Table 1: Most extensively prescribed medicines in the 2022/2023 financial year in New Zealand[34] used to identify the 10 most relevant medicines for treating acute conditions (ranked by annual number of prescriptions dispensed according to the national Pharmaceutical Management Agency of the New Zealand Government [Pharmac]).

Medicine	Therapeutic group (Pharmac)	Prescriptions (annual number)	Included in this study if relevant to acute treatment (even if also used for chronic disease management)
Paracetamol	Analgesics	3,460,000*	Yes—for acute pain relief; fever reduction (suitable for children)
Atorvastatin (statin)	Cardiovascular	1,840,000	No—since used for the prevention of cardiovascular disease (CVD)
Omeprazole (proton-pump inhibitor for heart burn/acid reflux)	Alimentary	1,690,000*	Yes—for acute gastritis and treating gastric ulcers
Amoxicillin (antibiotic)	Anti-infectives	1,230,000	Yes—for infections (potentially also life-saving e.g., severe bacterial pneumonia)
Ibuprofen (anti-inflammatory)	Analgesics	1,200,000*	Yes—for acute pain relief
Cholecalciferol (vitamin D)	Musculoskeletal	1,110,000*	No—typically used for prevention of osteoporosis
Aspirin	Antithrombotics	1,100,000*	Yes—for managing a heart attack or stroke (potentially life-saving); also (in adults) acute pain relief and fever control (low-dose aspirin is also used in non-acute disease management, i.e., for the secondary prevention of CVD)
Metoprolol succinate (an antihypertensive)	Cardiovascular	920,000	Yes—for managing acute cardiac conditions such as arrhythmias and heart failure (potentially life-saving); and for managing angina (it is also used in non-acute disease management, i.e., for treating high blood pressure, a risk factor for CVD)
Salbutamol (a bronchodilator)	Respiratory	860,000	Yes—for acute asthma attacks (potentially life-saving)
Levothyroxine (thyroid hormone)	Hormones	710,000	No—typically used for managing hypothyroidism. It is only life-saving in extremely rare forms of hypothyroidism, i.e., myxedema coma.
Prednisone (steroid)	Hormones	700,000	Yes—for severe allergic reactions, autoimmune crises and asthma attacks (potentially life-saving); acute management of chronic obstructive pulmonary disease, rheumatological conditions and other diseases
Cetirizine hydrochloride (antihistamine)	Antihistamines	690,000*	Yes—for allergic reactions; urticaria
Amlodipine (calcium channel blocker)	Cardiovascular	680,000	Yes—for certain types of angina (it is also used in non-acute disease management, i.e., for treating high blood pressure, a risk factor for CVD)

*Actual usage will probably be higher than suggested in this table as these particular pharmaceuticals are also sold over the counter in New Zealand, e.g., in pharmacies and/or supermarkets.

Table 2: Summary results relevant to potential New Zealand production capacity for the 10 selected pharmaceuticals after a trade-ending global catastrophe (see Table 1 and Table 3 for additional details).

Medicine (ranked as per Table 1)	Modern synthesis requires products from petrochemical refining that does not occur in New Zealand*	Modern synthesis requires other chemicals from compounds not produced in New Zealand	Modern synthesis requires catalysts from minerals not mined in New Zealand**
Paracetamol	Yes	No	Yes (platinum)
Omeprazole	Yes	No	Yes (molybdenum)
Amoxicillin	Yes	No	No
Ibuprofen	Yes	Yes (fluorite)	Yes (nickel, bauxite, palladium)
Aspirin	Yes	No	No
Metoprolol succinate	Yes	No	No
Salbutamol	Yes	Yes (lithium, bauxite)	Yes (palladium)
Prednisone	Yes	Yes (bauxite, chromite)	Yes (nickel, bauxite)
Cetirizine hydrochloride	Yes	Yes (borax)	No
Amlodipine	Yes	No	Yes (palladium)

*Excluding the production of methanol, which does occur in Taranaki.
**However, there could be scope for some minerals to be scavenged in a post-catastrophe environment, e.g., platinum and palladium from vehicle catalytic converters.

Table 3: More detailed results relevant to potential New Zealand production capacity for the 10 selected pharmaceuticals in a trade-ending global catastrophe situation (see Table 1 for additional details).

