

## Consumer Product Information for Protectyn®

**Active ingredient:** Dairy (bovine) colostrum powder containing high levels of Anti-LPS antibodies.

### What is Protectyn® used for?

Protectyn® is an oral biopharmaceutical product that is scientifically formulated to contain high levels of active antibodies. These antibodies target pathogenic bacteria and the harmful lipopolysaccharide (LPS) toxins they produce in the gut, reducing their ability to disrupt the healthy function of the gut, liver and immune system.

Protectyn® helps to:

- Enhance healthy digestive system function and enhance gastrointestinal system health.
- Promote good bacteria growth and restore friendly gut flora.
- Maintain liver health and support healthy liver function.
- Reduce mild gastrointestinal tract inflammation.
- Maintain healthy gastrointestinal mucosal membrane health.
- Aid and assist in the repair of the gut wall lining and
- Enhance immune defence and support healthy gastrointestinal immune function.

### What is the natural\* medical ingredient in Protectyn®?

The drug product contains 200 mg of hyperimmune bovine colostrum\* formulated as a 700 mg solid oral tablet. The 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?

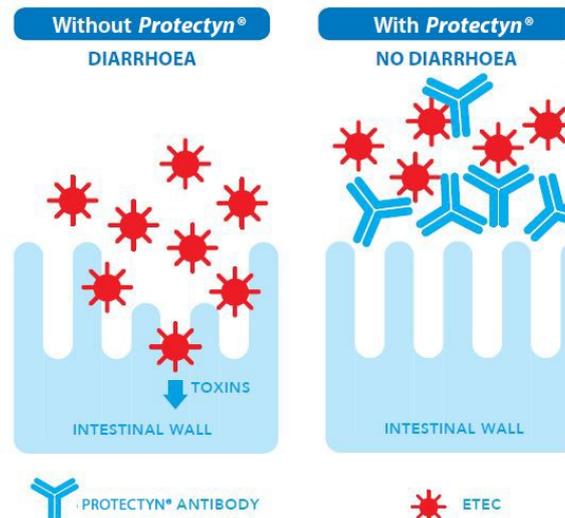
Colloidal silicone dioxide, croscarmellose sodium, glucose, magnesium stearate and microcrystalline cellulose.

### How Protectyn® helps to maintain healthy gastrointestinal function

Commensal (“good”) bacteria have a significant role in the maintenance of intestinal epithelial cell (IEC) homeostasis. The interaction of LPS toxins with its receptor (TLR4) in the gastrointestinal tract has been demonstrated to initiate acute inflammatory responses in mammals<sup>1</sup>.

Protectyn® contains high levels of antibodies that target pathogenic bacteria and the LPS toxins they produce in the gut. Protectyn® binds to and neutralises these bacteria and their toxins, allowing them to be eliminated from the GI tract before they can colonise, multiply, leak into the bloodstream and disrupt the digestive system. Clinical studies have shown protection of up to 90% from *E.coli* (ETEC) in those taking Protectyn®<sup>2</sup>.

Mechanism of action for Protectyn®:



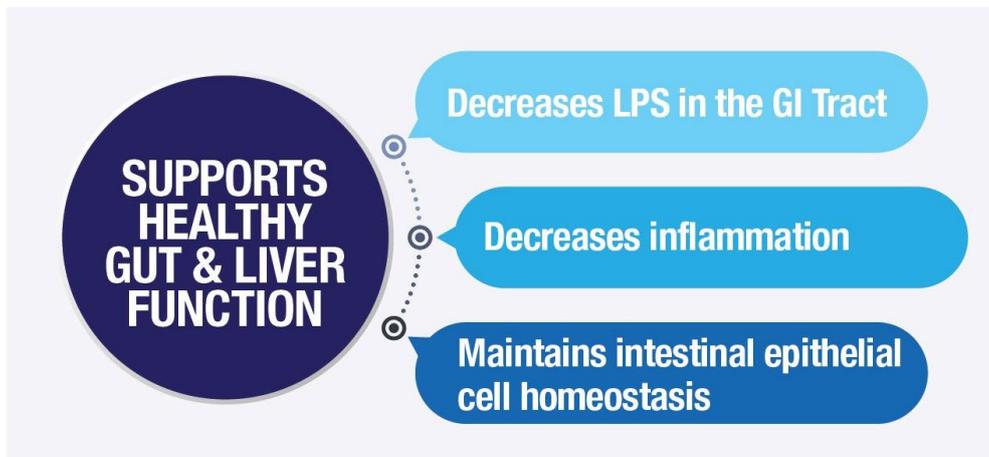
Protectyn® can help to restore friendly gut flora, enhance good bacteria growth, maintain GI mucosal membrane health, reduce mild GI tract inflammation and assist in the repair of the gut wall lining<sup>2,3,4,10</sup>. Protectyn® is antimicrobial but not an antibiotic. It will not cause dysbiosis of the gut microbiome like antibiotics do or cause bacterial antibiotic resistance, an increasing concern for medical authorities<sup>5</sup>.

