

Consumer Product Information for Travelan®

Active ingredient: Dairy (bovine) colostrum powder 200mg

What is Travelan® used for?

Travelan® is an oral biopharmaceutical product that targets pathogenic bacteria and the toxins they produce in the gastrointestinal (GI) tract which cause traveller's diarrhoea, a digestive tract disorder.

Travelan® helps to:

- Reduce the occurrence of symptoms of traveller's diarrhoea.
- Decrease symptoms of traveller's diarrhoea when travelling.
- Reduce the occurrence of diarrhoea when travelling.
- Decrease abdominal cramping and gastrointestinal pain.
- Reduce mild gastrointestinal tract inflammation.
- Maintain gastrointestinal function and enhance gastrointestinal system health and
- Enhance immune defence and support healthy gastrointestinal immune function.

What is the natural* medical ingredient in Travelan®?

The drug product contains 200 mg of highly immune bovine colostrum as powder formulated as a 700 mg solid oral tablet. This natural hyperimmune bovine colostrum* contains over 80% proteins by weight, approximately 35% to 45% of which are immunoglobulins. The very high levels of antibodies provide passive protection against a wide range of pathogens.

What are the non-medical ingredients?

Colloidal silicone dioxide, croscarmellose sodium, glucose, magnesium stearate and microcrystalline cellulose.

What is Travellers' Diarrhoea?

Travellers' Diarrhoea is a digestive tract disorder that is commonly caused by consuming food or water infected with pathogenic bacteria. According to Australian government agencies,^{2,3} the Public Health Agency of Canada⁴ and the Centers for Disease Control and Prevention⁵, Travellers' Diarrhoea is the most common illness that affects travellers. It is known by many colourful euphemistic names such as; Bali Belly, Montezuma's Revenge, Food Poisoning, Gastro, the Greek Gallops, Delhi Belly, the Aztec Two-Step, Back Door Sprint, Casablanca Crude, La Tourista and the Turkey Trots.

Travellers' Diarrhoea affects millions of international travellers to developing countries each year⁶ and can cause substantial disruption by interfering with travel itineraries and business opportunities. It can also cause significant medical costs and productivity losses if the disease persists when travelers return home⁷. Travellers' diarrhoea is generally defined as the passage of 3 or more unformed stools in a 24-hour period plus at least one additional symptom such as nausea, vomiting, abdominal cramps, fever, blood/mucus in

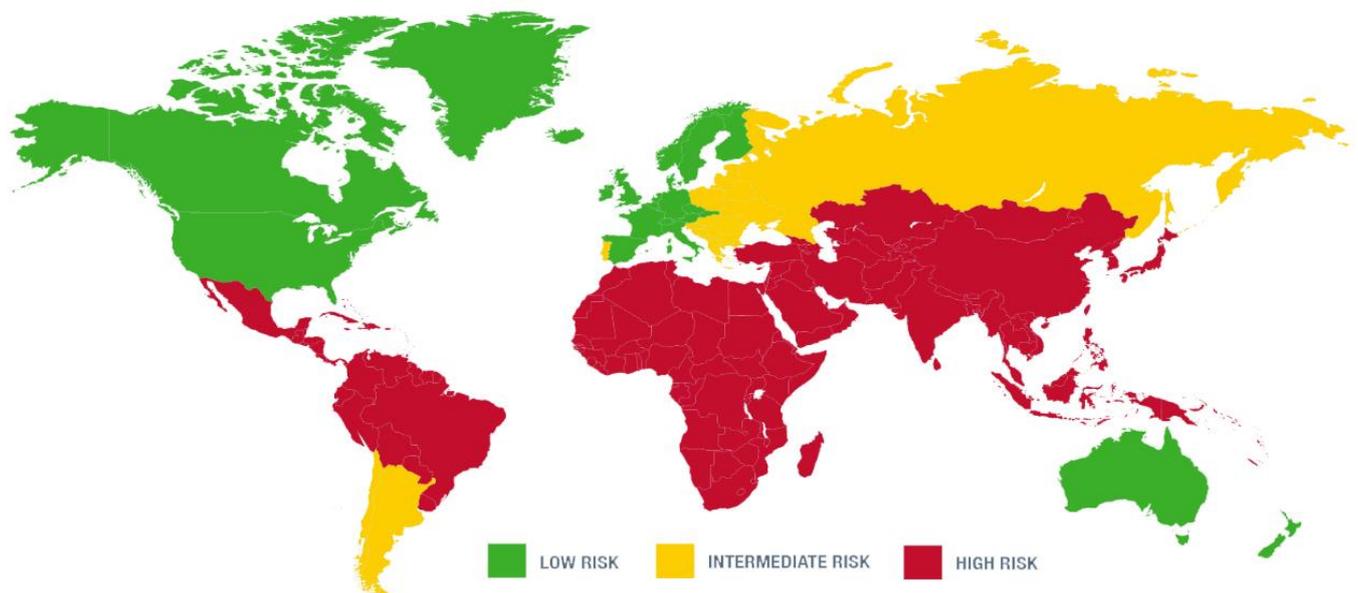
the stools, or feecal urgency⁶. Travellers' Diarrhoea develops while abroad or within 10 days of returning from a resource-limited destination⁶.

