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Why does Pharmac neglect inflammatory bowel disease?

Andrew McCombie, Malcolm Arnold, Marian O'Connor, Richard Stein, James Fulforth, Belinda Brown, Richard Gearry

Crohn's disease (CD) and ulcerative colitis (UC), collectively known as inflammatory bowel disease (IBD), are chronic, incurable, inflammatory diseases. Symptoms are severe and include bloody diarrhoea, abdominal pain, fatigue and inflammation in the anal area; extraintestinal comorbidities can also occur, including arthritis, liver disease, iritis and skin lesions. CD and UC follow a relapsing and remitting course and in times of flare can lead to hospitalisation, often coupled with abdominal and perianal surgery, followed by varying periods of recovery. New Zealand has the third highest prevalence of IBD in the world,[1] and the incidence is still increasing.[2,3] A burden-of-disease report published in 2017 reported that IBD costs New Zealand an estimated $245,000,000 in healthcare costs and lost productivity.[1]

What IBD treatments are presently available in New Zealand?

Treatments for IBD have improved over recent years, moving from corticosteroids to immunomodulators (such as azathioprine, mercaptopurine and methotrexate) to biological therapies. Biological therapies, such as the anti-tumour necrosis factor (anti-TNF) drugs infliximab and adalimumab, have made a significant difference to the lives of patients with IBD.[4,5] For many this has reduced steroid use, hospitalisation and surgery. However, not everyone responds to anti-TNF drugs, and others lose response after a period of time due to anti-drug antibodies and refractory disease.[6]

Patients who lose response to anti-TNF drugs are left with few medical options. Enduring ongoing symptoms leads to a reduced quality of life, a reduced ability to attend education and work and an increased healthcare utilisation. Many patients will require a bowel resection and some will require a permanent stoma, often at a young age.

Faced with few other options, New Zealand gastroenterologists often trial double dosing of either infliximab or adalimumab when patients lose response to standard doses. This can be effective for some but incurs a doubling of cost and an increased risk of adverse effects. Furthermore, many patients may not respond completely.[7]

What other options are available?

Internationally there are numerous other drugs available (Table 1) for the treatment of IBD. Many of these drugs are funded by countries with a lower OECD ranking than New Zealand. The two most established drugs are ustekinumab (approved in New Zealand by Medsafe in early 2018) and vedolizumab (currently awaiting Medsafe registration). Importantly, these drugs have a different mechanism of action to the anti-TNF drugs, meaning that patients who do not respond to an anti-TNF drug will be more likely to respond to either ustekinumab or vedolizumab, rather than another anti-TNF drug. Ustekinumab blocks the interleukin (IL)-23/12 receptor, leading to a reduced inflammatory response. Vedolizumab provides gut-specific immunosuppression by blocking α4β7 integrin, leading to a reduction in leucocyte trafficking to areas of inflamed gut. Both

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drugs have been shown to be safe, efficacious and cost effective, including in patients who have lost response to anti-TNF drugs. They are available and funded in most western countries.

Despite compelling Phase 3 trial efficacy and safety data,[8–11] multiple supportive cost utility analyses[12–14] and real-world data from many countries,[11, 14–16] New Zealanders with IBD do not have access to these drugs. Furthermore, despite positive recommendations from the Pharmacology and Therapeutics Advisory Committee's Gastrointestinal Sub-committee (which exists to provide objective evidence to Pharmac)[17,18] and intensive lobbying from the New Zealand Society of Gastroenterology, Crohn's and Colitis New Zealand and the New Zealand IBD Nurses Group, Pharmac refuses to fund these drugs.

How does this compare to other diseases?

Pharmac has been celebrated as a successful organisation that has reduced the cost of buying pharmaceuticals for New Zealanders. However, there is also a dark side to the current Pharmac decision-making model for drug funding. There are now major inequities in access to drugs for different diseases. Over time, the lack of investment in new drugs has left New Zealand patients with some diseases worse off than others. For example, IBD is often grouped with a number of rheumatological diseases (eg, rheumatoid arthritis and ankylosing spondylitis) and psoriasis as immune-mediated inflam-

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.

matory diseases (IMIDs). As shown in Table 2, ongoing investment in treatments for rheumatological diseases and psoriasis has continued over time, whereas no new drug has been funded for IBD since 2009. This is despite the availability of new drugs and the documented multifactorial impact of IBD on patients and the healthcare system. Furthermore, in recent years the cost of infliximab and adalimumab have fallen substantially, with no reinvestment of the resultant savings into these diseases.

