Tēnā koutou e te Komiti,

Submission from Crohn's and Colitis New Zealand Charitable Trust

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Dear Panel Members:

While the following is just one example of how Pharmac fails in "creating better health outcomes for New Zealanders", it is very representative of the countless and repeated failures of the agency raised by patient groups and professional organisations over the last several years. At the end of this example is a summary and list of our recommendations to the Panel. Note that the professional members of Crohn's and Colitis NZ Charitable Trust serve in a voluntary capacity, and are presenting this submission only in the interest of bringing the health care of New Zealanders up to the basic standards of other OECD countries.

In sharing this example, we need to first explain some basics about Crohn's disease and ulcerative colitis and their treatment. Following this is a discussion about our serious concerns about Pharmac's funding decisions.

At the end of this discussion we present our most important recommendations as medical practitioners to the Panel.

What are Crohn's disease and ulcerative colitis (collectively known as inflammatory bowel disease or IBD)?

Crohn's disease and ulcerative colitis are chronic, incurable diseases that attack to the intestines. The large and small intestines become red, swollen, and ulcerated. Often fistulae form which are tunnels between the intestines and the skin which then drain stool, blood, and pus, usually from small openings around the anus. Symptoms of bloody diarrhoea, debilitating abdominal pain, and weight loss are common. Over time, the intestines can become severely scarred and narrowed from the inflammation which can cause blockages requiring urgent surgery. There is also an array of "extra-intestinal" manifestations, including liver disease, sometimes requiring transplant surgery, skin involvement, arthritis, and serious eye involvement. There is also a significant increased risk of bowel cancer.

Who are affected by these diseases?

The impact of these diseases is compounded by the fact that Crohn's disease and ulcerative colitis most often affect the young, when they are in the middle of their schooling, when they are starting their careers, or raising young families. These diseases can even present in infancy. Twenty percent of patients are children and teens. And, for those who are diagnosed, they will be burdened with these illnesses for their entire lives. New Zealand has the third highest prevalence[1] of these diseases in the world, and the incidence is increasing.[2,3] 20,000 people are affected.

How were these diseases treated prior to 2009 in New Zealand?

Treatment rests on suppressing the immune system since the immune system is responsible for the inflammation in the intestines. In Crohn's disease and ulcerative colitis, the body literally attacks itself.

Suppressing the immune system requires medications that have multiple side effects. For years, doctors struggled to treat patients with steroids and other drugs called immunosuppressants that are also used

in chemotherapy to treat cancer patients. For those patients who did not respond to medications, surgery is the only recourse.

Surgery for ulcerative colitis involves removing the entire colon (large intestine), requiring either an ileostomy bag or reconstructive surgery to connect the small intestine to the anus. Surgery for Crohn's disease requires removing areas of affect bowel, also often resulting in a permanent ileostomy bag. Despite surgery, Crohn's disease always returns.

How did treatment for many of the sickest patients with IBD change with the introduction of "biologicals"?

In 1998, there was a breakthrough in medical options. A new class of medications, called "biologics" or "biologicals" became available. They worked by inactivating a protein called "TNF" which triggers inflammation in the body. Two "anti-TNF" medications came to market: adalimumab (Humira) and infliximab (Remicade). For many patients they were exceedingly effective[4,5], ***although New Zealanders had to wait until after 2009 for them to be finally funded.***

What happens if the "anti-TNF" medications don't work or stop working?

Unfortunately, even if adalimumab and infliximab work initially, they stop working for about half of patients within five years. The reason is that a person's body can develop antibodies to the drugs which renders them ineffective[6]. In frustration and without other options, doctors will often double the dosage of these medications (at twice the cost), hoping they might help, to avoid life-altering surgery. This strategy, while often employed, doubles the expense and rarely works[7].

In 2016 the FDA approved a new biological medication for the treatment of Crohn's disease. It has a different mechanism of action than the anti-TNF medications. It blocks different protein mediators of inflammation called "interleukins". It has the potential to help people who never responded to the anti-TNF medications in the first place and those who developed antibodies. It gives patients another chance to achieve remission and avoid surgery and a life with an ileostomy bag. This medication is called ustekinumab (the brand name is Stelara). Ustekinumab has been fully funded for people with Crohn's disease in Australia since 2017. It is also fully funded in 36 other countries throughout the Western world. Another biological medication, vedolizumab, which has another mechanism of action is also available throughout the world. It is currently undergoing review by Medsafe.