## How Protectyn® helps to support liver health

The presence of LPS toxins in the body can induce inflammation and have a detrimental effect on liver health<sup>6</sup>. Under normal circumstances LPS remains contained within the confines of the GI tract and causes no pathology. LPS toxins can gain access to the circulatory system via a multitude of routes and can then leak into the surrounding tissues and initiate inflammatory processes. In situations where there is no obvious physical breach of GI barrier integrity, LPS can translocate across the barrier by being absorbed with the digestion of lipids associated with a high fat diet.<sup>7,8</sup>

By targeting and removing harmful LPS toxins in the gut, Protectyn® helps to:

- Support liver health<sup>9</sup> and
- Enhance and maintain healthy liver function<sup>9</sup>



## How Protectyn® enhances immune defense

Protectyn® is rich in nutrients and immune components which can enhance immune defense by protecting against a wide range of pathogenic bacteria and the toxins they produce.<sup>10, 11</sup>

## What are Lipopolysaccharide (LPS) toxins and Gut Dysbiosis?

The human gastrointestinal tract or gut is naturally colonised by trillions of bacteria<sup>12</sup>. These bacteria play an important role in human health, aiding digestion, metabolism and supporting the immune function<sup>6,13</sup>. Collectively, these microorganisms are known as intestinal microbiota and they are essential to the normal function of the gut<sup>14</sup>.

Gut dysbiosis occurs when the ratio of good (commensal) and bad bacteria in the gut becomes imbalanced. It can be caused by many factors such as poor diet, alcohol consumption, poor dental hygiene, lack of sleep, stress, antibiotic use and even disease<sup>15,16</sup>. Once the gut microbiota is altered, pathogenic bacteria such as *E.coli* may over colonise the gut and release the toxic by-product known as LPS or endotoxins.<sup>17,18</sup>

Increasing scientific evidence suggests that LPS is a potent activator of inflammatory responses in the body. Inflammation has been linked to many intestinal conditions including Inflammatory Bowel Disease (IBD)<sup>19</sup> as well as dysfunction of the organs such as the liver.<sup>9,12,6,20-25</sup>

## What is Leaky Gut Syndrome / Bacterial Translocation?

Tight openings in the intestinal walls allow nutrients to pass through into the bloodstream while keeping harmful substances such as bacteria and their toxic LPS by-products inside. Leaky Gut Syndrome occurs when these openings become wider, allowing food particles, bacteria, and toxins to enter directly into the bloodstream<sup>26</sup>. It is believed that impaired gut epithelial integrity may be the underlying cause for bacterial translocation.<sup>27</sup> Symptoms may include, but are not limited to, constipation, diarrhoea, bloating, nutritional deficiencies, fatigue, headaches, eczema, joint pain, difficulty concentrating and widespread inflammation<sup>26</sup>.

## Scientific Evidence

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

Protectyn® 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 diarrhoea. Participants who took dose regimens of 1 caplet (200 mg) and 2 caplets (400 mg) of Protectyn® three times a day had significantly less discomfort and diarrhoea compared to those who did not receive Protectyn®<sup>2</sup>.

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

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 colitis<sup>3</sup>.

In another pre-clinical study stool samples were collected from mice treated with either Protectyn® or placebo for microbiome analysis. This mouse model demonstrated that Protectyn® 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 tract<sup>4</sup>.

Various in vitro studies have shown that the antibodies in Protectyn® 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 Protectyn® was able to bind and react to all 180 samples of pathogenic bacteria tested, including *Campylobacter*, *ETEC (E.coli)* and *Shigella*<sup>28</sup>. The second study found that Protectyn® was also able to bind and react to all 71 samples of *Vibrio cholera* tested<sup>28</sup>. Other studies conducted by Immuron's Research partners have demonstrated that Protectyn® was also able to bind and react to pathogenic strains of *Salmonella* and *Klebsiella*<sup>29</sup>.

Furthermore, in a pre-clinical study conducted by the US DoD, Protectyn® 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 Protectyn® treated group displayed any signs of dysentery. The remaining 75% (6 of 8) of the Protectyn® treated group remained healthy and without signs of dysentery post challenge<sup>28</sup>. 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 Protectyn® treated animals had signs of inflammation in the gastrointestinal tract. All other animals in the Protectyn® treated group were clinically healthy and overall, the results suggest that Protectyn® is functionally cross-reactive and may have some prophylactic activity against Shigellosis<sup>28</sup>.

## What is dairy Bovine Colostrum Powder (BCP)?

Colostrum is the first milk given by a cow after calving. Protectyn<sup>®</sup> 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 infectious diarrhoea. It is this process that differentiates Protectyn<sup>®</sup> from other forms of BCP.

Only the first milk is collected and processed for Protectyn<sup>®</sup> ensuring that Immuron hyperimmune bovine colostrum has the highest level of immunoglobulins.

## How do you use Protectyn<sup>®</sup>?

Protectyn<sup>®</sup> 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 or as directed by your healthcare practitioner.

## 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.

Protectyn<sup>®</sup> contains cows' milk proteins, lactose and added glucose: do not take Protectyn<sup>®</sup> 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 gas<sup>30</sup>.

Protectyn<sup>®</sup> contains calcium: if taking oral Tetracycline, do not take Protectyn<sup>®</sup> without advice from a healthcare professional.

Protectyn<sup>®</sup> 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 practitioner<sup>31</sup>.

Protectyn<sup>®</sup> is not on the TGA pregnancy database. However, Protectyn<sup>®</sup> 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.

### Adverse Events (AEs)

The safety and efficacy of 2 dose levels of Protectyn<sup>®</sup> 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, Protectyn<sup>®</sup> 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 group<sup>32</sup>. 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 Protectyn<sup>®</sup> are minimal. Treatment-related AEs were primarily GI disorders (e.g., abdominal pain, constipation, diarrhea, flatulence, nausea and vomiting), with relatively equal percentages across all three treatment groups (including placebo)<sup>32</sup>.

### Storage

Store below 25°C. Refrigeration is not required.

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This document was prepared in April 2021.

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