General Practitioner, Dr C

Rest Home

Auckland District Health Board

Pharmacy

A Report by the

Health and Disability Commissioner

(Case 13HDC01300)

Health and Disability Commissioner
Te Toihau Hauora, Hauātanga

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Executive summary

1. Mrs B (aged 78 years), a rest home resident, had high blood pressure, type 2 diabetes, osteoarthritis of her knees, dementia, high cholesterol and incontinence. Mrs B was taking simvastatin for her high cholesterol. General practitioner (GP) Dr C advised HDC that Mrs B's previous GP initiated Mrs B's simvastatin treatment after Mrs B experienced an episode of chest pain. In 2011, Mrs B developed a severe fungal rash on her lower abdomen and groin area. Dr C prescribed ketoconazole 200mg daily for four weeks to treat this. The Medsafe datasheet for ketoconazole states that it has a high risk of causing liver injury, and that administration of ketoconazole with simvastatin is contraindicated. Dr C did not discuss the risks of ketoconazole with Mrs B or her family.

2. A pharmacy dispensed the ketoconazole. The Pharmacy had MIMS[1] integrated into its dispensing software, which highlighted drug interactions by checking the medications entered into the dispensing software against the patient's current medications. No one from the Pharmacy contacted Dr C about the drug interaction between simvastatin and ketoconazole.

3. The rash occurred again in 2012, and Dr C again prescribed ketoconazole 200mg daily for four weeks. This was dispensed the same day by the Pharmacy. No one from the Pharmacy advised Dr C of the drug interaction.

4. A few months later, Mrs B presented again with the same rash. Dr C prescribed ketoconazole at 400mg daily for eight weeks. The ketoconazole was dispensed the same day by the Pharmacy. Again, no one from the Pharmacy advised Dr C of the drug interaction.

5. Contrary to the Medsafe datasheet, Dr C did not monitor Mrs B's liver function on any of the occasions on which he prescribed ketoconazole.

6. Approximately two months later, in late 2012, Mrs B fell, and could not raise herself from the floor. Mrs B was taken to a public hospital.

7. On arrival at the Emergency Department, Mrs B's medications were documented as aspirin, metoprolol, simvastatin and paracetamol. Ketoconazole was not included.

8. A creatine kinase (CK) test[2] was ordered. Mrs B's CK levels were recorded as 2,740 units per litre (normal levels being 30–180). On the third day of her admission (Saturday), a registrar viewed the result of the CK test electronically. Although the result was highlighted on the system as being abnormal, the registrar did not inform the ordering consultant of the result.

[1] Medical Information Management System.
[2] This measures the amount of CK (a protein) in the blood. The muscle cells in the body need CK to function. If the CK test shows that the CK levels are high, the patient may have muscle or heart damage.

9. On Monday, Mrs B's CK test was reviewed, and her CK level was noted as elevated. Mrs B's simvastatin was discontinued.

10. On Wednesday, clinicians reviewed Mrs B's computerised pharmacy dispensing records and discovered Mrs B's prescription for a two-month course of ketoconazole. Up until that point, staff had not been aware that Mrs B had been prescribed ketoconazole.

11. Mrs B suffered from acute kidney failure and, sadly, she died from a cardiac arrest.

Decision

Dr C

12. By failing to establish Mrs B's medical history appropriately, either by questioning Mrs B adequately or reviewing her medical notes, and by failing to monitor Mrs B's liver function adequately when prescribing ketoconazole, Dr C breached Right 4(1)[3] of the Code of Health and Disability Services Consumers' Rights (the Code).

13. By failing to communicate effectively with Mrs B in a manner that would have enabled her to understand the information provided to her, Dr C breached Right 5(1)[4] of the Code. In addition, by failing to provide Mrs B with information that a reasonable consumer in her circumstances would expect to receive, Dr C breached Right 6(1)(b)[5] of the Code. By not discussing the risks of ketoconazole with Mrs B, Mrs B was not in a position to make an informed choice and give her informed consent to taking ketoconazole, and, accordingly, Dr C also breached Right 7(1)[6] of the Code.

The Pharmacy

14. The Pharmacy failed to have in place an appropriate dispensing standard operating procedure, and failed to act on the alert when it was prompted. Several staff members, on three separate occasions, failed to follow the professional standards relating to dispensing medications. This was a systemic failure and, accordingly, the Pharmacy breached Right 4(2)[7] of the Code.

[3] Right 4(1) of the Code states that "[e]very consumer has the right to have services provided with reasonable care and skill".
[4] Right 5(1) of the Code states that "[e]very consumer has the right to effective communication in a form, language, and manner that enables the consumer to understand the information provided. Where necessary and reasonably practicable, this includes the right to a competent interpreter."
[5] Right 6(1)(b) of the Code states that "[e]very consumer has the right to the information that a reasonable consumer, in that consumer's circumstances, would expect to receive, including — an explanation of the options available, including an assessment of the expected risks, side effects, benefits, and costs of each option".
[6] Right 7(1) of the Code states that "[s]ervices may be provided to a consumer only if that consumer makes an informed choice and gives informed consent, except where any enactment, or the common law, or any other provision of this Code provides otherwise".
[7] Right 4(2) of the Code states that "[e]very consumer has the right to have services provided that comply with legal, professional, ethical, and other relevant standards".

Auckland District Health Board

15. Auckland District Health Board (ADHB) breached Right 4(1) of the Code by not having in place appropriate systems to ensure that Mrs B's recent medications were known to staff. Criticism is also made of the failure to ensure that an abnormal test result was acted on appropriately.

The Rest Home

16. Adverse comment is made about Mrs B's progress notes having been completed on an irregular basis while she resided at the Rest Home, and the lack of nursing support.

Complaint and investigation

17. The Commissioner received a complaint from Mr A about the services provided to his mother, Mrs B (deceased), by general practitioner (GP) Dr C. An investigation was commenced on 12 June 2014, and the following issues were identified for investigation:

- *Whether Dr C provided an appropriate standard of care to Mrs B in 2011 and 2012.*
- *Whether the Rest Home provided an appropriate standard of care to Mrs B in 2011 and 2012.*

18. On 28 September 2015 the investigation was extended to include the following issues:

- *The appropriateness of the care provided to Mrs B by the Pharmacy in 2011 and 2012.*
- *The appropriateness of the care provided to Mrs B by Auckland District Health Board during her admission.*

19. The parties directly involved in the investigation were:

Mr A	Complainant (consumer's son)
Dr C	Provider
Rest Home	Provider
Auckland District Health Board	Provider
Pharmacy	Provider

Also mentioned in this report:

Dr E	Registrar
Dr F	Internal medicine specialist physician
Mr G	Pharmacist and director of the Pharmacy

20. Information from Mr D, a pharmacist, was also reviewed.

21. Independent expert advice was obtained from in-house clinical advisor, general practitioner, Dr David Maplesden (**Appendix A**), expert pharmacist advice was obtained from Mr Glenn Mills (**Appendix B**), and expert general physician advice was obtained from Dr Denise Aitken (**Appendix C**).

Information gathered during investigation

Background

22. This report focuses on the care provided to Mrs B by Dr C while she was a resident at the Rest Home. The report also focuses on the care provided to Mrs B by the Pharmacy and Auckland District Health Board.

Dr C

23. At the time of these events, Dr C was a private contractor working as a visiting medical officer to several rest homes and private hospitals, including the residents at the Rest Home. He advised HDC that his contractual arrangement with the Rest Home was verbal only. Dr C said: "The terms agreed were such that I was able to visit [the Rest Home] on one set day every two weeks to attend to regular routine matters. In addition, I was contracted to be available for any acute illness by visiting the home …"

24. One of Dr C's patients at the Rest Home was Mrs B. Dr C was Mrs B's doctor from the time she was admitted to the Rest Home in early 2011 until she died.

25. Dr C told HDC that "[the Rest Home] operated a manual patient record system only". Each time Dr C assessed Mrs B he made handwritten GP notes and placed these into Mrs B's file, which was held at the Rest Home.

The Rest Home

26. The Rest Home provided limited responses to HDC's requests for information during this investigation. The Rest Home had a single integrated paper file for each patient. Mrs B's family provided HDC with a copy of her caregiver and nursing progress notes, which often have more than a week between entries. There are two incident reports in Mrs B's file relating to medication errors, with potential remedial actions referring to a need for more registered nursing staff. Shortly after these events, the Rest Home closed down.

27. The Pharmacy told HDC that it was difficult to contact a nurse at the Rest Home, as the number of nurses had reduced over time. Dr C told HDC that nurses were typically present in his two weekly reviews during the week, but they were not always present for acute events.

Mrs B

28. Mrs B (who was 78 years old at the time of these events) was admitted to the Rest Home in 2011. Her husband was also a resident at the Rest Home. Mrs B did not speak English, and had a history of:

1. hypertension (high blood pressure);
2. type 2 (mellitus) diabetes;
3. osteoarthritis (knees);
4. dementia;
5. hyperlipidaemia (high cholesterol); and
6. urinary and faecal incontinence (double incontinence).

29. Dr C advised HDC that Mrs B's hypertension was mild and well controlled with regular administration of metoprolol[8] tablets (trade name Betaloc). She was also taking aspirin for vascular risk.[9]

30. Mrs B's diabetes was mild and managed by diet alone, without the need for oral medication or insulin injections. Dr C advised HDC that Mrs B's osteoarthritis was also mild and managed quite well with paracetamol four times daily, and that Mrs B complained of intermittent knee pain for most of the time he was her GP.

31. Dr C advised HDC that, as Mrs B was not English-speaking, her degree of dementia was difficult to assess. He said that she was quite mobile and was able to feed herself, but she was disoriented in time and place, did not recognise her husband at times, and required supervision with most daily tasks, including dressing, toileting, and showering. Dr C said that in 2012 Mrs B's memory deteriorated and she became more confused and disorientated.

32. On admission to the Rest Home, Mrs B was taking simvastatin 40mg daily for high cholesterol. Dr C advised HDC that, prior to her admission to the Rest Home, Mrs B's previous GP initiated Mrs B's simvastatin treatment, following an episode of chest pain thought to be due to coronary insufficiency.[10] Dr C advised that he continued her on this dose because Mrs B's cholesterol levels were normal on admission, and that at no stage did Mrs B suffer any vascular complications or chest pain from high cholesterol. Mrs B's progress notes record that Dr C monitored her serum lipid levels[11] regularly.

33. Dr C attributed Mrs B's urinary incontinence to her dementia, and advised HDC that her urinary incontinence was worse when she developed urinary infections, which her progress notes document occurred regularly.

34. Dr C advised HDC that because Mrs B suffered from urinary incontinence and needed to wear incontinence pads, often she suffered skin infections in the lower abdominal

[8] A beta-blocking drug used to treat hypertension and angina.
[9] To help control the heart and blood vessels.
[10] Decreased supply of blood to the heart owing to obstruction of the coronary arteries.
[11] Blood tests undertaken to record the amount of cholesterol in the blood.

area. He said that he put Mrs B on a trial of topical therapy with miconazole,[12] but the rash was "very resistant" to miconazole.

Prescription for ketoconazole

35. In mid 2011, Mrs B developed a severe fungal rash on her lower abdomen and groin area. A swab grew the fungus *Trichophyton rubrum* (*T. rubrum*). Dr C advised HDC that it was his understanding that *T. rubrum* is difficult to eradicate using topical treatment, and that oral treatment is usually required.

36. Dr C prescribed Mrs B ketoconazole[13] 200mg daily for four weeks. The Medsafe datasheet for ketoconazole stated that this drug has a high risk of causing liver injury,[14] and that concomitant administration of ketoconazole with simvastatin is contraindicated. Dr C advised HDC that he did not discuss the risks of ketoconazole with Mrs B or her family.

37. The Pharmacy dispensed the ketoconazole for the Rest Home to administer to Mrs B. A pharmacist entered the prescription into the system and dispensed the ketoconazole. The Pharmacy advised HDC that it is not documented who checked the dispensing of the prescription. It also advised HDC that the Pharmacy had MIMS[15] integrated into its dispensing software, which would highlight drug interactions by checking the medications entered into the dispensing software against the medications the patient was currently taking. However, Dr C told HDC that no one from the Pharmacy contacted him.

38. Dr C advised HDC that the ketoconazole had "excellent results" for Mrs B. He said, however, that the rash recurred a few months later, and he again prescribed 200mg of ketoconazole daily for four weeks. This was dispensed the same day by the Pharmacy. A dispensary technician entered the prescription and dispensed the medication. Again, it is not documented who checked the dispensing of the prescription. No one from the Pharmacy contacted Dr C regarding this dispensing. Dr C advised HDC that the rash disappeared with the treatment.

39. Dr C advised HDC that he ordered liver function tests for Mrs B, as hepatoxicity is a risk associated with ketoconazole. Documentation from a medical testing laboratory indicates that two months after the completion of the second course of ketoconazole liver function tests were undertaken on Mrs B. These were documented as being normal. Dr C advised HDC that the normal results "reassured [him] somewhat that there had been no significant damage from the two courses of ketoconazole". Mrs B's creatine kinase (CK) level was not tested.

[12] Antifungal cream.
[13] Ketoconazole has recently been withdrawn from sale in New Zealand, and Medsafe's data sheets on ketoconazole are no longer available. HDC's clinical advisor stated that the cited information was current and freely available at the time of these events.
[14] Since December 2013 some manufacturers of ketoconazole in New Zealand have ceased making it owing to ongoing safety concerns regarding liver injury.
[15] A software system used in some pharmacies. The system provides interaction warnings when a medicine is being dispensed, and offers an ability to look up reference information at any time the software is operational.

