ETHICAL CONSIDERATIONS IN MEDICAL PRACTICE

Focus on section 21 of Act 101/65

KEY MESSAGES

- Section 21 is an important option for selected patients and should be considered in all ethically conducted medical practices in South Africa.
- The medical professional who applies for the use of unregistered medicines for a particular patient, using the concessions provided for in Section 21, becomes ethically responsible for the appropriate use of the medicine.
- As with any treatment option, informed consent from the patient is the cornerstone and must include a clear description of other general treatment options available to the patient (e.g., use of existing agents, available procedures).
- Informed consent of the patient must also cover the possibility of the medication becoming available in South Africa in future, possibly at a greater cost than under Section 21. Also, the patient must know that the right of use may be withdrawn by the Medicines Control Council (MCC) at any juncture, despite the best efforts of the medical practitioner.
- The best interest of the patient needs to prevail at all times in the usage of Section 21 medication.

“The provision of medicines in South Africa is legally regulated by the Medicines and Related Substances Act, Act 101 of 1965 (as amended). This Act governs the availability of medicines and prohibits the importation or/and sale of unregistered medicines in South Africa,” Ms Ulundi Behrtel pointed out as she set the scene for the ethical use of Section 21.

Section 21 of Act 101 provides an important mechanism to authorise the use and sale of unregistered medicines in South Africa. The two criteria that must be fulfilled when a Section 21 application is submitted by a registered medical professional is that the medication is needed by the patient and that no other ‘similar’ product is available in the country.

In terms of Section 21, the Medicines Control Council (MCC) of South Africa may authorise the sale of unregistered medicine for certain purposes:

The relevant section reads:

Council may authorize sale of unregistered medicine for certain purposes

(1) The council may in writing authorize any person to sell during a specified period to any specified person or institution a specified quantity of any particular medicine which is not registered.

(2) Any medicine sold in pursuance of any authority under subsection (1) may be used for such purposes and in such manner and during such period as the council may in writing determine.

(3) The council may at any time by notice in writing withdraw any authority granted in terms of subsection (1) if effect is not given to any determination made in terms of subsection (2).

“It is important to note that the MCC may impose conditions regarding the use of the medicine (e.g., the purpose of the medication, the manner in which it may be used and the period of its use),” Ms Behrtel pointed out. “Also, authorisation may be withdrawn at any stage by the MCC.”

The process is guided by a 6.12 Section 21 application form which is downloadable from the MCC website. The first four pages of the form relate to the MCC’s policy with regard to unregistered medicine.
use in South Africa. *(Full document link is provided under additional reading of this module.)*

“The applicant, in most instances the medical practitioner, must realise that the use of the medicine for a particular patient becomes the ethical responsibility of the applicant from the outset. The applying doctor must have a thorough knowledge of the medicine and be able to respond to any queries that the MCC may have about the efficacy, safety and any other relevant aspect thereof,” Ms Behrtel noted.

The form is comprehensive and must be completed meticulously. “Generally, the application is approved for a specific time period up to a maximum period of six months. If continuation of the medication is required or indicated, an applicant has to apply for new approval from the MCC by submitting a re-application together with a follow-up progress report,” Ms Behrtel said.

The clinical implication of the use of Section 21 medication is that the practitioner needs to provide closer monitoring than is the norm for registered medicines. Any adverse or unexpected events must be reported to the MCC. On termination of treatment using a Section 21-acquired medicine, the MCC must be informed and a full and final case report submitted to the organisation.

**A brief summation of ethics in medical practice**

Ethics is a branch of moral philosophy, but in a profession, e.g. medicine, adherence to the principles of ‘accepted professional ethics’ will determine whether a practitioner has behaved in a professional or unprofessional manner.

The four cornerstones of ethical principles in medical practice are: respect for the autonomy of each individual, beneficence – ‘the intention to do good’, non-maleficence – the principle of doing no harm and ‘justice’- behaving in a fair and just manner to all patients.

Rule 27A, as set out in the ethical rules published by the Health Professions Council of South Africa, provides a useful summation of the main ethical responsibilities of health professionals in South Africa (Table 1).

“Rule 23, which relates to prescribing medicines and medical devices, is also relevant to the use of Section 21,” Ms Behrtel pointed out (Table 2).

**Table 2. Rule 23**

<table>
<thead>
<tr>
<th>Health care professionals’ duty when prescribing medicines and medical devices:</th>
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<tbody>
<tr>
<td>• clinically appropriate or the most cost-effective option</td>
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<tr>
<td>• clinically indicated</td>
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<tr>
<td>• affords best possible care at a cost-effective rate compared to other choices available</td>
</tr>
<tr>
<td>• patient is informed of such other available options</td>
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</table>

**Ethical considerations when using Section 21**

In considering the ethical aspects of medicines supplied under Section 21, the structure of the approval process must be described carefully to the patient. The patient needs to understand that authorisation can be withdrawn, that circumstances and costs can change if the medicine is registered in the country. In the event of the MCC withdrawing a particular medicine from the Section 21 concession, a practitioner can argue and legally challenge the MCC’s decision to withdraw a medicine if his/her patient’s best interests are harmed by the withdrawal.