It is estimated that Travellers' Diarrhoea affects between 30% to 70% of travellers, depending on the destination and season of travel⁵. The attack rate is highest for travellers from a developed country who visit a developing country and children are at particular risk⁶. Unfortunately, Travellers' Diarrhoea can lead to significant limitation of activity, with approximately 10% of travellers seeking medical care and up to 3% requiring hospitalisation⁸.

Travellers' Diarrhoea is usually acquired through the ingestion of contaminated food and water⁶ with bacteria thought to account for 80% to 90% of cases⁵. The most common Travellers' Diarrhoea pathogen identified is Enterotoxigenic *Escherichia coli* (ETEC), followed by *Campylobacter jejuni*, *Shigella spp* and *Salmonella spp*. Intestinal viruses may account for 5% to 15% of cases⁵. Bacteria such as *E.coli* can be found in a street side stall or the finest of restaurants. Dehydration is the most common complication associated with Travellers Diarrhoea⁶.

In which countries should you use Travelan[®]?

Travellers' Diarrhoea can occur anywhere, but the highest-risk destinations are in Asia, India, the Middle East, Africa, Mexico, Central and South America⁹. In addition, areas where hygienic practices and sanitation are poor are also high-risk⁶.

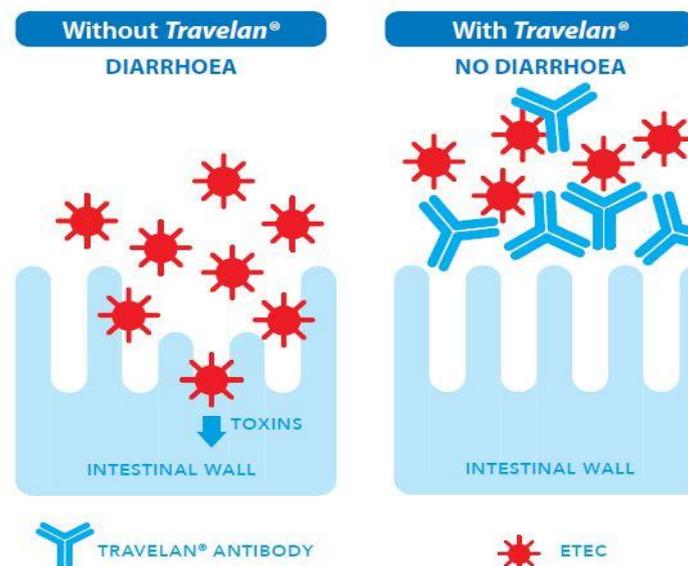


How does Travelan® work?

Travelan® contains high levels of antibodies that target pathogenic bacteria such as *E.coli* (ETEC) and the toxins they produce in the gut. Travelan® binds to and neutralises pathogenic bacteria, allowing them to be eliminated from the GI tract before they can colonise, multiply, leak into the bloodstream and cause Travellers' Diarrhoea.

Should you contract Travellers' Diarrhoea, Travelan® can also help to decrease its symptoms such as abdominal cramping and gastrointestinal pain.