People in New Zealand with Crohn's disease and ulcerative colitis have not had any funding for new medications since 2009 (note that infliximab was available through DHB's in 2007, but rarely approved for patient use. Funding was not widely available until 2009).

Table 1: Comparison of access to new drugs for IBD between New Zealand and other countries, including IBD incidence and prevalence.

Drug	New Zealand	Australia	United Kingdom	Canada	Spain	Israel
Infliximab	2007	2007	2002 (CD) and 2008 (UC)	2001	2000	2000
Adalimumab	2009	2008	2003	2004	2003	2008
Golimumab	Not funded	2017	2010	2013	2014	2012
Certolizumab	Not funded	Not funded	Not funded	Not funded	2014	2014
Vedolizumab	Not funded	2015	2015	2014	2015	2015
Ustekinumab	Not funded	2017	2017	2016	2017	2017
Tofacitinib	Not funded	Positive PBAC[1] recommendation likely 2020	2018	2018	2018	2018
Estimated IBD prevalence	0.5% (~)	0.3% (~)	0.5% (310,000)	0.7% (300,000)	Unknown	0.4% (35,000)
IBD incidence (cases/100,000)	39	37	26	52	35	30
OECD[2] ranking of gross domestic product per capita	20	10	16	15	24	22

[1]PBAC = Pharmaceutical Benefits Advisory Committee.
[2]OECD= Organisation for Economic Co-operation and Development.

Is there evidence that these drugs work and is a petition to obtain funding supported by New Zealand's gastroenterology specialists?

Yes. There is compelling Phase 3 trial efficacy data[8-11], multiple cost utility analyses[12-14] and real-world data from many countries[11,14-16] Furthermore, despite positive recommendations as a "high priority" medication from PHARMAC's own Pharmacology and Therapeutics Advisory Committee's Gastrointestinal Sub-committee (which exists to provide objective evidence to Pharmac[17,18]), these drugs are still not funded[19] [from NZJM, by permission of authors, appendix 2]

PHARMAC has repeatedly ignored their own experts' advice. The New Zealand gastroenterology community is of the opinion that PHARMAC's methods are faulty and based on incomplete data. Over 100 gastrointestinal specialists in New Zealand have strongly endorsed a petition, currently sitting in Parliament, to fund ustekinumab. That petition has over 30,000 signatures.

We are also aware that Pharmac, using selective data of its own choosing (which they do not release), has made the determination that the newer biologicals are "not cost-effective" and, hence, do not warrant funding. It is curious that Pharmac's data and decisions run counter to funding decisions

throughout the rest of the world: in Australia, the United Kingdom, Canada, and thirty four other countries, most of which rank below New Zealand in terms of GNP/capita.

Importantly, Pharmac does not take into account the cost and real-life quality of life ramifications of denying newer biologicals to patients who do not respond to the two medications that are currenty funded. People who are denied these newer medications, generally those with the most severe disease, have repeated hospitalisations, ED visits, are unable to work or care for their families, and often end up living with ileostomies (bags). Most of these patients are children, teens, and young adults under the age of 35.

Professor Richard Gearry, one of New Zealand's most distinguished medical researchers, Academic Head of the Department of Medicine at University of Otago, Christchurch, recipient of the Gold Medal for Research at the University, who has published over 160 scientific papers, Christchurch, writes:

"Pharmac states that they use best practice to assess the cost and benefit of introducing new medicines and that their methods are applied equally across all patient groups. However, it has become clear to scientists, doctors, and researchers that the methodology that they use is deeply flawed. Firstly, the direct costs associated with IBD are high, with hospitalisation for flares of active disease and complications common. These expensive costs are greater than for similar inflammatory diseases which are afforded more new drugs. When existing drugs do not work, double dosing is allowed which leads to double the cost. This is often less effective than a new drug would be. Therefore, patients cost twice as much to treat, but seldom do they attain remission. Although specifically allowed by Pharmac, when asked how many patients in NZ are being double dosed with infliximab for IBD, they have been unable to provide an answer and have asked gastroenterologists if we can provide this to them. It is inconceivable how Pharmac can make a fair and balanced cost effectiveness decision on IBD drugs when it admits to having no understanding of the current cost of the drugs, many of which are not working."