40. Later in the year, Dr C recorded in the GP notes for Mrs B that she presented with the same rash again. Dr C advised HDC that, owing to the persistence of the rash, he thought Mrs B needed a higher dose and a longer period on ketoconazole. He prescribed ketoconazole at 400mg daily (the maximum recommended dose) for eight weeks. Dr C did not order liver function and CK level tests for Mrs B when he prescribed the higher dose.

41. The ketoconazole was dispensed the same day by the Pharmacy. There is no documentation to show who entered the prescription and dispensed it. Pharmacist Mr D advised HDC that he checked the dispensing of the prescription.

42. Mr D advised HDC that he checked the dose of ketoconazole and saw that the dose prescribed was within the recommended range. Mr D advised HDC that he checked Mrs B's patient history electronically and noted that she had been prescribed ketoconazole on two previous occasions. He said that it "seemed appropriate to dispense on this instance". Mr D said he did not contact Dr C as he assumed Dr C would have been contacted at the time the ketoconazole was previously dispensed. Mr D advised HDC that he was not aware of an alert having been prompted in the dispensary software when the prescription was entered into the system.

43. While the Pharmacy has advised HDC that it can not tell who, if anyone, saw the alert, it admits that an alert would have been prompted on the software system of "a potential interaction between simvastatin and ketoconazole"[16] and acknowledged that no staff contacted Dr C about the interaction or the dispensing on this occasion.

44. Dr C reviewed Mrs B and documented in the GP notes that there was a marked improvement in the rash, but to continue ketoconazole for the remainder of the eight weeks. He advised HDC this was because of "the persistence and continued recurrence of the rash". Dr C did not order liver function and CK level tests.

Muscle pain, weakness and tiredness

45. Mrs B's son, Mr A, advised HDC that from late 2012 Mrs B complained to him of unexplained muscle pain, weakness and tiredness, and that she was in pain when she walked. Mr A said that he reported these symptoms to Dr C.

46. Dr C advised HDC that Mr A did not report such symptoms to him.

47. Prior to Mrs B's fall, there is no record in Mrs B's progress notes or GP notes that she was experiencing muscle pain, weakness or tiredness. Dr C stated to HDC that he was not aware of any such problems prior to the fall, except for the mild osteoarthritis in her knees, for which she was taking paracetamol.

48. Dr C advised HDC that there was no regular nursing supervision at the Rest Home, and often little was documented in Mrs B's progress notes. Both Dr C and Mrs B's

[16] This was documented in an incident report completed after these events and provided to HDC as part of the Pharmacy and Mr D's response.

son advised that, throughout this time, Mrs B was able to maintain her walks with her husband after dinner almost every day.

Fall

49. On the day of Mrs B's fall, staff at the Rest Home recorded in Mrs B's progress notes: "Feel restless, Pt pain on ankle and very painful to walk on. Check BP [blood pressure] 172/79, pulse 48 + temp 35 [degrees Celsius] … plus Dr to assess."

50. Dr C was contacted by the Rest Home staff and advised that Mrs B had experienced a fall. Dr C attended the Rest Home and reviewed Mrs B. He recorded in the GP notes that she had a "[p]ainful [left] buttock after fall against tap OE [on examination] bruising [left] buttock only + crepitus[17] both knees".

51. Dr C advised HDC that Mrs B had a bruised buttock, and that her knee pain "was more evident" following her fall. He stated that the crepitus was "due to the known osteoarthritis". He said that while the fall potentially explained her reports of pain, he considered the pain and the unsteadiness on her feet could have been due to polymyalgia rheumatica[18] (PMR). He ordered blood tests to exclude PMR and charted liquid paracetamol four times a day. The blood tests were carried out the next day, and the test results were documented as being normal. Dr C advised HDC that there was no explicit complaint of muscle pains at that time and, therefore, no liver function testing[19] was carried out.

Second fall

52. Two days later, it is documented in Mrs B's progress notes that at 9.48pm she slipped from her bed, and could not raise herself from the floor. Staff helped her up and back to bed. Staff noted in her progress notes: "[J]ust looks very weak so report to manager and manager contact with hospital."

53. The Rest Home organised for an ambulance to take Mrs B to a public hospital that night. The ambulance crew documented on the ambulance service's Patient Report Form that the ambulance was dispatched at 10.13pm, and that the paramedics were told by Mrs B's husband that over the past three days Mrs B had had general weakness in her legs, and that that evening she had slipped off her bed and fallen down the side of it. It is also noted that her urinary incontinence had worsened, and she had become bowel incontinent.

The public hospital

Assessment

54. At 10.49pm Mrs B arrived at the Hospital's Emergency Department (ED). The ambulance transfer records (provided to the Hospital) state that Mrs B's medications were Betaloc (metoprolol), aspirin, simvastatin and ketoconazole. Mrs B's Doctors Prescribed Medication Chart (from the Rest Home) lists Mrs B's medications as: "1)

[17] A grating sound or sensation produced by friction between bone and cartilage or the fractured parts of a bone.
[18] A disabling arthritic condition characterised by severe pain and stiffness in various muscles.
[19] Liver function tests are often carried out when a patient presents with weakness and fatigue.

betaloc 2) aspirin 3) simvastatin", then a series of crossed out medications followed by "12) Panadol liquid", then a space of four lines, followed by "17) Ketoconazole". ADHB advised HDC that it was not provided with a copy of [Mrs B's] medication chart.[20]

55. On arrival at ED, Mrs B's current medications were documented as aspirin, metoprolol, simvastatin and paracetamol. ADHB advised HDC that these were the medications advised to staff on Mrs B's admission by those who accompanied her. Ketoconazole was not included.

56. At 11.30pm Mrs B was assessed by a staff nurse who documented that Mrs B's current medications were aspirin, Betaloc, simvastatin and paracetamol. Mrs B's history, given in the presence of an interpreter, was a progressive deterioration in her mobility the previous week, to the point where she was unable to get out of bed at all without assistance. Her clinical notes document that she had pain in her left hip and knee following a fall. She complained of tiredness and generalised weakness.

Admission

57. At 4.32am the following day, an emergency medicine registrar assessed Mrs B and, at 6.30am, a general medicine registrar admitted Mrs B. Mrs B was described as alert and attempting to communicate verbally. Her temperature, blood pressure, respiratory rate and oxygen saturation were all documented as being normal. Her heart sounds were normal, her lungs were clear, and her abdomen was unremarkable and non-tender. There was mild oedema of both lower legs up to the level of the mid-shin.

58. Mrs B could lift her arms and legs off the bed on request, but they drifted back down. She made clinical staff aware that she was too weak to continue holding them up. Mrs B's medications were documented as aspirin, metoprolol, simvastatin and paracetamol.

59. That day, a general and obstetric physician was the consultant in charge of Mrs B's care. Following the consultant-led ward round, she requested several tests. These included a CT of Mrs B's head, thyroid function tests, cortisol[21] and a CK test. Mrs B's CK levels were recorded as 2,740 units per litre (U/L) (normal levels being 30–180U/L).

60. At 12.51pm on Saturday, registrar Dr E electronically viewed the result of the CK test but did not accept it (acknowledge electronically that the result had been seen). Although the result is highlighted on the system as abnormal, Dr E did not tell anyone of the result, and no one else viewed it.

[20] However, it was amongst Mrs B's clinical documentation when HDC requested her file from ADHB.

[21] Cortisol is a steroid hormone and is released in response to stress and low blood-glucose concentration. It functions to increase blood sugar to suppress the immune system, and to aid in the metabolism of fat protein and carbohydrates.

61. Mrs B was started on treatment for a possible bladder infection (the oral antibiotic trimethoprim).[22]

62. On Monday, internal medicine specialist physician Dr F took over Mrs B's care. He asked for Mrs B's most recent blood tests to be reviewed (including the CK test taken on Friday). A registrar viewed and "accepted" the CK test result at this time. On Tuesday, Dr F was made aware of the result. Dr F noted that Mrs B's CK was elevated. ADHB advised HDC that this is a "marker of muscle damage". ADHB further advised that high CK levels can have a wide range of causes, including muscle trauma due to injury, immobility or unaccustomed exertion, intrinsic muscle disorders due to congenital enzyme defects, hormonal problems such as underactive thyroid gland, bacteria and viral infections, and drug, toxin and medication side effects. Dr F asked clinicians to check Mrs B's urine for myoglobin.[23]

63. Also on Tuesday, Mrs B's CK level was re-tested and had risen to over 20,000, and her urine myoglobin level was very high at 27.7mg/L (normal being less than 1mg/L). The results indicated that Mrs B was suffering from acute kidney injury. Mrs B's simvastatin was discontinued and active measures put into place to treat the acute kidney injury. Mrs B's clinical notes document that over the next few days her kidneys progressively shut down.

64. On Wednesday, the registrar reviewed Mrs B's computerised pharmacy dispensing records. He discovered Mrs B's earlier prescription for a two-month course of ketoconazole, 200mg twice daily. ADHB advised HDC that up until that point, staff had been unaware that Mrs B had been prescribed ketoconazole.

Acute renal failure

65. ADHB advised HDC that despite "aggressive intravenous fluid therapy", in an attempt to flush the muscle breakdown products from Mrs B's kidneys, her kidney failure could not be reversed.

66. On Wednesday, Dr F documented in Mrs B's clinical notes that Mrs B's family were advised (at a translated family meeting) that the drug combination of simvastatin and ketoconazole had most likely caused her muscle pains and weakness and subsequent kidney failure. Mrs B became progressively more unwell and less responsive, and passed into a coma.

67. Sadly, Mrs B died at the Hospital from a cardiac arrest. It is documented that she had suffered from acute kidney failure secondary to rhabdomyolysis[24] and high potassium levels.

[22] She was treated for a bladder infection for four days until a urine culture result came back indicative of a contaminated sample, rather than a bladder infection.
[23] An iron- and oxygen-binding protein found in muscle tissue. It is found in the bloodstream only after muscle injury (including severe rhabdomyolysis) and, if present, is an abnormal finding.
[24] Rhabdomyolysis clinically presents as generalised muscle pains and weakness (myalgia).

Events following Mrs B's death

68. Following Mrs B's death ADHB sent a clinical summary to Dr C. It is recorded in the clinical summary that it appears most likely that the rhabdomyolysis resulted from the interaction between the ketoconazole and simvastatin.

69. Dr C contacted the Pharmacy advising them of Mrs B's death and asking whether an interaction had been prompted on their software system when the ketoconazole was dispensed. Dr C advised HDC that the pharmacist to whom he spoke (pharmacist and director of the Pharmacy at the time, Mr G) told him that an interaction would have been prompted.

70. Mr G advised HDC: "[Dr C] asked me if the pharmacy's software was set-up to pick up drug interactions. I explained to him that we had MIMS integrated into our dispensing software which would highlight drug interactions by checking the medication(s) when entered in to the dispensing software with the medications the patient was currently taking. He informed me that he had not been contacted regarding this interaction."

71. Following this telephone call, another pharmacist was asked by Mr G to complete an incident report for the third dispensing, which she did. She documented on the incident report that "[a]n interaction was prompted on the lots software system of a potential interaction between simvastatin and ketoconazole …".

72. The incident report documented that the incident was one of "overlooking drug interactions when patient has been on similar/same combination in past". It documented that this would result "in a change in policy" to now state that "all [MIMS] pop-up interactions [are] to be printed and all interventions recorded accordingly". The Pharmacy advised that the Standard Operating Procedure *C10 — Dispensing Prescriptions, medical practitioner supply orders (MPSOs) and bulk supply orders (BSOs)* (the dispensing prescriptions SOP) was "amended accordingly".

73. Shortly after these events the Pharmacy was sold.

Subsequent information

Dr C

74. Dr C advised HDC that he was aware of the interaction between ketoconazole and simvastatin but, "as there were no apparent vascular problems, the prescription of simvastatin was not in the forefront of [his] mind when [he] prescribed the Ketoconazole". Because of Mrs B's pre-existing osteoarthritis of the knees, he "mistakenly attributed the increasing pain in the legs to this problem".

75. Dr C acknowledged that he failed to check all of Mrs B's other medications prior to prescribing ketoconazole. Dr C said: "I accept without reservation that I made an error, but it was that I did not check and review all other medications she had been taking at the times I initiated prescription of the Ketoconazole, rather than not being aware of the contraindications of combining these two medications."

76. Dr C said that had he been using a computer, a red warning signal would have appeared when he entered the prescription for ketoconazole, and this would have been an immediate reminder about the interaction with simvastatin, which "would have prompted reconsideration". He also said that trying to provide optimal treatment to elderly patients who present with a range of complex problems requiring multiple medications "necessarily involves prescribing medications that may have interactions, so it is a matter of fine clinical judgment, which is not always straightforward".

77. In regard to not checking Mrs B's liver function when prescribing the higher dose of ketoconazole, Dr C advised HDC: "I deeply regret this omission." He further advised: "[I had] no indication to perform CK levels on [Mrs B's] blood as there was at no stage a clear complaint of muscle pain, and no such symptoms were reported to me. I acknowledge the communication difficulties (dementia, language and no regular nursing supervision) which may have contributed to the absence of reported symptoms."

78. Dr C said that as Mrs B did not speak English and therefore required translation from the Rest Home staff (who would translate for her), often the accuracy of her symptoms, clinical complaints or other information being given was difficult to interpret.