Travelan®'s mechanism of action:



Clinical studies have shown protection of up to 90% from *E.coli* (ETEC) in those taking Travelan®¹⁰.

How Travelan® helps to support healthy gastrointestinal function

Travelan® binds to and neutralises pathogenic bacteria and their endotoxins, allowing them to be eliminated from the GI tract before they can trigger inflammation and disrupt healthy GI function. In doing this, Travelan® also helps to restore friendly gut flora, enhance good bacteria growth, maintain GI mucosal membrane health, reduce mild GI tract inflammation and assist in the repair of the gut wall lining^{10,13}.

Travelan® is antimicrobial but not an antibiotic. It will not cause dysbiosis of the gut microbiome like antibiotics do or cause bacterial antibiotic resistance, an increasing concern for medical authorities¹.

How Travelan® helps to enhance immune defense

Travelan® is rich in nutrients and immune components which can enhance immune defense by protecting against a wide range of infectious disease-causing pathogens.^{11, 12} These same ingredients may also enhance general health and wellbeing.¹⁴

Scientific Evidence

Clinical trials of IMM-124E (the active pharmaceutical ingredient used in Travelan®)

Travelan® underwent independent double-blinded placebo-controlled *E.coli* (ETEC) challenge trials in Europe and the USA. The trials showed protection of up to 90% against infection with *E.coli* (ETEC) and the development of Travellers' Diarrhoea. Participants who took dose regimens of 1 caplet (200 mg) and 2 caplets (400 mg) of Travelan® three times a day had significantly less discomfort and diarrhoea compared to those who did not receive Travelan®¹⁰.

The safety of Travelan® is also supported by a phase II study which examined doses of up to 3600 mg/day for 24 weeks¹³.

In vitro & pre-clinical studies of IMM-124E (the active pharmaceutical ingredient used in Travelan®)

Various in vitro studies have shown that the antibodies in Travelan® can bind to a wide range of pathogenic gram-negative bacteria and the toxins they produce. The U.S. Department of Defense (DoD) conducted two studies using bacteria samples retrieved from infected personnel deployed in Southern Asia. The first study demonstrated that Travelan® was able to bind and react to all 180 samples of pathogenic bacteria tested, including *Campylobacter*, *ETEC (E.coli)* and *Shigella*¹⁵. The second study found that Travelan® was able to bind and react to all 71 samples of *Vibrio cholera* tested¹⁵. Other studies conducted by Immuron's Research partners have demonstrated that Travelan® was also able to bind and react to pathogenic strains of *Salmonella* and *Klebsiella*¹⁶.

Furthermore, in a pre-clinical study conducted by the US DoD, Travelan® was shown to reduce the risk of infection with a pathogenic strain of *Shigella* in non-human primate challenge trials. All 100% (4 of 4) placebo treated animals displayed acute clinical signs of dysentery within 24 - 36 hours of a *Shigella* challenge. Only 2 of the 8 Travelan® treated group displayed any signs of dysentery. The remaining 75% (6 of 8) of the Travelan® treated group remained healthy and without signs of dysentery post challenge¹⁵. Histopathological analysis, which provides a comprehensive view of the clinical disease and its effect on tissues of the gut, revealed that all animals in the placebo-treated group displayed severe inflammation in different parts of the gastrointestinal tract. Only 3 of the 8 Travelan® treated animals had signs of inflammation in the gastrointestinal tract. All other animals in the Travelan® treated group were clinically healthy and overall, the results suggest that Travelan® is functionally cross-reactive and may have some prophylactic activity against Shigellosis¹⁵.

Pre-clinical studies were conducted to investigate the anti-inflammatory potential of Protectyn® in two mouse models of colitis. The results demonstrated that oral treatment with Protectyn® significantly reduces intestinal inflammation and confirmed that the administration of Protectyn® may represent a novel therapeutic strategy to induce or maintain remission in chronic colitis¹⁷.

In another pre-clinical study stool samples were collected from mice treated with either Travelan® or placebo for microbiome analysis. This mouse model demonstrated that Travelan® increased the abundance of potential gut-beneficial bacteria, such as the genus *Akkermansia*, and reduced *Clostridium* (Clade III) without disrupting the underlying ecology of the gastrointestinal tract¹⁸.

