cancer. 2012 Apr; 48(6): 875-81.

4. Sharma A, Tilak T, Bakhshi S, et al. Lactobacillus brevis CD2 lozenges prevent oral mucositis in patients undergoing high dose chemotherapy followed by haematopoietic stem cell transplantation. ESMO Open. 2017;1(6):e000138.

Marketed in India By:

Wembrace Biopharma Pvt.Ltd

B-6/5 first floor, Okhla Phase 2,

New Delhi-110020

Manufactured in India By:

Cosmas Pharmacls Ltd.

Buranwala Road, Village : Kotla,

P.O. Barotiwala, Solan (H.P.) 174103