79. Dr C said that a patient with normal cognition (as opposed to one with dementia) would likely be better able to recognise and distinguish different types of muscle pain, which would greatly assist in warning that a weakness might be present. He advised HDC: "[K]nowing, in retrospect, that she had rhabdomyolysis, she would likely have been experiencing a generalised pain in all major muscle groups, arms and legs. An accurate history of such symptoms was not provided to me. Had I been alerted to the presence of such a history, the myalgia due to the drug interaction may have been more evident to me." He further stated that if there had been "regular nursing supervision [at the Rest Home] [he] might have been alerted earlier about [Mrs B's] severity of symptoms such as tiredness and unsteadiness on her feet or inability to walk properly".

80. Dr C stated that he does not recall ever receiving any contact from the Pharmacy alerting him about the drug interaction between ketoconazole and simvastatin on any of the three occasions on which he prescribed ketoconazole.

81. Dr C stated: "Upon hearing of [Mrs B's] death I immediately visited [her husband] … and explained to him that her death may have resulted from the reaction between the two medications."

82. Dr C advised HDC that he has made the following changes to his practice since this incident:

> "(a) I am now acutely conscious of the need to always check current drugs before adding a new one on the prescribing chart. This is a very basic rule for all prescribing doctors, and which I failed to follow in this instance.

(b) I will never prescribe Ketoconazole again nor any of its group …

(c) I have also undertaken the following actions:

…

(ii) I presented this case anonymously to a group of 20 general practitioners as an educational message, and reminder to other practitioners.

(iii) I have reduced my work commitments by arranging that three of the smaller rest homes for which I was caring for at the time have now been transferred to other doctors. This allows me to take more time and care for reflection and checking."

83. In response to the provisional opinion, Dr C outlined the following additional changes he has since made to his practice:

(i) In the event of "any future language difficulties" he will either transfer the care of such patients or use a translator.

(ii) He is now prescribing by computer for half of his current rest home patients and says this is expected to be in place for the other half sometime later this year. He said "[t]his computer prescribing system (MediMap) will have a red flag system installed by the end of April. This will give warning about all serious drug interactions".

(iii) He contacted the pharmacies that dispense his scripts asking them to contact him before dispensing anything when the 'red flag' appears on their system.

(iv) He has asked rest home practice dispensing nurses to check the list of drug interactions before handing out medications.

The Pharmacy

84. The Pharmacy acknowledged to HDC that staff did not contact Dr C when ketoconazole was dispensed on the second and third occasions but former director Mr G advised: "I do firmly believe that [Dr C] was contacted when the ketoconazole [was initially dispensed]. However I am unable to find any notes to support this …"

85. The Pharmacy further stated that staff rosters for this period were not retained, and that it is not possible now to determine which staff members were on duty. Although names were provided for who entered the prescription into the dispensing database for the first and second dispensing, names of who checked the dispensing could not be provided. For the third dispensing, the name of the person who entered the prescription could not be established, although it could be established who checked the dispensing on that occasion.

86. The Pharmacy advised that when it updated its SOPs, older ones were "usually discarded to ensure everyone [used] the most current SOP". It stated that the SOPs

from 2011–2012 have been deleted. Page three of the *dispensing prescriptions SOP* formed part of the incident report and was provided to HDC. The relevant part of this states:

> "4.8. Appropriately deal with any adverse reactions, interactions or other queries associated with the prescribed medicines."

87. The *dispensing prescriptions SOP* did not state what should happen if a drug interaction was alerted. Following the incident report, the following addition was made to the *dispensing prescriptions SOP*:

> "4.9. For any Mims prompted drug interactions print out a copy of the drug interaction and consult the pharmacist. All appropriate interventions to be recorded on the printed copy of interaction and filled [sic] in the drug interaction folder."

ADHB

88. ADHB said that the ambulance records (which were scanned onto Mrs B's clinical file on admission) document that Mrs B was prescribed both ketoconazole and simvastatin "but this [dual prescription] was regrettably missed". ADHB advised: "It is clear that the admitting Emergency Department staff was not aware of the [ketoconazole], nor was the admitting medical registrar who saw Mrs B without the benefit of a translator some hours later. Both list her regular medications without reference to ketoconazole."

89. ADHB told HDC that if "medicines reconciliation on the day of admission" had occurred, it is likely it would have identified the true nature of Mrs B's illness at an earlier stage. ADHB stated that simvastatin on its own can cause minor degrees of rhabdomyolysis, but the addition of some drugs, including ketoconazole, can make the problem much worse.

90. ADHB further stated that it is well known that the combination of ketoconazole and simvastatin can induce rhabdomyolysis. Other risk factors for statin-induced rhabdomyolysis[25] are advanced age, female gender, diabetes and chronically impaired kidney function. Hypertension and Mrs B's descent are also thought to be risk factors. On admission to the Hospital, Mrs B's kidney function was normal (55mL/min, with normal being under 90). ADHB advised HDC that, therefore, simply in relation to her impaired kidney function, the dose of simvastatin was not considered excessive.

91. ADHB stated that had the registrar on Saturday noted the abnormal CK result and discussed it with the consultant or flagged it for follow-up, the cause of Mrs B's weakness would have been identified much earlier.

[25] Statins are a class of drug prescribed to help lower cholesterol levels in the blood. By lowering the levels, they help prevent heart attacks and stroke. Their use can be associated with muscle complaints ranging from muscle weakness and cramps, to myalgia with and without elevated CK levels, mild CK elevations, or myositis and rhabdomyolysis (rhabdomyolysis is breakdown of muscle fibres and can cause acute renal failure). Myalgia is the least severe but most common presentation of muscle toxicity.

92. ADHB told HDC that since these events, there has been "an increased presence of pharmacists both on the ward and in the Emergency Department … with the expectation that prescribing errors in the community (as in this case) will be detected at the time of admission".

Relevant professional standards

93. The following standards were in place at the time of these events:

Standards New Zealand — Health and Disability Services Pharmacy Services Standard (NZS 8134.7:2010)

> "Standard 1.7: Consumers receive services of an appropriate standard.
>
> Standard 3.5: Consumers shall receive adequate and appropriate services in order to meet their assessed needs and desired outcomes.
>
> Standard 3.8: Consumers shall receive medicines in a safe and timely manner that complies with current legislative requirements and safe practice guidelines.
>
> Standard 5.2: A disciplined dispensing procedure shall ensure that the appropriate product is selected and dispensed accurately and efficiently.
>
> Standard 5.2.4: Prescriptions are interpreted and evaluated for correctness, appropriateness and completeness, their authenticity verified and their priority for dispensing determined."

Good prescribing practice (April 2010):[26]

> "Take an adequate drug history of the patient, including: any previous adverse reactions to medicines; current medical conditions; and concurrent or recent use of medicines."

Responses to provisional opinion

94. Mrs B's family, Dr C, ADHB, the Rest Home and the Pharmacy responded to relevant sections of my provisional opinion.

95. Dr C's responses have been incorporated into the report where relevant. Dr C accepted the findings and the recommendations made. In response to recommendations made in my provisional opinion, Dr C provided a written apology

[26] A Medical Council of New Zealand publication.

for Mrs B's family and provided evidence showing that he had recently completed several workshops relating to good prescribing practice.

96. The Pharmacy's responses have been incorporated into the report where relevant. It stated it had no objections to the substance of the opinion or to the recommendations.

97. Mrs B's family and ADHB had no further comment to make.

Opinion: Dr C — Breach

Prescription for simvastatin

98. Prior to her admission to the Rest Home, Mrs B was taking 40mg simvastatin daily for high cholesterol. On admission to the Rest Home, Dr C continued her on this dose and monitored her serum lipid levels regularly.

99. During the course of this investigation I obtained clinical advice from in-house clinical advisor GP Dr David Maplesden. Dr Maplesden advised that because Mrs B had an elevated cardiovascular risk, it was reasonable for her to have been prescribed simvastatin at a dose of 40mg, and that her serum lipid levels were monitored adequately. I accept this advice.

Continuing use of simvastatin

100. Mrs B developed symptoms of muscle pain and weakness. Although her recent fall could have accounted for her musculoskeletal symptoms, Dr C thought her condition "sufficiently atypical to warrant considering a diagnosis of PMR". However, he did not order tests of Mrs B's CK levels.

101. Dr Maplesden advised:

> "If there were atypical features of the presentation with respect to extent of myalgia and/or muscle weakness, and leaving aside for the moment the issues of concomitant prescribing of ketoconazole, best practice would have been to stop simvastatin while CK levels were checked to exclude statin induced myopathy as a cause of the symptoms."

102. Dr Maplesden referred me to a May 2004 Prescriber Update[27] report, which stated:

> "[R]eports of myopathy and rhabdomyolysis with statins are a reminder to prescribers to measure creatine kinase (CK) levels in patients presenting with muscle pain or weakness. The risk of myopathy may be increased by high doses of statins, especially in patients with co-morbidities, or in the presence of interacting medicines …"

[27] Myopathy with Statins: Check CK Levels and Interactions. Prescriber Update 2004;25(1):4–5. Available at: http://www.medsafe.govt.nz/profs/puarticles/Statinmyop.htm.

103. Likewise, a 2010 BPAC article on prescribing of statins[28] included the following recommendations:

> "After initiating statin treatment, creatine kinase should be checked when there are unexplained muscular symptoms … If there is unexplained muscle pain, tenderness or weakness, statin treatment should be stopped and creatine kinase levels checked; Factors that may increase the risk of statin induced myopathy are: advanced age (>80 years old), female sex, low body mass index, multisystem diseases (for example, diabetes mellitus), diseases affecting kidney or liver function, hypothyroidism (untreated), drug interactions, especially with drugs that are inhibitors … (for example, … antifungals …), … intercurrent infections …"

104. Mrs B had all of the above factors (advanced age, female, low body mass and multisystem diseases). Dr Maplesden advised that Mrs B's ethnicity is mentioned in other publications as being an additional risk factor for statin-induced rhabdomyolysis.

105. Dr Maplesden also advised, however, that mitigating factors included that Mrs B had taken simvastatin at a constant dose for at least a couple of years without problems, and that the language barrier would have made interpretation of Mrs B's musculoskeletal symptoms somewhat difficult to clarify. He also advised that, under the circumstances (recent fall and symptoms apparently consistent with that fall), there was no obvious reason to consider statin-induced myopathy in the differential diagnosis and, therefore, to check CK levels.

106. I acknowledge Dr Maplesden's comments regarding best practice but I also accept Dr Maplesden's advice that, in these circumstances, there was no obvious reason to consider statin-induced myopathy and, therefore, to check Mrs B's CK levels. I consider that in all of the circumstances, this aspect of Dr C's care did not breach the Code.

Prescriptions for ketoconazole

Commencement of oral therapy

107. Mrs B suffered recurrent skin infections on her lower abdominal area. Dr C attempted to treat the infections with an antifungal cream, but said the infections were "very resistant" to the cream. In mid 2011 Mrs B developed a severe fungal rash on her lower abdomen and groin area. A swab grew *Trichophyton rubrum* (*T. rubrum*). Dr C advised that *T. rubrum* is difficult to eradicate with topical treatment, and that oral treatment is usually required.

108. On two occasions, Dr C prescribed ketoconazole 200mg daily, for four weeks, and on the third occasion he prescribed ketoconazole at 400mg daily for eight weeks, while Mrs B continued to take simvastatin.

109. The Medsafe data sheet for ketoconazole[29] included the following relevant information:

[28] Available at: http://www.bpac.org.nz/BPJ/2010/August/statins.aspx.

> "(i) Adult dosage: The recommended dose of [ketoconazole] tablets for all indications is one tablet (200 mg) once daily with a meal, … If no adequate response is obtained with this dose after a reasonable trial period, the dosage may be increased to two tablets (400 mg) once daily with a meal …
>
> (ii) Duration: … the risk of serious hepatic toxicity increases with longer duration of treatment. Therefore, long duration of treatment should only be given after full consideration of the extent of treatment response and the risks and benefits of continuing treatment. … The usual duration of treatment is as follows: … Dermatophytosis [as suffered by Mrs B]: approximately 4 weeks.
>
> …
>
> (iv) WARNING: because of the risk for serious hepatotoxicity, [ketoconazole] tablets should be used only when the potential benefits are considered to outweigh the potential risks, taking into consideration the availability of other effective antifungal therapy."

110. Dr Maplesden advised that, as Mrs B had received an adequate trial of topical therapy for her fungal rash before oral therapy was considered, commencement of oral therapy was reasonable.

Liver function testing

111. Dr C ordered a liver function test two months after completion of Mrs B's second course of ketoconazole and the results were normal. However, her liver function was not monitored on the preceding occasions on which ketoconazole was prescribed. This is contrary to the Medsafe data sheet for ketoconazole, which states:

> "… [L]iver function should be closely monitored …
>
> (iv) … Assess liver function, prior to treatment to rule out acute or chronic liver diseases. Liver function should then be monitored at frequent and regular intervals during treatment (for example, after two and four weeks of treatment and then on a monthly basis). Liver function should also be assessed at the first signs or symptoms of possible hepatotoxicity."

112. I acknowledge Dr C's response that, as the liver test result had been normal, he assumed there had been no liver damage from the previous courses of ketoconazole and was confident that a third course would be similarly tolerated. However, Dr Maplesden advised me that the failure to ensure that recommended monitoring of liver function was undertaken was "particularly significant" when the longer course at a higher dose was initiated.