What is dairy Bovine Colostrum Powder (BCP)?

Colostrum is the first milk given by a cow after calving. Travelan[®] is produced by harvesting colostrum from the first milking of dairy cows that have been specifically immunised with proprietary vaccines manufactured for Immuron. The vaccines have been specifically developed to produce high levels of antibodies against selected surface antigens from the most common strains of pathogenic *E.coli* (ETEC), a major causative agent of Travellers' Diarrhoea. It is this process that differentiates Travelan[®] hyperimmune BCP from other forms of BCP.

Only the first milk is collected and processed for Travelan[®] ensuring that Immuron hyperimmune bovine colostrum has the highest level of immunoglobulins.

How do you use Travelan[®]?

Travelan[®] is a caplet which should be taken orally before every meal.

Directions for use:

- Take one or two caplets before every meal, three times per day, starting 48 hours before travel and during the period of travel.
- Additional caplets may be taken when increased protection is required.
- Travelan[®] should be used in addition to good hygiene practices.

WARNINGS

If symptoms persist, talk to your health professional.

Seek medical advice if diarrhoea persists for more than 48 hours in adults and children over 6 years.

Travelan[®] contains cows' milk proteins, fat, lactose and added glucose: do not take Travelan[®] without advice from a healthcare professional if you have an allergy to milk or bovine proteins or a lactose intolerance. Symptoms may include digestive problems, such as bloating, constipation, diarrhoea or gas¹⁹.

Travelan[®] contains calcium: if taking oral Tetracycline, do not take Travelan[®] without advice from a healthcare professional.

Travelan[®] contains glucose: if you have diabetes you should seek independent medical advice before using this product.

For children under 6 years of age consult your medical practitioner²⁰.

Travelan[®] is not on the TGA pregnancy database. However, Travelan[®] has not been specifically tested on pregnant and nursing mothers. It is recommended that pregnant and nursing mothers should seek independent medical advice before using this product.

If you have a history of cancer, consult a healthcare professional before using this product.

If you have liver or kidney disease or have been instructed to follow a low protein diet, consult a healthcare professional before using this product.

If you suffer from an immune system disorder (e.g. HIV/AIDS) consult a healthcare professional before using this product.

What to do if you contract Travellers' Diarrhoea

The major cause of Travellers' Diarrhoea is *E.coli* (ETEC) however it may also be caused by other bacteria, viruses or parasites.

If you get the symptoms of Travellers' Diarrhoea when taking Travelan[®], other appropriate treatment should be started in addition to consulting a healthcare professional. Dehydration is the main risk associated with Travellers' Diarrhoea. The recommended treatment for dehydration is to rest and drink plenty of clean water (up to about 2L or 8 1/2 cups a day) including specific rehydration fluids containing salts (electrolytes) and glucose (if allowable for your health condition).

Consult a healthcare professional if symptoms of Travellers' Diarrhoea persist for over 48 hours or if the symptoms include any of the following: dehydration, a persistent temperature over 39°C, blood or mucus in the stool, or severe abdominal or rectal pain.

Adverse Events (AEs)

The safety and efficacy of 2 dose levels of Travelan[®] were evaluated in a phase 2, randomised, double-blind, placebo-controlled, 3-arm parallel group, multidose, multicentre study. Subjects were randomised into 3 treatment arms, Travelan[®] 600 mg (n=46) or 1200mg (n= 43) or high milk protein placebo (n=44) 3 times daily for 24 weeks. No treatment related deaths or serious adverse events (SAEs) were reported, and safety measures (e.g., clinical chemistry, hematology, electrocardiogram [ECG]) remained stable across each treatment group¹³. Overall laboratory, vital signs, and physical exam data did not display any differential patterns and remained constant throughout the study regardless of treatment group, suggesting that safety concerns regarding Travelan[®] are minimal. Treatment-related AEs were primarily GI disorders consistent with milk allergy ¹⁹ (e.g., abdominal pain, constipation, diarrhea, flatulence, nausea and vomiting), with relatively equal percentages across all three treatment groups (including placebo)¹³.

Storage

Store below 25°C. Refrigeration is not required.

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This document was prepared in April 2021

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