Unlike other IMIDs, IBD is a frequent cause of hospital admission, surgery and unplanned care, including emergency department visits. Furthermore, patients are, on average, younger than those with other IMIDs yet have at least as much disability, work impairment, educational disruption and psychological distress.[19] Recently, the paediatric IBD population was shown to be at an increased risk of suicide,[20–22] which aligns with similar reports for the adult population.[23]

What are the consequences of not funding new therapy?

As Pharmac ignores these mainstream treatments, it is patients and their families who are faced with less-desirable alternatives, including invasive surgery that often leads to permanent stoma, repeat hospitalisations, prolonged steroid use with associated adverse effects and, perhaps worst of all, a need to live with devastating and embarrassing symptoms that keep them away from work, study and social and interpersonal relationships. Despite patients with IBD having fewer educational opportunities and increased difficulty maintaining their employment and sometimes their relationships,[1] Pharmac continues to ignore these indirect costs.

Recently, a meeting was held between Dr Malcolm Arnold (President, NZSG), Professor Richard Gearry (gastroenterologist) and Pharmac staff via Zoom at 3pm on Monday 31 August 2020. It is telling that when questioned about the frequency of double dosing of infliximab for patients with IBD and how this would affect cost–utility analyses for new drugs, Pharmac staff admitted that they do not have these data and do not know how often double dosing occurs, nor whether it is effective. They did admit that double infliximab dosing would cost twice as much as standard dosing. It is disturbing that Pharmac continues to deny New Zealand patients effective treatments despite not having collected the crucial data on which to base these decisions.

Conclusion

In our opinion, at the very least, new medical therapies should be funded by Pharmac for patients who fail to respond to, or lose response to, anti-TNF therapy. Gastroenterologists, IBD nurses and patients in New Zealand have grown increasingly frus-

Table 2: Comparison of funded drugs for immune mediated inflammatory diseases in New Zealand.

Drug	Rheumatology (RhA, AS, JA)[1]	Dermatology (psoriasis)	Gastroenterology (IBD)
Infliximab	Registered by Medsafe in 2000. Individual DHB funding with variable use across specialties since mid-late 2000s		
Adalimumab	RA 2006; AS/PsA 2009; JA 2013	2009	2009
Etanercept	<2003	Not effective	Not effective
Rituximab	2013	Not effective	Not effective
Tocilizumab	JA 2013; RA 2014	Not effective	Not effective
Secukinumab	Not effective	2018	Not effective (may worsen)

[1]Rha=Rheumatoid Arthritis; AS=Ankylosing spondylitis; JA=Juvenile arthritis.

trated with the treatment of IBD being well behind the rest of the western world and the inequity with which IBD is treated compared with other diseases in New Zealand. A petition "That the House of Representatives urge the Government to provide funding for the drug ustekinumab to be made available to those New Zealanders with severe Crohn's disease and ulcerative colitis, for whom all other funded medical treatments have failed" (https://www.wecantwait.nz/) has so far garnered more than 30,000 signatures in less than two months. This was presented to parliament on 2 December 2020. It is time for patients with IBD, and the medical practitioners who endeavour to provide them with expert care, to be able to access treatments that are routinely available in other countries and for Pharmac to be held to account for the decisions they make and the way in which they make them.

Competing interests:
Nil.

Author information:
Andrew McCombie, Research Officer and Data Analyst,
Department of General Surgery, Canterbury District Health Board;
Honorary Senior Research Fellow, University of Otago, Christchurch;
Executive Committee Elected Member, New Zealand Society of Gastroenterology.
Malcolm Arnold, Consultant Gastroenterologist, Department of Gastroenterology,
Canterbury District Health Board; President of the New Zealand Society of Gastroenterology.
Marian O'Connor, Clinical Nurse Specialist, Taranaki District Health Board;
Co-chair of the NZ IBD Nursing Group, GENCA Board Director.
Richard Stein, Chairman, Crohn's and Colitis New Zealand Charitable Trust;
Clinical Senior Lecturer, University of Otago, Wellington.
James Fulforth, Consultant Gastroenterologist,
Department of Gastroenterology, Waikato District Health Board.
Belinda Brown, Operations Manager, Crohn's and Colitis New Zealand Charitable Trust.
Richard Gearry, Consultant Gastroenterologist, Department of Gastroenterology,
Canterbury District Health Board; Head of Department, Department of Medicine,
University of Otago, Christchurch.

Corresponding author:
Professor Richard Gearry, Consultant Gastroenterologist, Department of Gastroenterology,
Canterbury District Health Board; Head of Department, Department of Medicine, University
of Otago, Christchurch; P.O. Box 4345, Level 5,
2 Riccarton Avenue, Christchurch, +64 3 364 0530.
richard.gearry@otago.ac.nz

URL:
www.nzma.org.nz/journal-articles/why-does-pharmac-neglect-inflammatory-bowel-disease

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