The entire gastroenterology medical community is appealing to the Panel to help correct this situation which affects the lives of so many New Zealanders. New Zealand has one of the highest rates of these diseases in the world. We should be leaders in providing effective medical treatment, rather than being singled out as an outlier across the world on how we treat our patients[19]. In our example, we maintain that the funding of at least one new biological for IBD patients will be highly cost-effective, not even taking into account quality of life issues. The fact that our patients are suffering runs counter to Pharmac's main purpose, that of ensuring "best health outcomes".

We are hopeful that the panel will do an in depth review of Pharmac's processes, specifically to address our concerns that their methodology is, in Professor Geary's words, "deeply flawed".

Summary:

As noted at the beginning of this submission, the above example is very representative of countless and repeated concerns raised by several patient and professional groups about Pharmac's practices. Pharmac's data is often incomplete and their decision-making processes do not fully consider the economic and social implications of denying standard of care treatment to New Zealanders. Their methods lack any semblance of transparency. There are no public minutes regarding their decisions, we do not have access to their rankings or timeline of drugs awaiting funding, and there is no standardised pathway in determining what treatments warrant funding.

Crohn's and Colitis New Zealand is a charitable trust, governed by a volunteer Board of medical professionals and consumers. We have been meeting regularly with representatives of Pharmac for the past several years. We have actively participated in Pharmac's consultative processes and are very well versed in the steps required for eventual funding of medications. We keep up to date on all of

Pharmac's publications, in particular the recommendations of the Gastrointestinal PTAC sub-committee. What happens afterwards, however, is not transparent. Decisions are often not based on best health outcomes, but seem to be clouded by extraneous considerations that involve negotiations with pharmaceutical companies, bundling of medications, and incomplete data such as described by Professor Gearry above. Engagement with medical professionals and consumers, who meet with Pharmac in good faith, seems to have no bearing on their decisions.

Additionally, Pharmac's repeated failures to fund medications that are regularly funded throughout the developed world creates huge inequities in our health care system. Despite our country's self-mandate to assure equity in health care, particularly for Maori, Pacifika, and our disabled populations, those with the ability to self-fund their treatments are rewarded with a better quality of life. The rest of the population simply does without.

Finally, Pharmac operates in a reactive manner. Treatments are usually funded years after they have been shown to be efficacious throughout the rest of the world, and often not until the consequences of not funding these treatments becomes glowingly apparent. We should have a health care system that is proactive in finding the best proven therapies as soon as they become available.

From the standpoint of a medical practitioner who has been in practice since the early 1980's, the practice of medicine and available therapies has changed dramatically since Pharmac was founded almost thirty years ago. There have been tremendous advances, but at an economic cost. While funding is not to be considered by the panel, asking Pharmac to operate within a fixed budget, places the agency in an untenable position in fulfilling its mission. The system needs to be overhauled.

We make the following recommendations:

1) That Pharmac or an independent agency of medical professionals and economists, not politicians, submit an annual budget which realistically reflects the resources necessary to assure the agency can fulfil its objectives.
2) That there be complete transparency with professionals and consumers. It hardly bears mentioning that the Panel should familiarise itself with how similar agencies function in other countries. The U.K.'s National Institute for Care and Health Excellence (NICE) is a good point of reference for comparison. Their emphasis is on being proactive and transparent in providing best health outcomes for their citizenry, based on objective data and input from professionals and consumers. Below is a link to their 2021-2026 strategy.

   https://static.nice.org.uk/NICE%20strategy%202021%20to%202026%20-%20Dynamic,%20Collaborative,%20Excellent.pdf

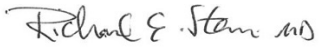
3) That there be a mechanism for professionals or patient groups to appeal Pharmac's determinations via an independent body of medical researchers, practitioners, and economists, who have the skills necessary to provide an objective review, factoring in real quality of life data and future economic costs. They should not have to resort to petitioning Parliament or appealing to the media to try to get access to basic health care.
4) As this is the first review of Pharmac since its inception 27 years ago, we ask that the Panel request enough time and resources to thoroughly review the agency.

I need to note at the end of this written submission that the professional members of Crohn's and Colitis NZ have repeatedly asked, over the past two months, for a face-to-face meeting with the five member panel. Our professional members include Professor Richard Gearry, Academic Head of the Department of Medicine, University of Otago, Christchurch, and Professor Michael Schultz, researcher and Head of the Department Medicine of University of Otago, Dunedin. These experts have been willing to re-

arrange their clinical and teaching activities to meet with the full panel to more fully explain their concerns and answer questions.

Thank you for the opportunity to present this submission.

Respectfully,



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