[29] While the cited references were current at the time of these events, recently the oral formulation of ketoconazole was withdrawn from sale in New Zealand, and the references are no longer available. However, Dr Maplesden stated that at the time of these events the cited information was current and freely available.

113. Dr Maplesden advised me that this "delayed" testing was not in accordance with the manufacturer's recommendations. He also stated that the first two courses of ketoconazole were of short duration (one month) and a lower dose than the October 2012 course. He said: "Leaving aside the issue of co-prescribing of simvastatin and ketoconazole, I am mildly critical of liver function monitoring during [Mrs B's] first two courses of ketoconazole but I remain moderately critical of her monitoring during [the third course] which involved a higher dose of ketoconazole (400mg daily) for a longer period (eight weeks)."

114. I accept Dr Maplesden's advice and am critical that Dr C failed to monitor Mrs B's liver function adequately prior to and during ketoconazole therapy, especially when he doubled the dose and duration of treatment.

Co-prescribing of ketoconazole with simvastatin

115. Dr Maplesden advised me that the potential interaction between statins (drugs such as simvastatin) and CYP3A4[30] inhibitors[31] (drugs such as ketoconazole) is well recognised.

116. Dr Maplesden referred me to an April 2011 Prescriber Update,[32] which reinforced the warning regarding statin interactions and the co-prescribing of simvastatin and potent CYP3A4 inhibitors:

> "Prescribers are reminded of the potential for serious adverse reactions when statins are prescribed with medicines that inhibit the CYP3A4 isoenzyme. Recent reports to the Centre for Adverse Reactions Monitoring (CARM) indicate that the concomitant treatment with medicines that interact with simvastatin or atorvastatin has led to serious myopathies. These reports have included life-threatening and fatal cases of rhabdomyolysis."

117. The Medsafe data sheet for simvastatin[33] specifically mentions ketoconazole as a contraindication. It also states:

> "Myopathy sometimes takes the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria,[34] and rare fatalities have occurred. … The risk of myopathy/rhabdomyolysis is increased by concomitant use of simvastatin with … ketoconazole … If short-term treatment with potent CYP3A4

[30] Cytochrome P450 3A4 (CYP3A4) is an important enzyme in the body, mainly found in the liver and in the intestine.
[31] An inhibitor in this context is something that is used to slow down a reaction or to prevent an unwanted chemical change.
[32] Statin interactions: reports of serious myopathy. Prescriber Update 2011;32(2):13–14. Available at: http://www.medsafe.govt.nz/profs/PUArticles/StatinInteractionsJune2011.htm.
[33] Available at: http://www.medsafe.govt.nz/profs/datasheet/l/Lipextab.pdf. While the Medsafe data sheet pertaining to simvastatin has been updated recently, Dr Maplesden advised that the cited information was current and freely available at the time of these events.
[34] Myoglobinuria is the presence of myoglobin in the urine, usually associated with rhabdomyolysis or muscle destruction. Myoglobin is present in muscle cells as a reserve of oxygen.

> inhibitors is unavoidable, therapy with [simvastatin] should be suspended during the course of treatment."

118. The Medsafe data sheet for ketoconazole includes the following relevant information:

> "(iii) Concomitant administration of [ketoconazole] tablets with any of the following medicines is contraindicated: … CYP3A4 metabolised HMG-CoA reductase inhibitors such as simvastatin or lovastatin."

119. I note that Dr C was aware of the interaction between ketoconazole and simvastatin when he prescribed ketoconazole for Mrs B on three occasions. However, Dr C did not recall and did not check the GP notes for Mrs B's existing medications, which included simvastatin, when he prescribed her ketoconazole.

120. The Medical Council of New Zealand's publication *Good prescribing practice* (April 2010) states: "Take an adequate drug history of the patient, including: any previous adverse reactions to medicines; current medical conditions; and concurrent or recent use of medicines …"

121. I note that it was Dr C's expectation that if such a drug interaction was detected, he would be contacted by the Pharmacy when the medication was dispensed. I also note that, as the Rest Home operated only a manual patient record system, Dr C could prescribe only manually at the time, without the benefit of a computerised prescribing module flagging potential medication interactions. However, as advised by Dr Maplesden, the prescribing clinician has the primary responsibility to take all appropriate steps (including checking of existing medications) to prescribe safely, rather than prescribing without due care with the expectation that others will provide a "failsafe backstop".

122. Dr Maplesden advised that Dr C's co-prescribing of simvastatin and ketoconazole to Mrs B on three separate occasions represents a moderate to severe departure from accepted practice, "even if the primary reason was a failure to check her existing medications rather than a failure to be aware of the potential risk of such co-prescribing". I agree with Dr Maplesden's advice. Given that Dr C was aware of the potential risks, it was imperative that he assess the risk of prescribing ketoconazole for Mrs B.

123. I consider that Dr C should have ensured that Mrs B's medication records were readily accessible to him and reviewed prior to prescribing. Previously I have highlighted the importance of taking a comprehensive history from the patient, reviewing the risk factors, and having a discussion with the patient about the medication before prescribing it.[35] While I acknowledge, in this instance, the language barrier and Mrs B's cognitive impairment, Dr C was aware of these difficulties and should have had systems in place to work within these limitations (discussed below). I am critical that Dr C failed to check Mrs B's regular medications when prescribing,

[35] See opinions 10HDC00753, 12HDC01062 and 13HDC01041 available at www.hdc.org.nz.

on three separate occasions, a medication (ketoconazole) known to have potential for interaction with several drugs.

Conclusion

124. Under Right 4(1) of the Code, Mrs B had the right to have services provided by Dr C with reasonable care and skill. When prescribing medication to a patient, doctors must ensure they are familiar with the patient's medical history in order to assess the patient's needs adequately and to satisfy themselves that the medication will be in the patient's best interests. Failing to do so can have serious and potentially fatal consequences for the patient.

125. The co-prescribing of ketoconazole and simvastatin is clearly contraindicated and, as outlined above, over several years there has been significant information conveyed to the medical profession on the risks of such co-prescribing.

126. Dr C had a duty to check Mrs B's existing medications and to prescribe safely. He failed to do so. This prescribing error occurred not once but on three separate occasions over two years. In addition, he failed to monitor Mrs B's liver function adequately prior to and during ketoconazole treatment. Overall, I consider that by failing to establish Mrs B's medical history appropriately, either by communicating adequately with Mrs B or by reviewing her medical records; by not monitoring Mrs B's liver function adequately when prescribing ketoconazole; and by co-prescribing ketoconazole with simvastatin, Dr C did not provide services to Mrs B with reasonable care and skill and, therefore, breached Right 4(1) of the Code.

Communication

127. Dr C said that the language barrier made interpretation of Mrs B's musculoskeletal symptoms difficult and, as a result of these communication difficulties, he did not discuss the risks of ketoconazole with Mrs B.

128. I note Dr Maplesden's comment that "this situation [significant language barrier] is becoming increasingly common as immigration increases and affordable and appropriate translation services are not always available". However, the Code states that consumers have the right to effective communication, which includes the right to receive information in a manner that enables them to understand that information.

129. Dr C accepted the responsibility of caring for a patient who could not speak English. While I acknowledge the difficulties this caused him, it was his responsibility to provide Mrs B with the standard of care she was entitled to. If the language barrier prevented him from doing this, he could have transferred her care to a more suitable doctor, or put in place initiatives, such as ensuring a translator was available at their appointments. He did not do so.

130. I am critical that Dr C made insufficient arrangements to communicate effectively with Mrs B and, accordingly, I find that Dr C breached Right 5(1) of the Code.

131. Mrs B was also not provided with information that a reasonable consumer in her circumstances would expect to receive, in particular the potential risks and side effects

of the ketoconazole therapy. Accordingly, Dr C also breached Right 6(1)(b) of the Code. It follows that Mrs B was not in a position to make an informed choice, and give her informed consent to taking ketoconazole. Accordingly, Dr C also breached Right 7(1) of the Code.

Opinion: The Pharmacy — Breach

132. Dr C told HDC that he expected that if a drug interaction was detected on the Pharmacy's system when the medication was dispensed, the Pharmacy would contact him. Following Mrs B's death, Dr C contacted the Pharmacy and was told that it had been aware of the interaction between ketoconazole and simvastatin at the time the medication was dispensed. However, Dr C said that the Pharmacy did not notify him or withhold the prescription on any of the three occasions on which Dr C prescribed ketoconazole to Mrs B.

133. I note that, although the Pharmacy believes Dr C was contacted when the ketoconazole was dispensed initially, it was unable to provide any evidence to support this. My expert pharmacy advisor, Mr Glenn Mills, advised that this "highlights the necessity for interventions to be thoroughly recorded electronically". I agree and, in the absence of any evidence to support the assertion that Dr C was contacted, and in light of Dr C's assertion that he was not contacted, I do not accept that the Pharmacy advised him of the drug interaction on the first dispensing.

134. The Pharmacy accepted that Dr C was not contacted on the other two occasions on which ketoconazole was dispensed for Mrs B, even though a red flag alert would have appeared on its dispensing software on those occasions.

135. Mr Mills advised that, when prompted with a "red flag" alert during the process of entering a prescription, the staff member entering would be expected to do the following:

> "1. Review the alert;
>
> 2. In the case of a dispensing technician, advise the dispensing pharmacist of the alert (either verbally, or by annotation on the prescription etc); who would then continue the process detailed below;
>
> 3. Review the patient's dispensing history, including, in the case of a drug–drug interaction, identifying if the concomitant drug therapy had previously been dispensed;
>
> 4. Review any notes in the patient's dispensing history, including but not limited to whether the interaction had on a previous dispensing occasion been identified, researched and/or the prescriber contacted;
>
> 5. Discuss with other colleagues where appropriate;
>
> 6. Review appropriate reference information, to further understand the clinical mechanism and nature of the drug interaction and to assess its severity;

> 7. Contact the prescriber to alert them of any potential prescribing issue, provide them with clinical information as researched, and agree on a clinically appropriate plan;
>
> 8. Make clear and thorough electronic notations of the intervention on the patient's file, for future reference, including the issue raised, information obtained and outcome, contact with prescriber etc. as well as on the prescription, in case it is referenced in future (e.g. when dispensing repeats etc.);
>
> 9. Where appropriate, discuss the outcome with the patient, providing an explanation [of] any changes to the original prescription (whilst maintaining professional courtesy), ensuring the patient is confident about their therapy and is fully informed."

136. Mr Mills advised that Dr C's expectation that the Pharmacy would advise him of any interactions alerted to it is reasonable and valid. He stated that this forms part of "the fundamental responsibility of a pharmacist during the dispensing process i.e. that of assessing suitability of prescribed medication(s)". I accept this advice.

137. Mr Mills also advised that "the concomitant dispensing of incompatible medications to a patient distinctly breaches the fundamental standard of care a patient should reasonably expect". He said that, in his opinion, "drug interactions, such as between simvastatin and ketoconazole, are well understood and recognised and would generally be considered a 'well known' drug interaction by pharmacists".

138. A number of relevant standards that apply in New Zealand in relation to the completion of the dispensing process (outlined above) were not followed by the Pharmacy on any of the occasions on which ketoconazole was prescribed for Mrs B. In particular, Standard 5.2 of the Health and Disability Services Pharmacy Services Standard states that "[a] disciplined dispensing procedure shall ensure that the appropriate product is selected and dispensed accurately and efficiently", and Standard 5.2.4 states that "[p]rescriptions are interpreted and evaluated for correctness, appropriateness and completeness, their authenticity verified and their priority for dispensing determined".

139. Due to the lack of written documentation available, it has been difficult to evaluate the extent to which each particular individual pharmacist and dispensing technician was responsible for the dispensing in this case. For the first dispensing, this Office has established who entered the prescription and dispensed it, but the Pharmacy has been unable to advise who checked the dispensing. For the second dispensing this Office has established who entered the prescription and dispensed the medication, but the Pharmacy has been unable to advise who checked the dispensing. For the third dispensing this Office has established who checked the dispensing, but the Pharmacy has been unable to advise who entered the prescription and dispensed it. Therefore, I consider that several staff members failed to provide Mrs B with an appropriate standard of care.

140. Mr Mills advised me that the relevant part of the dispensing prescriptions SOP failed to outline the appropriate procedure to be followed when an alert was prompted,

including reviewing reference material, assessing severity and contacting the prescriber. Furthermore, there was no reference to detailing any interventions electronically on the patient's medical record in the dispensing software. I also note Mr Mills' advice that the alteration made to the Pharmacy's dispensing prescriptions SOP, in place at the time of these events, is not adequate.

141. The Pharmacy advised that a red flag alert would have been prompted on the dispensary software on the three occasions on which ketoconazole was dispensed. The alert was not documented, and Dr C was not contacted about it. As there were several pharmacists and technicians involved, I consider that there were systemic issues for which the Pharmacy must be held responsible. The relevant part of the dispensing prescriptions SOP, in place to guide staff in dealing with alerts and contraindicated drugs, was inadequate as it did not require the alert to be documented, communicated and investigated. A pharmacy has an obligation to ensure that it has in place adequate policies to facilitate safe dispensing. In my view, the Pharmacy failed to have in place an appropriate dispensing SOP that required its staff to act on an alert when prompted. Accordingly, the Pharmacy did not comply with Standard 5.2 of the Health and Disability Services Pharmacy Services Standard.