Medicine (ranked as per Table 1)	Year first produced commercially (globally)	Capacity to produce the necessary chemical ingredients and catalysts in New Zealand without trade
Paracetamol	1952[37]	We considered the modern continuous flow method for the synthesis of paracetamol involving hydrogenation, Bamberger rearrangement and amidation.[38] The raw materials for this synthesis (using the intermediate of p-aminophenol) mainly include nitrobenzene, p-nitrophenol and p-nitrosophenol.[38] These are all typically derived from petroleum products (i.e., benzene). The ingredient tetrahydrofuran is also typically derived from petroleum products, although it can also be made from furfural, a biomass-derived compound. Another ingredient, acetic anhydride,[38] is also typically derived from petroleum products, although methanol (which New Zealand produces) could in theory be used to produce it instead. While some ingredients could probably continue to be produced in New Zealand without trade (e.g., hydrogen gas and sulphuric acid), platinum (for the catalyst) is not mined in New Zealand. **Assessment:** Probably no capacity due to there being no petrochemical refining in New Zealand and no mining of platinum in New Zealand. However, for this catalyst (and some others in this table), post-catastrophe scavenging might be possible, e.g., from vehicle catalytic converters.
Omeprazole	1998 (Omeprazole was the first proton pump inhibitor to market)	Modern synthesis[39] of omeprazole involves the starting materials of: 1) chloromethyl-4-methoxy-3,5-dimethylpyridine hydrochloride and 2) 5-methoxy-1H-benzimidazole-2-thiol. While the former might be feasible to produce in New Zealand (it is not dependent on petroleum products), the latter is typically derived from benzene or toluene (both petroleum-derived products and not produced in New Zealand). Also, the molybdenum catalyst may not be available as this mineral is not mined in New Zealand. However, other ingredients are produced in New Zealand (i.e., methanol) or could probably be readily produced (i.e., hydrogen peroxide and sodium hydroxide). **Assessment:** Probably no capacity due to there being no petrochemical refining and no mining of molybdenum in New Zealand.
Amoxicillin	1972[40]	Modern amoxicillin production typically involves fermentation of *Penicillium chrysogenum* to produce penicillin G (Pen G), followed by the enzymatic conversion of Pen G to amoxicillin.[41] Here we considered those ingredients detailed for one well-described modern method (albeit for after the glucose production phase—which can use corn starch, wheat starch and even waste paper).[42] Of the other ingredients, some could probably be produced in New Zealand, e.g., ammonium hydroxide, butyl acetate, *P. chrysogenum* (sourced from the environment, if not laboratories), potassium acetate and sulphuric acid (with the latter already produced in New Zealand). The enzyme penicillin G acylase (PGA) could also be produced via fermentation (with *E. coli* representing the most common host for the production of recombinant PGA[43]). The feedstock p-hydroxyphenylglycine methyl ester (PHPGME) is derived from p-hydroxybenzaldehyde and glycine methyl ester as key precursors. Of these, the former is derived from phenol, which is mainly produced via the cumene process starting from benzene and propylene (both of which are derived from petroleum). **Assessment:** Probably no capacity due to there being no petrochemical refining in New Zealand.

Table 3 (continued): More detailed results relevant to potential New Zealand production capacity for the 10 selected pharmaceuticals in a trade-ending global catastrophe situation (see Table 1 for additional details).

Medicine (ranked as per Table 1)	Year first produced commercially (globally)	Capacity to produce the necessary chemical ingredients and catalysts in New Zealand without trade
Ibuprofen	1969[44]	The modern Boots-Hoechst-Celanese process for manufacturing ibuprofen was considered.[45] This starts with a skeleton of aromatic acetic acid or propionic acid. Both of these are typically derived from petroleum products, i.e., benzene and ethene respectively. Some ingredients could probably be produced in New Zealand: acetic anhydride (from methanol), carbon monoxide and hydrogen gas (already produced). But other ingredients that would probably not be available in New Zealand without trade include: • Hydrogen fluoride (the source of the fluoride is the mineral fluorite, which is not mined in New Zealand). • Raney nickel catalyst (which is derived from a nickel and aluminium alloy, with neither nickel nor bauxite mined in New Zealand). • Palladium catalyst (palladium is not mined in New Zealand). **Assessment:** Probably no capacity due to no petrochemical refining in New Zealand, no mining of three minerals for catalysts and no mining of a mineral for producing hydrogen fluoride.
Aspirin	1874 (powder) and 1904 (tablet form)[46]	The key chemical feedstock for modern aspirin (acetylsalicylic acid) production is sodium phenoxide[47] (synthesis can also involve a yeast-derived enzyme[48]). The sodium phenoxide is derived from phenol,[47] which itself comes from petroleum-derived feedstocks (benzene and propylene). Other ingredients could all probably be produced in New Zealand, i.e., sulphuric acid (already produced) or phosphoric acid, and acetic anhydride (from methanol). **Assessment:** Probably no capacity due to no petrochemical refining in New Zealand. But in the Discussion (below) we consider potential plant-sourced production using much less efficient historical methods.
Metoprolol succinate	1978[49]	We considered the modern four-step chemo-enzymatic protocol to achieve (S)-metoprolol with 99% enantiomeric excess and high yield.[50] The core chemical building block in this process is 4-(2-methoxyethyl)phenol. This is derived from petroleum, typically benzene derivatives. This is also the case for one ingredient: the solvent vinyl butanoate (which is normally made from the petroleum-derived ethylene). Some ingredients in the production of methanol could probably be produced in New Zealand, i.e., potassium hydroxide and isopropylamine (e.g., if an acid catalyst was used for the latter instead of a metal catalyst). The specific enzyme catalyst *Candida antarctica* lipase B (CALB) could probably be produced in New Zealand if the relevant recombinant production methods were set up. **Assessment:** Probably no capacity due to no petrochemical refining in New Zealand (relevant for two ingredients).

