



THE COLLEGES OF MEDICINE OF SOUTH AFRICA

Incorporated Association not for gain
Reg No 1955/000003/08

Final Examination for the Fellowship of the
College of Clinical Pharmacologists of South Africa



2 March 2017

Paper 1

(3 hours)

All questions are to be answered. Each question to be answered in a separate book (or books if more than one is required for the one answer)

- 1 A 68-year-old man with type 2 diabetes mellitus (T2DM) diagnosed 4 years ago has blood pressures of 148-156/92-96 mm Hg measured on 3 occasions. His body mass index is 35 kg/m²; HbA1c = 8.5%; eGFR = 55 mL/min; urine albumin/creatinine ratio 50 mg/mmol (normal range 2.5-25); serum potassium 5.5 mmol/L (normal range 3.5-5.5); LDL-cholesterol = 3.4 mmol/L; HDL-cholesterol = 0.9 mmol/L; total cholesterol = 5.6 mmol/L. His current treatment is basal insulin and metformin 1000mg 12 hourly. He has been admitted twice for hypoglycaemic episodes in the last month. He was unable to tolerate simvastatin 20mg daily due to myalgia.
- a) Discuss the pharmacological approach to the treatment of T2DM in this patient. (10)
- b) Discuss the pharmacological approach to the treatment of hypertension and dyslipidaemia in this patient. (10)
- [20]
- 2 There is an outbreak of extended spectrum beta lactamase-producing *Klebsiella pneumoniae* at the intensive care unit (ICU) in your hospital. The only antimicrobial available at the hospital to which the organism is susceptible is amikacin. You are asked to develop a short guideline for the dosing and monitoring of amikacin for treating severe sepsis in critically ill patients in the ICU. Include your reasons for the proposed patient management. [10]
- 3 A 55-year-old male with type II diabetes mellitus is treated with glimepiride 2mg/day, metoclopramide 10mg/day for gastroparesis, and omeprazole 20mg/day for gastro-oesophageal reflux disease. He is admitted with an acute coronary syndrome and has a drug-eluting stent inserted into his right coronary artery. He is commenced on aspirin 100mg/day and clopidogrel 300mg immediately, followed by 75mg/day.
- a) Describe the mechanisms of action of metoclopramide, omeprazole, aspirin and clopidogrel. (12)
- b) Discuss the mechanism and management of potential drug-drug interaction between his chronic therapy and the antiplatelet agents. (8)
- [20]

- 4 You are a project manager for the Medicines for Malaria Venture, responsible for designing the Phase 3 clinical trial of a fixed dose combination of artemether combined with a novel antimalarial compound (MMV123) with a novel mechanism of action, good efficacy against uncomplicated falciparum malaria, a long duration of action, and a favourable safety profile demonstrated up until and including the Phase 2b studies. African children under 5 years of age carry at least two-thirds of the global malaria disease burden, raising the debate of when best to enrol young children with uncomplicated malaria in clinical trials
- a) Outline the advantages and disadvantages of first enrolling young children in Phase 2b, Phase 3, or Phase 4 clinical trials. (10)
 - b) List key elements of study design to minimise risk and maximise evidence needed for policy makers to recommend the novel fixed dose combination for the treatment of young children once licensed. (15)
- [25]
- 5 a) What is Hy's law to assess drug hepatotoxicity? Discuss its regulatory and clinical importance. (10)
- b) A patient presents with derangement of routine liver function tests on a medicine. What criteria would you use in order to decide if the medicine should be stopped, and whether or not rechallenge should be attempted? (15)
- [25]



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3 March 2017

Paper 2

(3 hours)

All questions are to be answered. Each question to be answered in a separate book (or books if more than one is required for the one answer)

Please answer Question 1 – 2 in one book.

- 1 A 52-year-old man is brought to casualty by paramedics. He is known with bipolar mood disorder for more than 20 years for which he takes lithium. He was diagnosed with hypertension 3 months ago and was started on hydrochlorothiazide and enalapril. He was found in his home collapsed, but conscious with diarrhoea. The acute problem list by the attending physician was: gastroenteritis complicated by renal impairment (eGFR 24 ml/min). His lithium concentration is 3.49 mmol/L (therapeutic range 0.6 to 1.2 mmol/L for bipolar mood disorder). White cell count $32.1 \times 10^9/L$. Discuss the following and highlight aspects of relevance to this patient
- a) Symptoms and signs of lithium toxicity. (5)
 - b) The relationship between lithium concentrations and symptoms. (5)
 - c) Factors which predispose to lithium toxicity. (5)
 - d) Proposed further management of this patient. (5)
- [20]
- 2 You are contacted by a medical officer who notes in the SA Standard Treatment Guideline (Adult Hospital level) that haloperidol, risperidone and chlorpromazine are all options for the acute management of a first psychotic episode. She cites a recent meta-analysis which concluded that there are no differences in efficacy between these antipsychotics. She seeks advice on which antipsychotic to choose for her patient. Her patient is a 36-year-old man, presenting with a first episode of psychosis. He is not receiving any medication. On examination additional findings are that he has a body mass index of 42 kg/m^2 , a blood pressure of 159/89 mmHg, and blood glucose of 15 mmol/l. Outline the general principles of selecting one of these three antipsychotics and make a recommendation for this patient. [10]

Please answer Question 3 – 4 in one book.

- 3 Discuss interactions between allopathic and complementary or traditional medicines, giving 3 examples with different interaction mechanisms. [20]
- 4 Answer the following questions on cannabis:
- a) Discuss the pharmacology of the main active ingredient of cannabis. (10)
 - b) Write short notes on potential medical uses of cannabinoids. (10)
- [20]

Please answer Question 5 – 6 in one book.

- 5 A 68-year-old patient with a history of hypertension, well controlled on hydrochlorothiazide 25mg daily, developed chronic atrial fibrillation and warfarin was commenced. However, the clinic reports that they have been unable to maintain INR in the therapeutic range for 5 months.
- a) Discuss the role of antiplatelet agents for chronic atrial fibrillation. (5)
 - b) Discuss the efficacy and mechanism of action of the novel oral anticoagulants for chronic atrial fibrillation. (10)
 - c) How would you manage a severe bleed in patients on a novel oral anticoagulant? (5)
- [20]
- 6 Electronic cigarettes (e-cigarettes) are battery-powered devices that vaporise a flavoured propylene glycol or glycerine solution, with or without nicotine. Although e-cigarettes have the potential to act as harm reduction devices, due to the absence of combustion-related toxins and carcinogens produced by conventional cigarettes, the long-term health effects of vapour inhalation are unknown. You have been approached to provide advice regarding the regulatory approval for the nicotine containing e-cigarettes. Write short notes on the information that would be required for the regulator to approve e-cigarettes with nicotine. [10]