142. In addition, on three separate occasions, several staff members dispensed an inappropriate product, failed to evaluate the prescription for correctness (including its compatibility with other medications) and, on each occasion, failed to notify Dr C when the alert was prompted. Therefore, the Pharmacy also failed to comply with Standard 5.2.4 of the Health and Disability Services Pharmacy Services Standard. Accordingly, by failing to comply with professional standards, I find that the Pharmacy breached Right 4(2) of the Code.

Opinion: Auckland District Health Board — Breach

Admission process — Breach

143. In late 2012, Mrs B was transferred by ambulance to the public hospital. The ambulance transfer records state that Mrs B was taking Betaloc, aspirin, simvastatin and ketoconazole.

144. ADHB advised HDC that, after these events, as it could not find Mrs B's Doctors Prescribed Medication Chart from the Rest Home, it assumed that this was not provided to it on admission. However, a copy was provided to HDC by ADHB amongst Mrs B's clinical notes. This lists Mrs B's medications as "1) betaloc 2) aspirin 3) simvastatin", followed by a series of crossed out medications, followed by "12) Panadol liquid", a space of four lines, then "17) Ketoconazole". Accordingly, ketoconazole is listed as a current medication in two places (the ambulance transfer note and the medication chart). These documents appear to have been missed or overlooked by ADHB staff.

145. Mrs B's medications transcribed on admission were aspirin, metoprolol, simvastatin and paracetamol. ADHB advised HDC that these were the medications advised to staff on Mrs B's admission by those who accompanied her. Ketoconazole was not included. This list of medications appears to have been re-transcribed by the doctor who admitted Mrs B as an inpatient, repeating the error. The clinicians involved in Mrs B's care at ADHB were not aware of Mrs B's previous prescriptions of ketoconazole.

146. My expert advisor, consultant physician Dr Denise Aitken, advised me that failing to record Mrs B's medication accurately in this situation is an understandable mistake, "given the form of documentation of medications from the Residential Care Facility" and that it was difficult to correct because of language and cognition barriers with regard to Mrs B. However, I note that ADHB has acknowledged that if "medicines reconciliation on the day of admission" had occurred, it is likely it would have identified the true nature of Mrs B's illness at an earlier stage.

147. I am critical that, at the time, ADHB did not have in place an effective medicines reconciliation system.

Conclusion

148. Two documents listed ketoconazole as a current medication of Mrs B's, and both documents appear to have been missed or overlooked by ADHB staff, both on Mrs B's admission to ED and when she was admitted as an inpatient. ADHB has acknowledged that if "medicines reconciliation on the day of admission" had occurred, it is likely it would have identified the true nature of Mrs B's illness at an earlier stage. I am critical that Mrs B's notes were not reviewed adequately, and that medicines reconciliation did not occur. Had this happened, appropriate treatment could have been initiated much earlier. Accordingly, I find that ADHB failed to provide Mrs B services with reasonable care and skill and breached Right 4(1) of the Code.

Failing to review test result — Adverse comment

149. Mrs B was admitted on Friday as an inpatient to the public hospital. A physician requested a CK test. The abnormal result was posted (reported electronically) that afternoon. On Saturday, a registrar Dr E reviewed the abnormal result but did not bring it to the attention of a senior clinician. There is also no documentation in Mrs B's clinical notes requesting that the CK result be reviewed by the consultant even though the result was abnormal.

150. Dr Aitken advised me that inpatient services work in teams, and that a test result requested by the consultant is expected to be followed up and acted on, if abnormal, by the junior team. She also advised that, if it is not clear what action should be taken, escalation for advice to the next most senior person should occur. This did not occur on this occasion.

151. Dr Aitken advised me that when Mrs B's elevated CK was noted, the following should have occurred: "[R]eview of the patient's notes and medication list,

discontinuation of [s]imvastatin, repeat of all blood tests including electrolytes, renal function, CK and measurement of urinary myoglobin." This did not occur.

152. Had registrar Dr E on Saturday noted the abnormal CK result and discussed it with the consultant or flagged it for follow-up, diagnosis of the cause of Mrs B's weakness could have been made much earlier. Dr Aitken advised that she would view the failure to act on the abnormal CK result as a failure of process of moderate severity. I am critical that the abnormal CK result was not acted on.

Opinion: The Rest Home — Adverse comment

153. Mrs B's progress notes at the Rest Home were completed on an irregular basis, often with more than a week between entries. Generally, entries were also brief. In my view, Mrs B's progress notes were of a suboptimal standard in terms of frequency of entry and content of notes. I also note that there are two incident reports in Mrs B's file relating to medication errors, where the potential remedial actions refer to a need for more regular registered nursing staff. Both Dr C and the Pharmacy said that there had been periods at the Rest Home during which there was no registered nurse oversight of patients.

154. Dr C said if there had been "regular nursing supervision [at the Rest Home] [he] might have been alerted earlier about [Mrs B's] severity of symptoms such as tiredness and unsteadiness on her feet or inability to walk properly".

155. The failure by staff to document Mrs B's progress and observations appropriately appears to have led to Dr C's inability to pick up on the subtle changes in her condition. Dr C told HDC that he was very dependent on nursing and caregiver observations to aid his assessment of Mrs B because of the language barrier and her cognitive impairment.

156. I am critical that Mrs B's progress notes were completed only on an irregular basis, and that there was infrequent nursing support at the Rest Home. A lack of documentation in Mrs B's progress notes led to failings in communication between staff at the Rest Home and Dr C, and I am critical of this. However, I note that the Rest Home has since closed down and its residents have moved to other facilities.

Recommendations

157. I recommend that the Medical Council of New Zealand consider whether a review of Dr C's competence is warranted.

158. In response to recommendations made in my provisional opinion Dr C:

a) Provided a written apology to Mrs B's family for his breaches of the Code; and

b) Underwent further training on good prescribing practice.

159. I recommend that the company that traded as the Pharmacy:

a) Provide a written apology to Mrs B's family for its breach of the Code. The apology should be sent to HDC within three weeks of the date of the final report, for forwarding to Mrs B's family.

b) Obtain an independent review of the dispensing SOPs for all pharmacies that it owns and report to HDC on the outcome of the review within **three months** of the date of the final report.

c) Provide training to its pharmacists on its dispensing SOPs within **six months** of the date of the final report.

160. I recommend that ADHB provide a written apology to Mrs B's family for its breach of the Code. The apology should be sent to HDC within three weeks of the date of the final report, for forwarding to Mrs B's family.

Follow-up actions

161.
- A copy of the final report with details identifying the parties removed, other than the experts who advised on this matter and ADHB will be provided to the Medical Council of New Zealand and the Royal New Zealand College of General Practitioners, and they will be advised of Dr C's name.
- A copy of the final report with details identifying the parties removed, other than the experts who advised on this matter and ADHB, will be provided to HealthCERT, the Health Quality and Safety Commission and the NZ Pharmacovigilance Centre.
- A copy of the final report with details identifying the parties removed, other than the experts who advised on this matter and ADHB, will be placed on the Health and Disability Commissioner website, www.hdc.org.nz, for educational purposes.

Appendix A — In-house clinical advice to the Commissioner

The following expert advice was obtained from general practitioner David Maplesden:

> "1. Thank you for providing this file for advice. I have reviewed the available information: letter to HDC from [the Coroner] dated 8 October 2013; letter from geriatrician [Dr C] to Coroner dated 19 February 2013; letter from ADHB physician [Dr F] to Coroner dated 30 January 2013; document (undated) from the son of [Mrs B] outlining his concerns at her management; very limited [public hospital] clinical notes; [the rest home's] care documentation.
>
> 2. [Mrs B] died in [the public hospital]. Cause of death was felt to be hyperkalaemia secondary to acute renal failure, the renal failure being secondary to acute rhabdomyolysis — that condition most likely being a consequence of [Mrs B] taking the contraindicated combination of simvastatin and ketoconazole. [Mrs B's] past medical history and the sequence of events leading to her death has been well documented in the Coronial reports and will not be reiterated in detail here.
>
> 3. [Dr C] acknowledges he prescribed a contraindicated combination of medications and this was an error on his part. He failed to recall the potential interaction between simvastatin (one of [Mrs B's] long term medications) and ketoconazole on any of the three occasions he prescribed short courses of ketoconazole to treat [Mrs B's] fungal skin infection (confirmed on culture [date]), those dates being [first occasion] (one month course at 200mg daily), [second occasion] (one month course at 200mg daily) and [third occasion] (two month course at 400mg daily). This is discussed further below.
>
> 4. [Rest home] caregiver/nursing progress notes are available from [mid] 2012. These have been completed on an irregular basis with often more than a week between entries. The entries are generally brief and certainly do not indicate [Mrs B] was having problems with mobility and weakness prior to [her fall] as indicated by her son in his report. Notes for [the day of her fall] state *Feel restless, Pt pain on ankle and very painful to walk on. Check BP 172/79, pulse 48 + temp 35°C, handover to PM staff + Dr to assess.* [The following day] *Seen by [Dr C] yesterday due to painful ankle + buttock. Charted liquid paracetamol, take four times a day.* Next entry is [two days later] — *At 2148 when she use commode she slipped and sitted on the floor, help her back to bed. Check blood pressure 170/69, pulse 52 but she can answer question and can hold my hand, just looks very weak so report to manager and manager contact with hospital.* The care notes appear to be of a suboptimal standard in terms of frequency of entry and content of notes. There are at least two incident reports on file relating to 'medication errors' with potential remedial actions noted referring to need for registered nursing staff. [Dr C] noted in his report to the Coroner that four months of notes were missing and could not be found, and that there have been long periods at the facility where there has been no registered nurse oversight of patients. He feels the failure by care staff to report perhaps subtle changes in [Mrs B's] condition to him may have

impaired his ability to suspect the true nature of her condition. **These are all concerning issues with respect to rest home care and processes and I think require further investigation. The nursing advisor may be able to give some direction in this regard.**

5. GP notes are generally brief but probably adequate. If the notes are complete and sequential, it appears [Mrs B] was not seen for review between [mid 2011 and early 2012] which would be a departure from the expected practice of at least three-monthly review of rest home patients. GP notes [on the third occasion] are: *Recurrence fungal rash lower abd. 130/70. Chest √ Rx ketoconazole 8wks, Lamisil Cr.* [Two weeks later] *rash markedly improved. Continue ketoconazole for total 8 weeks.* On [day of fall] *Painful L buttock after fall against tap OE bruising L buttock only + crepitus both knees. Rx Panadol, Bloods to exclude PMR* [polymyalgia rheumatica]. The notes do not mention any generalised unwellness, weakness or myalgia or discoloured urine despite the report from [Mrs B's] son regarding his mother's condition over this period. The care notes did not record any concerns other than those documented by [Dr C], and given the difficulties gaining an accurate history from [Mrs B] (language barrier and cognitive impairment) [Dr C] was very dependent on nursing or caregiver observations to aid his assessment of [Mrs B]. There may have been a deficiency in this aspect of inter-provider communication.

6. Examination of sequential blood results on [rest home] files indicates tests were undertaken on [seven occasions]. Results of note include: evidence of adequately controlled diabetes (managed with diet only); adequate control of hyperlipidaemia (on simvastatin); normal blood count and thyroid function each time they were tested; suboptimal renal function in January and April 2009 (eGFR 53 and 54 respectively, normal >60) but serum creatinine within normal limits, renal function returning to normal [mid] 2011 and [mid] 2012, slight deterioration (eGFR 59 and normal creatinine) [mid] 2012 with further deterioration (eGFR 47 and creatinine mildly elevated at 98 µmol/L (normal 45–90) [in late] 2012); C-reactive protein normal on [in late] (making a diagnosis of PMR unlikely); liver function tested once [in mid] 2012 (not done at any time immediately preceding or during [Mrs B's] ketoconazole courses) and normal at this point.