Table 3 (continued): More detailed results relevant to potential New Zealand production capacity for the 10 selected pharmaceuticals in a trade-ending global catastrophe situation (see Table 1 for additional details).

Medicine (ranked as per Table 1)	Year first produced commercially (globally)	Capacity to produce the necessary chemical ingredients and catalysts in New Zealand without trade
Salbutamol	1966[51]	All the four general modern pathways for salbutamol production[51] require petroleum-derived chemicals. That is: using acetophenones (derived from benzene), using salicylic acid derivatives (derived from benzene—see above for aspirin), using benzoic acid derivatives (derived from toluene) and using benzaldehyde (derived from toluene). If the salicylic acid pathway utilised New Zealand-based plant sources instead of petroleum-derived products (see as for aspirin in the Discussion), then the following ingredients would be required: • Bromine (potentially could be produced in New Zealand from brine evaporation ponds). • Hydrogen gas (is produced in New Zealand). • Tetrabromobisphenol A (TBBA), which ultimately is synthesised from the petroleum-derived products benzene and propylene (used to produce phenol). • Lithium aluminium hydride (which requires sources of lithium and aluminium [bauxite], and neither are mined in New Zealand). • Palladium catalyst (palladium is not mined in New Zealand). **Assessment:** Probably no capacity due to no petrochemical refining in New Zealand, no mining of one metal for a catalyst and no mining of two metals used for one ingredient.
Prednisone	1955	When considering modern prednisone synthesis,[52] many of the required materials could probably be produced in New Zealand (e.g., acetic acid, acetic anhydride [from methanol], calcium chloride, calcium oxide, DMF [dimethylformamide], ethanol, iodine [I^2], methanol, potassium acetate, potassium hydroxide and sodium hydroxide). The starting material (diosgenin) could be derived from soya beans (which are grown in New Zealand), and the fungus *Rhizopus nigricans* used in the fermentation process is readily accessible in the natural environment. (Also, instead of soya beans, lanolin from wool grease is a source of cholesterol, which can be a starting point for steroid synthesis.) The specific strain of *Corynebacterium simplex* (ATCC 6946) that produces a key enzymatic system could probably be produced in New Zealand if the relevant recombinant production methods were set up. Hydrobromic acid could be produced using bromides extracted from brine evaporation ponds. But materials that would probably not be produced in New Zealand include: • Cyclohexanone (derived from petroleum products, e.g., benzene). • Toluene (a petroleum product). • Aluminium isopropoxide (Al[iPrO]$_3$) (since no bauxite is mined in New Zealand). • The oxidising agent chromium trioxide (CrO3) (chromite is no longer mined in New Zealand[36]). • Raney nickel catalyst (which is derived from a nickel and aluminium alloy, with neither nickel nor bauxite mined in New Zealand). **Assessment:** Probably no capacity due to no petrochemical refining in New Zealand (two ingredients), no mining for two metals for a catalyst and no mining for two other metals needed for two ingredients.

Table 3 (continued): More detailed results relevant to potential New Zealand production capacity for the 10 selected pharmaceuticals in a trade-ending global catastrophe situation (see Table 1 for additional details).

Medicine (ranked as per Table 1)	Year first produced commercially (globally)	Capacity to produce the necessary chemical ingredients and catalysts in New Zealand without trade
Cetirizine hydrochloride	1987[53]	Of the various modern processes for producing cetirizine, we considered the one described by Reiter et al. (specifically the more modern "Scheme 3").[54] Some of the ingredients could probably be produced in New Zealand: hydrochloric acid, sodium hydroxide, thionyl chloride and the phase transfer catalyst, which is the quaternary ammonium salt: methyltrioctylammonium chloride. Two ingredients could probably be produced using New Zealand-produced methanol: 1) sodium methoxide and 2) N,N-dimethyl-2-chloroacetamide. But the following would probably not be able to be produced in New Zealand: • A starting ingredient: 4-chlorobenzophenone (it is derived from the petroleum product benzene). • An additional starting ingredient: N-(2-hydroxyethyl)piperazine (it is derived from the petroleum product ethylene). • The reducing agent sodium borohydride (which requires the metalloid boron from borax, which is not mined in New Zealand). • The solvent toluene (which is derived from petroleum products). **Assessment:** Probably no capacity due to no petrochemical refining capacity in New Zealand (relevant for three ingredients), and there being no borax mining in New Zealand.
Amlodipine	1990[55]	A review article[56] covering the modern synthesis of amlodipine (to amlodipine besylate) was considered. Some of the required materials could probably be produced in New Zealand (e.g., the source of the heterocycle ring: 1,4-dihydropyridine [and its precursors], ammonium acetate and hydrogen gas [which is already produced in New Zealand]). But materials that would probably not be available include: • Benzenesulphonic acid, which requires benzene to produce (a petroleum product). • The catalyst "palladium on calcium carbonate" (palladium is not mined in New Zealand). Another path to amlodipine synthesis is via the aza-Diels-Alder approach.[56] But this also depends on a petroleum product: toluene. **Assessment:** Probably no capacity due to no petrochemical refining in New Zealand and there being no mining of palladium in New Zealand.