7. The potential interaction between statins and CYP3A4 inhibitors (such as ketoconazole) has been recognised for at least 15 years[1]. The risk of rhabdomyolysis with statins alone is also recognised but is rare. However, the risk of myopathy is increased when statins are coadministered with medications that inhibit their metabolism. Simvastatin is a CYP3A4 substrate and when coadministered with potent CYP3A4 inhibitors the incidence of myopathy is increased by about five-fold[2]. In New Zealand, Medsafe has communicated with doctors on several occasions warning of the risk of statin interactions. In May

[1] Gilad R et Lampl Y. Rhabdomyolysis induced by simvastatin and ketoconazole treatment. Clin Neuropharmacol. 1999;22(5):295–7

[2] Jacobson TA. Comparative pharmacokinetic interaction profiles of pravastatin, simvastatin, and atorvastatin when coadministered with cytochrome P450 inhibitors. Am J Cardiol. 2004;94:1140–6

2004 a Prescriber Update[3] report stated *reports of myopathy and rhabdomyolysis with statins are a reminder to prescribers to measure creatine kinase (CK) levels in patients presenting with muscle pain or weakness. The risk of myopathy may be increased by high doses of statins, especially in patients with co-morbidities, or in the presence of interacting medicines such as diltiazem … The Centre for Adverse Reactions Monitoring (CARM) has received eight recent reports (including two fatalities) of rhabdomyolysis occurring in patients taking between 20mg and 80mg of a statin daily … All patients in the eight cases initially complained of myalgia or muscle weakness and were later diagnosed with rhabdomyolysis. Two of the patients on simvastatin presented with urinary discoloration; one went on to develop acute renal failure. The duration to onset of symptoms ranged from 2–12 weeks from initiation of, or change in, statin therapy. The patients were between 54–79 years of age; five were taking other medicines known to interact with statins … Three patients had significant co-morbidities including chronic renal failure and hepatic cirrhosis; two patients had recently had their simvastatin dose increased to 60mg and 80mg daily… It is advisable to monitor patients for signs and symptoms of muscle pain, tenderness or weakness, particularly during both the initial months of statin therapy and subsequent dose increases. Creatine kinase measurements must be performed when symptoms occur. Patients with additional risk factors (e.g. diabetes, older age, hypothyroidism, liver or renal disease) merit closer monitoring as they may be more at risk of rhabdomyolysis … Statin treatment should be discontinued immediately if an elevated CK level is found … or where myopathy is suspected or diagnosed … Consider temporarily discontinuing* [simvastatin] *if short-term courses of azole antifungals* [such as ketoconazole] *or macrolide antibiotics are required …*

8. A 2010 BPAC article on prescribing of statins[4] included the following recommendations: *After initiating statin treatment, creatine kinase should be checked when there are unexplained muscular symptoms, however no other monitoring is routinely required; Monitoring of creatine kinase is not required in people who are asymptomatic. If there is unexplained muscle pain, tenderness or weakness, statin treatment should be stopped and creatine kinase levels checked; Factors that may increase the risk of statin induced myopathy are: advanced age (>80 years old), female sex, low body mass index, multisystem diseases (for example, diabetes mellitus), diseases affecting kidney or liver function, hypothyroidism (untreated), drug interactions, especially with drugs that are inhibitors or substrates of the cytochrome P450 pathway (for example, fibrates, nicotinic acid, calcium channel blockers, ciclosporin, amiodarone, thiazolidinediones, macrolide antibiotics, azole antifungals, protease inhibitors, warfarin), vigorous exercise, excess alcohol, intercurrent infections, major surgery or trauma, diet (excessive grapefruit or cranberry juice), and genetic factors.* [Mrs B's] ethnicity as an additional risk factor was not mentioned in this publication but is in other publications.

[3] Myopathy with Statins: Check CK Levels and Interactions. Prescriber Update 2004;25(1):4–5. Available at: http://www.medsafe.govt.nz/profs/puarticles/Statinmyop.htm
[4] Available at: http://www.bpac.org.nz/BPJ/2010/August/statins.aspx

9. In April 2011 a further Prescriber Update[5] reinforced the warning regarding statin interactions and the co-prescribing of simvastatin and potent CYP3A4 inhibitors was noted to be contraindicated. *Prescribers are reminded of the potential for serious adverse reactions when statins are prescribed with medicines that inhibit the CYP3A4 isoenzyme. Recent reports to the Centre for Adverse Reactions Monitoring (CARM) indicate that the concomitant treatment with medicines that interact with simvastatin or atorvastatin has led to serious myopathies. These reports have included life-threatening and fatal cases of rhabdomyolysis. In some cases more than one interacting medicine was prescribed.*

The adverse reaction reports describe common situations such as: The use of macrolides for acute infection without stopping the patient's regular simvastatin; Initiating diltiazem in patients taking over 40 mg simvastatin daily; A lack of clarity in the treatment plan when care of the patient is transferred from primary to secondary care. [This comment may have been particularly relevant in [Mrs B's] case — see later discussion on hospital care.]

10. The Medsafe data sheet for simvastatin[6] includes the following relevant information:

(i) Contraindications include: *Concomitant administration of potent CYP3A4 inhibitors (eg. itraconazole, **ketoconazole,** posaconazole, voriconazole, HIV protease inhibitors, boceprevir, telaprevir, erythromycin, clarithromycin, telithromycin nefazodone and drugs containing cobicistat (see Warnings and Precautions, Myopathy/Rhabdomyolysis and Interactions).*

(ii) *Myopathy sometimes takes the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria, and rare fatalities have occurred. The risk of myopathy is increased by high levels of HMG-CoA reductase inhibitory activity in plasma. Predisposing factors for myopathy include advanced age (≥65 years), female gender, uncontrolled hypothyroidism, and renal impairment. The risk of myopathy/rhabdomyolysis is increased by concomitant use of simvastatin with the following medicines:* [contraindicated medication list as above, including ketoconazole, is reproduced] … *If short-term treatment with potent CYP3A4 inhibitors is unavoidable, therapy with* [simvastatin] *should be suspended during the course of treatment.*

11. The Medsafe data sheet for ketoconazole[7] includes the following relevant information:

(i) Adult dosage: *The recommended dose of* [ketoconazole] *tablets for all indications is one tablet (200 mg) once daily with a meal, with the exception of vaginal candidosis … If no adequate response is obtained with this dose after a*

[5] Statin interactions: reports of serious myopathy. Prescriber Update 2011;32(2):13–14. Available at: http://www.medsafe.govt.nz/profs/PUArticles/StatinInteractionsJune2011.htm
[6] Available at: http://www.medsafe.govt.nz/profs/datasheet/l/Lipextab.pdf
[7] Available at: http://www.medsafe.govt.nz/profs/datasheet/n/nizoraltab.pdf

reasonable trial period, the dosage may be increased to two tablets (400 mg) once daily with a meal …

(ii) Duration: *Treatment should be continued without interruption until clinical parameters or laboratory tests indicate that the fungal infection has resolved. An inadequate treatment period may lead to recurrence of the active infection. However, the risk of serious hepatic toxicity increases with longer duration of treatment. Therefore, long duration of treatment should only be given after full consideration of the extent of treatment response and the risks and benefits of continuing treatment. If treatment is continued, liver function should be closely monitored. Treatment should be stopped immediately and liver function testing should be conducted when signs and symptoms suggestive of hepatitis such as anorexia, nausea, vomiting, fatigue, jaundice, abdominal pain or dark urine occur … The usual duration of treatment is as follows: … Dermatophytosis* [as suffered by Mrs B]: *approximately 4 weeks.*

(iii) *Concomitant administration of* [ketoconazole] *tablets with any of the following medicines is contraindicated: … CYP3A4 metabolised HMG-CoA reductase inhibitors such as simvastatin or lovastatin.*

(iv) *WARNING: because of the risk for serious hepatotoxicity,* [ketoconazole] *tablets should be used only when the potential benefits are considered to outweigh the potential risks, taking into consideration the availability of other effective antifungal therapy. Assess liver function, prior to treatment to rule out acute or chronic liver diseases. Liver function should then be monitored at frequent and regular intervals during treatment (for example, after two and four weeks of treatment and then on a monthly basis). Liver function should also be assessed at the first signs or symptoms of possible hepatotoxicity.*

12. On 1 December 2013 the manufacturers of ketoconazole for the New Zealand market advised they were discontinuing production of the drug. The Medsafe announcement[8] was: *Oral ketoconazole tablets are a prescription medicine used to treat fungal infections. Due to ongoing safety concerns regarding liver injury with the use of oral ketoconazole tablets, the manufacturer has decided to stop making this medicine. This adverse reaction is well known with oral ketoconazole and was most recently discussed by the Medicines Adverse Reactions Committee (MARC) in September 2011.*

13. General background on prescribing errors

(i) A 2009 prospective study in the UK[9] documented errors in prescriptions from 28 general practitioners as they occurred over a 3-day period in 12 community pharmacies. From a total of 3,948 prescriptions, 491 (12.4%) contained one or more errors. From a total of 8,686 drug items, 546 (6.2%) contained one or more errors. Of the errors the majority were minor (398, 72.9%), a smaller number (135, 24.7%) were major nuisance errors, and there were 13 (2.4%) potentially serious errors. The most common errors related to drug directions and dosage.

[8] Available at: http://www.medsafe.govt.nz/Projects/B2/2013/oral-ketoconazole.asp
[9] Sayers YM et al. Prescribing errors in general practice: A prospective study. Eur J Gen Pr 2009;15

(ii) A more recent comprehensive UK study[10] including systematic and retrospective reviews concluded: *Prescribing or monitoring errors occurred in one in 20 prescription items and most of these were judged to be of mild to moderate severity; one in 550 prescription items contained a severe error. The risks of error were higher in young people, the elderly, males and those on multiple medications. Several groups of drugs were associated with higher risks of error including those requiring blood test monitoring, and those used for musculoskeletal problems and malignant disease/immunosuppression* [methotrexate fulfils these criteria]. *A wide range of different types of error were identified with a wide range of underlying causes. The general practices involved in the study identified a large number of strategies for minimising the risks of error … Prescribing errors in general practices are common, although severe errors are unusual. Many factors increase the risk of error. Strategies for reducing the prevalence of error should focus on GP training, continuing professional development for GPs, clinical governance, effective use of clinical computer systems, and improving safety systems within general practices and at the interface with secondary care.*

14. The Medical Council of New Zealand[11] states that prescribers should *be familiar with the indications, side effects, contraindications, major drug interactions, appropriate dosages, effectiveness and cost-effectiveness of the medicines that you prescribe.*

15. Comments regarding [Dr C's] management of [Mrs B]

(i) [Mrs B] had an elevated cardiovascular risk and it was reasonable for her to be prescribed simvastatin at a dose of 40mg daily. This medication had been initiated by [Mrs B's] previous provider and it is not possible for me to comment on whether risks and benefits were adequately discussed at the time of initiation. Serum lipid levels were monitored regularly. There was no indication to monitor creatine kinase (CK) levels until [Mrs B] developed mylagia in [late] 2012. However, at this point there was a recent injury to account for [Mrs B's] musculoskeletal symptoms, although [Dr C] had apparently thought the condition was sufficiently atypical to warrant considering a diagnosis of PMR. If there were atypical features of the presentation with respect to extent of myalgia and/or muscle weakness, and leaving aside for the moment the issues of concomitant prescribing of ketoconazole, best practice would have been to stop simvastatin while CK levels were checked to exclude statin induced myopathy as a cause of the symptoms. Mitigating factors were that [Mrs B] had taken simvastatin at a constant dose for at least a couple of years without problems, the history of recent injury and perhaps difficulties recognising subtle aspects of the history as discussed in section 5.

[10] Avery T et al. Investigating the prevalence and causes of prescribing errors in general practice: The PRACtICe Study. A report for the GMC, May 2012. Available at: http://www.gmc-uk.org/Investigating_the_prevalence_and_causes_of_prescribing_errors_in_general_practice___The_PRACtICe_study_Reoprt_May_2012_48605085.pdf

[11] Medical Council of New Zealand. Good prescribing practice. April 2010. Available at: http://www.mcnz.org.nz/assets/News-and-Publications/Statements/Good-prescribing-practice.pdf

(ii) [Mrs B] suffered from culture confirmed tinea corporis (fungal infection of the skin on the trunk). The most common cause of this infection is tricophyton rubrum as was cultured from [Mrs B] in 2011. Such infections are usually treated initially with topical antifungal agents but if the treatment is unsuccessful, oral antifungal agents may be considered[12]. I cannot determine from the available documentation whether [Mrs B] was given an adequate trial of topical antifungal treatment before the use of oral ketoconazole was considered. I am unable to determine whether the potential risks of ketoconazole therapy, with respect to liver toxicity, were discussed with [Mrs B] (or her representative) before oral ketoconazole was prescribed. Assuming [Mrs B's] skin condition had failed to respond adequately to appropriate topical treatment, and she made an informed choice (most likely through her representative) to take the medication, had she not been taking simvastatin concomitantly it was probably reasonable to prescribe the regimes recorded [on the first two occasions], particularly as a response to treatment was noted. However, it appears there was no monitoring of liver function as advised in the prescribing information sheet on any of the occasions the medication was prescribed and this was particularly significant following the prescribing of a higher dose of ketoconazole for a longer than usual period [on the third occasion]. Leaving aside the issue of concomitant prescribing of ketoconazole and simvastatin, the failure to ensure recommended monitoring of liver function was undertaken (and there is no evidence such monitoring was intended [on the third occasion]) prior to and during ketoconazole therapy was a significant (**at least moderate**) departure from expected standards, particularly when the longer course at higher dose was initiated [on the third occasion] (although such prescribing was still within accepted practice had [Mrs B] been appropriately informed, monitored and had not been taking a statin). I would be **moderately critical** if the potential risks of ketoconazole therapy had not been discussed with [Mrs B] or her representative at least prior to the first course of treatment in 2011. I would be **moderately critical** if oral ketoconazole had been initiated without an adequate trial of appropriate topical therapy in the first instance.

(iii) The co-prescribing of ketoconazole and simvastatin is contraindicated and there has been significant information conveyed to the medical profession on the risks of such prescribing over several years. Any prescriber has a duty to be aware of contraindications to particular prescribing or co-prescribing. Therefore, the prescribing error in this case must be regarded as a **severe departure** from expected standards particularly as it occurred on three separate occasions over two years. There are mitigating factors which deserve consideration but do not alter the degree of departure from expected standards: As discussed in section 13, prescribing errors are common in medical practice. There are some 'safety-net' processes which attempt to reduce the risk of harm to patients from such errors. Many computerised prescribing modules will flag potential medication interactions at the time of prescribing although such systems are not optimal in that many do not differentiate between trivial and significant interactions and can eventually be disregarded by the provider for this reason. In any case, [Dr C] did

[12] See: http://www.dermnetnz.org/fungal/tinea-corporis.html

not have access to such assistance as he was prescribing manually at the rest home. Perhaps more importantly, there is an expectation that any prescribing errors including significant interactions will be detected when the medication is dispensed (pharmacy), although this relies to some extent on the pharmacy being aware of all medications the patient is taking. It appears from [Dr C's] response that the pharmacy was aware of the interaction but did not notify him or withhold the prescription. **This may represent a significant departure from expected pharmacist practice and a response, and any relevant records, should be obtained from the pharmacy concerned with independent expert pharmacist advice possibly warranted**.

16. Treatment of [Mrs B] at [the public hospital]: The letter from ADHB outlining [Mrs B's] management in [the public hospital] does not in itself raise any immediate concerns regarding her management and I agree that even had the cause of her rhabdomyolysis been recognised earlier following admission, the clinical outcome may not have altered. However, there is insufficient information currently available to comment in any more detail. I note [Mrs B's] simvastatin was not stopped until [Tuesday] (admitted [previous Thursday]) which could be criticised given her presentation with an apparent myopathy and elevated CK (although the date of receipt of the first CK result is unknown). The issue of whether sufficient regard was paid to her admission medication regime is dependent to some extent on whether a copy of her [rest home] medication list was amongst her [transfer documentation] (could be confirmed with the rest home and/or should be present in DHB documentation). This list clearly shows she was taking simvastatin and ketoconazole concomitantly. **Given there may be some issues with DHB management I recommend in the first instance a copy of hospital notes for the admission in question be obtained (entire file including lab results, medication charts etc) and specifically noting the transfer documentation available from [the rest home]. Expert advice from a general physician may also be required depending on what is revealed in the notes.**"

Further expert advice was received from Dr Maplesden:

"I have reviewed additional responses from [Dr C] dated 25 June 2014 and 5 August 2015. I make the following observations and comments:

1. [Dr C] states he was aware of the interaction between ketoconazole and simvastatin when he prescribed ketoconazole for [Mrs B] [on three occasions] while she was taking simvastatin concurrently. He states he failed to realise [Mrs B] was taking simvastatin. The failure to check [Mrs B's] regular medications when prescribing a medication (ketoconazole) known to have potential for interaction with many drugs was a moderate to severe departure from expected standards. The Medical Council of New Zealand states, in the publication 'Good prescribing practice (April 2010)': *Take an adequate drug history of the patient, including: any previous adverse reactions to medicines; current medical conditions; and concurrent or recent use of medicines.* While there was a significant language barrier present in this case, [Mrs B's] medication records should have been readily accessible and accessed prior to the prescribing in

question. An aggravating factor is that such prescribing was undertaken on three separate occasions. However, I accept [Dr C] was aware of the potential interaction between the two drugs as he should have been given the amount of clinical information available on the interaction.

2. I accept [Dr C] tested [Mrs B's] liver function [two months after completion of her second course of ketoconazole] and these were normal. He assumed on this basis there had been no liver damage from the previous courses of ketoconazole and was confident [a third course] would be similarly tolerated. I note this 'delayed' testing was not in accordance with manufacturer recommendations (see sections 11(ii) and 15(ii) of my original advice) but also that the first two courses of ketoconazole were of short duration (one month) and lower dose. Leaving aside the issue of co-prescribing of simvastatin and ketoconazole, I am mildly critical of liver function monitoring during [Mrs B's] first two courses of ketoconazole but I remain moderately critical of her monitoring during [the third course] which involved a higher dose of ketoconazole (400mg daily) for a longer period (eight weeks).

3. I accept [Mrs B] had received an adequate trial of topical therapy for her dermatomycosis before oral therapy was considered and have no adverse criticism of this aspect of her care (change from previous advice). [Dr C] has explained the difficulty attempting to explain the risks and benefits of any treatment to [Mrs B] and her husband because of the language barrier, and the impracticality of trying to get appropriate interpretation of information every time a medication change was to be considered. While this situation was a significant barrier to provision of informed consent, I am aware of the Medical Council of New Zealand's recommendations (as per the previously cited reference): *Ensure that the patient (or other lawful authority) is fully informed and consents to the proposed treatment and that he or she receives appropriate information, in a way they can understand, about the options available; including an assessment of the expected risks, side effects, benefits and costs of each option.* Given the circumstances, I am mildly critical the potential risks of ketoconazole treatment were not discussed with [Mrs B] or her representative on any of the three occasions it was prescribed (change from previous advice), and the remedial measures since undertaken (appointment of a [bilingual] doctor to the rest home) may assist with provision of appropriate information in the future. However, I note this situation (significant language barrier) is becoming increasingly common as immigration increases and affordable and appropriate translation services are not always available.

4. I accept the language barrier also made interpretation of [Mrs B's] musculoskeletal symptoms following her fall in [late] 2012 somewhat difficult to clarify, and that under the circumstances (recent fall and symptoms apparently consistent with that fall) there was no obvious reason to consider statin induced myopathy in the differential diagnosis and therefore to check CK levels. I am not critical of this aspect of [Dr C's] care of [Mrs B].

5. Taking into account the discussion above, and comments in my original advice, I feel [Dr C's] co-prescribing of simvastatin and ketoconazole to [Mrs B] on three

separate occasions represents a moderate to severe departure from expected practice (change from previous advice) even if the primary reason was a failure to check her existing medications rather than a failure to be aware of the potential risk of such co-prescribing. This opinion takes into account the mitigating factor of the language barrier, but also the aggravating factor of the co-prescribing occurring on three separate occasions. I acknowledge the potential interaction should have been detected by the dispensing pharmacy if the pharmacy had a record of [Mrs B's] regular medications but I think the clinician has a primary responsibility to take all appropriate steps (including checking of existing medications) to prescribe safely rather than prescribing without due care with the expectation that the pharmacy will provide a failsafe backstop.

6. [Dr C] states he was in a contractual arrangement with a PHO (ProCare) to enable him to claim GMS benefits. This is a standard arrangement for all GPs providing services to patients (enrolled service users) registered with that GP, and avoids the need for multiple individual contracts between GPs and the DHB (through which primary care funding is channelled). The PHO holds the contract with the DHB for primary care funding and GPs sign a 'back to back' contract with the PHO to access that funding. [...] [Dr C] appears to have contracted his services to the rest home in question and for the purposes of the investigation is probably best regarded as being a self-employed contractor."

Appendix B — Independent pharmacy advice to the Commissioner

The following expert advice was obtained from registered pharmacist Mr Glenn Mills:

> "I have been asked to provide an opinion to the … Health and Disability Commissioner on Case Reference 13/01300, regarding [Mrs B]. I confirm I have read and agree to follow the Commissioner's Guidelines for Independent Advisors.
>
> I have no personal or financial connections with the provider(s) or the consumer(s) in this case. I also confirm that no professional connection exists with the provider(s), I am free of bias and it is of my opinion that no conflict of interest exists.
>
> I am a registered pharmacist with the Pharmacy Council of New Zealand, a member of the Pharmaceutical Society of New Zealand and an Associate Member of the New Zealand College of Pharmacists. I have been registered as a Pharmacist since 2002.
>
> I am a shareholder and director of Life Pharmacy Albany Limited, a large, busy community pharmacy in Albany, on Auckland's North Shore. I am employed in a full-time capacity by Green Cross Health, in the position of Executive — Pharmacy Partners, and am responsible for the operation, performance and development of approximately 75 pharmacies in which Green Cross Health has an equity shareholding.
>
> **Referral Instructions**
>
> I have been requested by [a] Legal Investigator, by letter dated 29 April 2015, to provide advice to enable the … Commissioner to determine whether, from the information available, there are concerns about the pharmacy care provided to [Mrs B] by [the Pharmacy] and/or its staff, as outlined further in this report. In particular, I have been requested to provide my opinion to the questions below:
>
> a) The pharmacy has changed ownership and apparently little information has been retained, however it would be appreciated if you can advise us of anything else we should try to obtain that is not enclosed;
>
> b) What is the expected response from a pharmacist when a 'red flag' appears on the pharmacy's dispensing system;
>
> c) Your thoughts with regard to the Doctor's comment to this Office that he had an expectation that when prescribing, the pharmacy would advise him of any interactions if they were alerted to them;
>
> d) Whether you have any comments on the policies that we have been provided also whether there are any additional policies we should try to obtain;
>
> e) Any other comments or advice would also be appreciated.

Material Reviewed (as provided)

1. Complaint from [Mrs B's] son, Mr A (undated);

2. Response from [the Pharmacy] (legal owner of [the] Pharmacy at the time of these events), dated 28/8/14;

3. Incident Reporting Form, dated [late 2012], completed by [the pharmacist];

4. Medication Chart for [Mrs B];

5. Phoned Prescriptions Form for the [Rest Home], dated [2012];

6. Amended Standard Operating Procedure C10 — Dispensing Prescriptions, MPSOs and BSOs (undated);

7. Response from dispensing pharmacist [Mr D], dated 28/8/14;

8. Response from [the] new owner of [the] Pharmacy, dated 5/8/14;

9. Patient History Report provided by [the new owner of the Pharmacy], dated 16/7/14;

10. Various standard operating procedures (SOPs) from [the new owner], including:

a. SOP C34: Dispensing 1 — Receive prioritise and validate prescription

b. SOP C35: Dispensing 2 — Prescription assessment and clinical check

c. SOP C36: Dispensing 3 — Labelling and dispensing medicines

d. SOP C37: Dispensing 4 — Accuracy check

e. SOP C38: Dispensing 5 — Counselling for dispensed medicines

f. SOP K06: Dispensing errors and near miss

g. SOP K12: Incident reporting

Factual Summary

[Mrs B], aged 79 at the time of these events, was a patient of a residential care facility, [the Rest Home]. Under the care of a doctor (anonymised) who would visit the resthome, [Mrs B] was taking Simvastatin for high cholesterol and, whilst taking this drug, was prescribed Ketoconazole, for chronic skin infections, following failed topical treatments. Ketoconazole 200mg daily for four weeks was prescribed on two occasions, and on a third occasion, 200mg twice daily for eight weeks was prescribed.

The prescribing doctor advised HDC that as he was prescribing in a rest home, that he used manual notes, not a computer, and therefore no alert popped up advising him of a potential drug interaction. He also advised that when he prescribed the Ketoconazole to [Mrs B], he had forgotten she was being co-prescribed Simvastatin.

Following hospitalisation, [Mrs B] unfortunately [passed away], and it was found that the co-prescribing of these two drugs were highly likely to have led to her death.

The Office of the HDC was advised by the pharmacy that a potential interaction was prompted on its software system; however, the pharmacist deemed it appropriate to dispense the third (and higher dose) on this instance, as [Mrs B] had been prescribed the drug on previous occasions.

The pharmacy has also advised that it is not possible to tell who dispensed the earlier two prescriptions of Ketoconazole.

[In 2013, the Pharmacy] was sold to a new proprietor.

Advisor Opinion & Commentary

Please find below my opinion and comments, with regard to the specific questions presented for my comment, as well as general comments for consideration.

a) The pharmacy has changed ownership and apparently little information has been retained, however it would be appreciated if you can advise us of anything else we should try to obtain that is not enclosed;

It is my opinion that it could be beneficial to obtain the following further information:

1. Copies of the original proprietor's standard operating procedures, valid at the time of these dispensings. Whilst [Mr G] has advised these have been replaced, they may have been retained in an electronic format? Alternatively, if the pharmacy had been audited by the Ministry of Health, they may have been provided to the Auditor at this time. Copies of these SOPs would further assist in clarifying whether there was a failure in the duty of care to the patient by the Pharmacy and/or the Pharmacist(s), through unacceptable operating procedures. Of particular interest would be the procedures around the full dispensing process (SOP C10), including the dispensing of repeat prescriptions.

2. A list of the reference sources available at the time of dispensing, including any approved reference text(s) for drug interactions;

3. Copies of the prescriptions generated by the pharmacy and signed by the prescriber. These could be obtained under a request to HealthPAC (as they are sent by the pharmacy to Sector Operations after retention for five months). It would be deemed best practice that these would be annotated by the person entering, dispensing and checking the prescription (and could be confirmed upon receipt of the SOPs described above), and may assist in identifying the persons responsible in each of the Ketoconazole dispensings.

4. In his letter dated 28/8/14, [Mr D] describes that '… the blister packs were put through the computer and packed by the technician …". There is no statement

provided by the dispensing technician, and this could warrant further investigation, to assist in clarifying the action(s) taken when the interaction 'alert' was prompted during the entering of the prescription record on this third occasion and to establish the general procedures followed within the pharmacy on a day to day basis.

b) What is the expected response from a pharmacist when a 'red flag' appears on the pharmacy's dispensing system;

It is my opinion that it would generally be expected by my peers that, when prompted with a 'red flag' alert during the process of entering a prescription, the staff member entering would:

1. Review the alert;

2. In the case of a dispensing technician, advise the dispensing pharmacist of the alert (either verbally, or by annotation on the prescription etc.); who would then continue the process detailed below;

3. Review the patient's dispensing history, including, in the case of a drug–drug interaction, identifying if the concomitant drug therapy had previously been dispensed;

4. Review any notes in the patient's dispensing history, including but not limited to whether the interaction had on a previous dispensing occasion been identified, researched and/or the prescriber contacted;

5. Discuss with other colleagues where appropriate.

6. Review appropriate reference information, to further understand the clinical mechanism and nature of the drug interaction and to assess its severity;

7. Contact the prescriber to alert them of any potential prescribing issue, provide them with clinical information as researched, and agree on a clinically appropriate plan.

8. Make clear and thorough electronic notations of the intervention on the patient's file, for future reference, including the issue raised, information obtained and outcome, contact with prescriber etc. as well as on the prescription, in case it is referenced in future (e.g. when dispensing repeats etc.).

9. Where appropriate, discuss the outcome with the patient, providing an explanation [of] any changes to the original prescription (whilst maintaining professional courtesy), ensuring the patient is confident about their therapy and is fully informed.

c) Your thoughts with regard to the Doctor's comment to this Office that he had an expectation that when prescribing, the pharmacy would advise him of any interactions if they were alerted to them;

It is my opinion that the Doctor's expectation that the pharmacy would advise him of any interactions alerted to them is reasonable, valid and would be shared by his peers. Further, it is my opinion that my peers would agree that this forms part of

the fundamental responsibility of a pharmacist during the dispensing process i.e. that of assessing suitability of prescribed medication(s).

Regrettably, the concomitant dispensing of incompatible medications to a patient distinctly breaches the fundamental standard of care a patient should reasonably expect, when presenting a prescription to a pharmacy for dispensing.

It is relevant to note that, in my opinion, cytochrome P450 drug–drug interactions, such as between Simvastatin and Ketoconazole, are well understood and recognised and would generally be considered a 'well known' drug interaction by pharmacists.

There are a number of relevant professional standards that apply to pharmacists in New Zealand in relation to the completion of the dispensing process. These standards include legislative requirements and, for a process failure such as on this occasion, notably Standards New Zealand's Health and Disability Services Pharmacy Services Standard (NZS 8134.7:2010) and the Pharmacy Council of New Zealand's Competence Standards for the Pharmacy Profession. Below, I refer to key standards that in this instance, in my opinion, have unfortunately clearly been breached.

Standards New Zealand — Health and Disability Services Pharmacy Services Standard (NZS 8134.7:2010):

Standard 1.7: Consumers receive services of an appropriate standard;

Standard 3.5: Consumers shall receive adequate and appropriate services in order to meet their assessed needs and desired outcomes;

Standard 3.8: Consumers shall receive medicines in a safe and timely manner that complies with current legislative requirements and safe practice guidelines;

Standard 5.2: A disciplined dispensing procedure shall ensure that the appropriate product is selected and dispensed accurately and efficiently.

Standard 5.2.4: Prescriptions are interpreted and evaluated for correctness, appropriateness and completeness, their authenticity verified and their priority for dispensing determined.

Guidance G.5.2.4: (d) Compatibility with other medication

Pharmacy Council of New Zealand — Competence Standards For The Pharmacy Profession (January 2011)[1]:

Standard 1.1.5: Works accurately;

Standard 6.2.2: Follows workplace dispensing criteria when dispensing a prescription item.

[1] Please note these standards have recently been re-published in January 2015; however the Standards valid at the time of these incidents have been referenced.

Standard 6.5.1: Confirms that each selected medicine is suitable for the patient;

Standard 6.6.2: Maintains a logical, safe and disciplined dispensing procedure

d) Whether you have any comments on the policies that we have been provided also whether there are any additional policies we should try to obtain;

Please refer to my previous advice under the heading a).

Further Commentary for Consideration

It is difficult to provide comprehensive commentary on this unfortunate incident, due to the lack of written documentation available to review. Importantly, the absence of standard operating procedures, current at the time of these dispensings, makes it difficult to assess [the Pharmacy's] role in this incident. Additionally, the lack of information provided pertaining to the first and second dispensings is frustrating, as it is possible the pharmacist(s) and/or dispensary technician(s) involved on these occasions may have been culpable for not identifying the non-suitability of this drug combination. This warrants further consideration.

It is important to note that there is no evidence presented that pharmacist [Mr D] was advised of the 'alert' having been prompted in the dispensary software. As previously described, in my opinion this warrants further investigation, as a pharmacy technician may have in fact received this alert and chosen to ignore it and failed to discuss it with the pharmacist. However, it is my opinion, based on the facts and responses presented, that pharmacist [Mr D] did not provide an appropriate standard of care to [Mrs B] on this occasion. It is reasonable that [Mrs B] would expect to receive her prescription to be dispensed accurately, with the appropriateness of her co-prescribed medications having been referenced; however regrettably this did not occur. It is unclear to me from the evidence presented whether in fact [Mr D] recognised the drug interaction at the time of dispensing, despite his own reference to checking reference sources to confirm the dose prescribed was within the recommended range, as well as a reference to checking the patient's dispensing history. This is worsened by [Mr D's] own admission that he 'assumed he (the doctor) had been contacted at previous dispensings'. In my opinion, this assumption is significant, and deviates from what would generally be considered reasonable practice to a moderate degree. I consider his peers would view this error with moderate disapproval.

SOP C10: 'Dispensing Prescriptions, MPSOs and BSOs' was reviewed by the pharmacy following this incident, and page 3 has been provided for review (it would be useful as commented to view it in its entirety). It is my opinion that the alteration made is not sufficient, and lacks a reasonable level of detail. For example, it references 'All appropriate interventions to be recorded on the printed copy of interaction and filed in the drug interaction folder'. This does not detail the appropriate procedure to be followed however when an alert is prompted, including reviewing reference material, assessing severity, contacting the prescriber etc. as per my description earlier of what would generally be accepted as best practice. Furthermore, there is no reference to detailing any interventions

electronically on the patient's medical record in the dispensing software, which is requisite for ease of future reference.

In my opinion, the standard operating procedures supplied by the new proprietor of the pharmacy bear little importance to the investigation of this incident. Accordingly, I have spent little time reviewing their suitability; however it is pleasing to note that SOP C35: 'Dispensing 2 — Prescription assessment and clinical check' does specifically refer to an assessment of 'compatibility with other medication'.

It is important to note that in the letter written by [Mr G], dated 28/8/14, he states that the doctor 'informed me that he had not been contacted regarding this interaction'. [Mr G] then later comments 'I do firmly believe that he was contacted when the Ketoconazole was [initially dispensed]. However I am unable to find any notes to support this when I checked the back-up disks'. This further highlights the necessity for interventions to be thoroughly recorded electronically. It may be useful obtaining a statement from the doctor confirming this.

Summary

Any dispensing error, such as those described in this case, is a highly regrettable incident, which all pharmacists fear occurring within their practice.

I trust these incidents, particularly given the seriousness of the outcome from these errors, have provided an important opportunity for both the Pharmacy and the Pharmacists involved to review their dispensing processes, particularly with regard to the assessment of suitability of prescribed medicines for a patient.

Glenn Mills

9/07/15"

Appendix C — Independent general physician advice to the Commissioner

The following expert advice was obtained from general and respiratory physician Dr Denise Aitken:

> "I have been asked to provide an opinion to the Health and Disability Commissioner on case 13HDC01300. I have read and agreed to follow the commissioner's guidelines for independent advisors.
>
> I am trained as a General and Respiratory Physician and have been working at Consultant level since 1997. I practise solely in an acute general hospital treating undifferentiated illness in patients presenting to that hospital.
>
> In providing this report I have reviewed all the documents provided to me from the Health and Disability Commissioner's office. These include the full set of photocopied clinical documents from ADHB, the letter from [Mrs B's] family, the response from ADHB, and the report to the coroner from [Dr F].
>
> Briefly in summary [Mrs B] was a resident at a Residential Care Facility. Her routine medications were Betaloc, Simvastatin and Aspirin. [She was started] on Ketoconazole orally for an abdominal rash by her general practitioner. Subsequently she developed progressive decline in mobility with deteriorating function and increasing impairment of continence. She was admitted by ambulance to [the public hospital] arriving at the Emergency Department at 22.49 at night. She was seen by the Emergency Doctor and assessed and then accepted as an acute inpatient admission and was seen by the Medical Registrar. She was seen the following day on a Consultant ward round. Results were reviewed on [Saturday morning]. She was next reviewed on [Monday] by a new Consultant and on [Tuesday] the cause of her deterioration was identified with muscle injury secondary to the combination of Ketoconazole and Simvastatin. The Ketoconazole had not been continued since admission since its prescription was overlooked, however her Simvastatin was not discontinued until [Tuesday]. She had developed acute kidney injury by [Tuesday] and died subsequently.
>
> I have been asked to address specific questions:
>
> **Whether sufficient regard was paid to [Mrs B's] medication regime on admission. I note in particular ADHB advised that the scanned ambulance records detail both Ketoconazole and Simvastatin as medication but this was regrettably missed.**
>
> [Mrs B] was transferred by ambulance to ADHB. The ambulance transfer records states that her medications were Betaloc/Aspirin/Simvastatin/Ketoconazole. The Residential Care Facility medication chart was included in the ADHB papers photocopied to me. I note [a DHB representative] comments that she was unable to find such documentation in the scanned medical record; however this was available to me and this medication chart lists the medications in numerical order:
>
> 1. Betaloc
> 2. Aspirin
> 3. Simvastatin 40mg daily

There is then a series of crossed out medications followed by 12. Panadol liquid. There is then a space of 4 lines and then at number 17. Ketoconazole 200mg daily is started with what appears to be a date of […] indicating an 8 week course of Ketoconazole. It is likely that the Emergency Department admitting officer missed the medication lower in the list assuming that the regular medications were those at the top of the list. Thus there are 2 places that Ketoconazole is listed as a current medication, in the Ambulance transfer note and in the Residential Care Facility medication list. The second doctor who admitted [Mrs B] to the Inpatient Service appears to have transcribed the Emergency Department doctor's error without correction, to the next admitting document, thus repeating the drug error.

This failure to accurately record the medication the patient was taking, falls below the standard of care. It is a mistake. This was compounded by replication and difficult to correct because of language and cognition barriers with regard to the patient.

It is notable that most treatment related harm takes the form of drug error, approximately 50% of drug errors occur at transitions of care.

I think this is an understandable mistake given the form of documentation of medications from the Residential Care Facility, but nevertheless is a failure. I would view this as mild. My peers would consider this an understandable error.

Whether there were any other issues related to [Mrs B's] admission or around the recording of her medication on admission.

The issue on medication errors has been noted by the NZ Health Quality and Safety Commission as a high risk area. They promote medicine reconciliation. Had medicine reconciliation by a Clinical Pharmacist been available for this patient, the transcription error would have been identified. The unsafe combined prescription of Ketoconazole and Simvastatin would have been recognized and the diagnosis reached earlier in this admission. Regrettably, Pharmacist led medicines reconciliation is not currently the standard of care.

The standard of care surrounding the abnormal CK result from [Friday] being overlooked.

[ADHB's response] of the 3rd July 2014 [said] that the CK result was posted early [on Friday afternoon]. It is not clear from the documentation whether this result was electronically 'accepted' at that time, or the next day. This information would be extractable from the laboratory audit trail system. The CK was requested as the Consultant ward round on [Friday]. This comprehensive ward round assessment concludes with a plan to do a CT head, TFTs (thyroid function tests), CK (Creatinine Kinase), cortisol and an MDT referral. Essentially this plan is a job list for the junior staff.

The weekend hand over plan written that day places a tick along TFTs indicating they have been checked but requests weekend review of the CT head which is pending and the cortisol in the morning. No mention is made of follow up of the CK requested to be checked by the Consultant. At sometime on [Friday or Saturday] the elevated CK is viewed on the computer and accepted. This result

was abnormal and appears to be highlighted on the black and white photocopy I have received. Presumably it appears in red on the computer screen.

Inpatient Services work in teams. A test result requested by the Consultant is expected to be followed up and acted on if abnormal by the junior team. If it is not clear what action should be taken escalation for advice to the next most senior person should occur. This did not occur.

The standard of care when the elevated CK was noted, should have been review of the patient's notes and medication list, discontinuation of Simvastatin, repeat of all blood tests including electrolytes, renal function, CK and measurement of urinary myoglobin.

At this point institution of renal protective intravenous therapy would have been appropriate. This did not occur.

This was a failure in the standard of care. It was of a moderate level. It is not certain that earlier cessation of [Mrs B's] statin medication and institution of renal protective treatment would have resulted in a better outcome, but nevertheless it should have occurred.

It does not appear either, that this abnormal result was handed over or alerted to the incoming team on Monday. Thus on the Consultant ward round [on Monday] the Consultant requested for the most recent bloods to be checked, but this does not appear to have been acted on until the Registrar ward round [on Tuesday]. At this point the Simvastatin is finally discontinued and active measures taken to treat the acute kidney injury when a repeat CK is received showing a level of greater then 20,000.

The abnormal CK result should have been responded to when it was received. This was the responsibility of the receiving team on [Friday]. It is not clear who 'accepted' the abnormal result and whether that person was aware of the clinical context.

I note that the Saturday review was carried out by a Registrar who comments that he is completing the review as there is no H/O (House Officer to do this). This suggests they were short staffed at that time. He was not asked to review the CK.

Therefore it is not clear whether the admitting team did not check the CK or whether they did not perceive the relevance of the elevated abnormal CK. Which ever of these was the case an opportunity was lost to intervene. It is clear from the Consultant ward round that muscle injury was appropriately considered in the differential diagnosis on [Friday]. I would describe the responsibility of follow up as a delegated responsibility of a junior doctor team. I would review the failure to act on the abnormal CK result as a failure of process of moderate severity.

Finally I would comment that Ketoconazole is a drug almost never used by myself and my colleagues because of its multiple drug interactions. I note that the New Zealand Formulary categorically states that Simvastatin should be discontinued if Ketoconazole is started. The indications for Ketoconazole in this setting of care did not seem to be compelling to me.

Yours sincerely, Denise Aitken

CONSULTANT PHYSICIAN"