In all instances, the fundamental considerations for using Section 21 are:

1. The best interest of the patient
2. The accessibility of the medication, and
3. The cost implications and affordability of the medicine relative to the circumstances of the patient.
Cost-effective approaches to improve glycaemic control

KEY MESSAGES

• The cost burden of diabetes in South Africa is very high, due to a high prevalence of the disease (4.8-8%), its often being diagnosed when there is already existing microvascular disease and poor adherence and compliance with medical therapies

• HbA1c is a good proxy for associated health care costs with high HbA1c leading to increased medical costs (hospitalisation)

• Infrequent measurement of HbA1c in South Africa hampers risk assessment by funders and reduces the clinician’s ability to focus on high-cost, high-risk patients

• Compliant patients at goal reduce health care costs, including cost of medication

• Treatment goals should be targeted ‘irrespective’ of chronic medicine costs (needs to pass reasonability test) as this is a cost-effective long-term strategy for type 2 diabetes.

The cost of poor glycaemic control in diabetes leading to hospitalisation in South Africa results in a median expenditure of R23 000 (hospital cost alone, i.e. 48% of total cost of care) per patient – this is a significant cost as evaluated in 2015 by Agility Global Health’s Dr Jacques Snyman and his team. “This reflects only the hospitalisation costs and not the medical practitioner or medicine costs,” Dr Snyman pointed out, “which will add a further 52% to the cost of each event.”

This data were collected and analysed from a South African funder’s database. In the USA, with its diabetes prevalence of 9.3%, 28% of all health care expenditure on medications is attributed to diabetes. In South Africa, with its current diabetes prevalence of 4.8-8%, a high percentage is also likely. “In fact, our overall percentage of health care costs spent on diabetes may be higher as diagnosis in South Africa is frequently late, as seen in a retinopathy prevalence of 21-25% at the time of diagnosis of type 2 diabetes,” Dr Snyman noted.

What drives cost of care in poorly controlled patients – hypo- or hyperglycaemia?

In a study funded by Novo Nordisk, conducted in Argentina, Australia, Brazil, Israel, Mexico and South Africa, Dr Snyman and co-workers noted that of the patients experiencing hypoglycaemia, 18% cited that this was due to overall poor glycaemic control. “Non-severe hypoglycaemic events significantly impact on a patient’s quality of life and there is also a knock-on effect with regard to health care costs and loss of work productivity,” Dr Snyman said.

In an effort to quantify the relationship between costs and level of glycaemic control a recent Italian funders’ study evaluated retrospective data from an administrative database and clinical registry of 31 000 patients with diabetes. The study showed that adherence to therapy, which was measured based on medication possession rates (MPRs), needs to reach more than 80% in order to impact positively on the disease. In South African diabetes patients, a survey in the private sector of patient access to insulin has shown that 30% of patients do not have ongoing access to insulin throughout the year [SA Pharmacy Benefit Management database]. This figure is even higher for full annual access to oral anti-diabetic medication.

Evaluation of costs as influenced by HbA1c and medicine compliance shows that glycaemic control (as assessed based on HbA1c) is a useful surrogate for associated health care costs. “As prescribers, we are failing our patients if we do not determine HbA1c levels more than once a year and use the finding to intensify patient education firstly, and then to consider further medication. Our guidelines for HbA1c targets also need to be simple so that they can be followed easily in primary care practice,” Dr Snyman noted.
As a useful clinical rule, treatment targets for HbA1c should be lower in patients with short disease duration, long life expectancy, no significant cardiovascular disease and should be accompanied by patient motivation by the prescriber. Higher HbA1c goals are needed in patients with a history of severe hypoglycaemia, limited life expectancy, advanced complications and extensive comorbid conditions.

The cost of hypoglycaemia is difficult to ascertain accurately, but examination of events resulting in emergency hospitalisation highlights its importance. Also, more than 50% of patients on oral hypoglycaemic agents, who arrive at emergency units, are then admitted to hospital for surveillance of their hypoglycaemia (Figure 1).

“In South Africa, this figure may be even higher,” Dr Snyman noted.

An interesting study of the value of high-level intervention in cardiovascular medicine has shown the value of this approach in South Africa [Agility Global Health South Africa research on file]. This managed care approach did not focus on restricting medication, but on ensuring that drugs managing cardiovascular risk (lipid-lowering, managing blood pressure) were available at no extra cost to the patient. The overall drive of the programme was to achieve treatment goals irrespective of chronic medicine costs. Results showed that over an 18-month period this nurse-driven approach to enhancing compliance and adherence to prescribed medicine and treatment resulted in less hospitalisation and lower chronic drug costs in both the GP and specialist environment (Figure 1).

There was also a lower knock-on cost as patients experienced a lower event rate without a significant change in GP or specialist costs.

In conclusion, Dr Snyman advised, “Practitioners should seek to get compliant patients to goal, as good clinical outcomes translate into better financial outcomes at all cost-of-care levels.”

**References**


**Table 1. Cost of hypoglycaemia**

<table>
<thead>
<tr>
<th>Medication</th>
<th>% Implicated in Emergency Hospitalisations</th>
<th>Hospitalised:</th>
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<tbody>
<tr>
<td>Warfarin</td>
<td>33.3%</td>
<td>46.2%</td>
</tr>
<tr>
<td>Insulin</td>
<td>13.9%</td>
<td>40.6%</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>13.3%</td>
<td>41.5%</td>
</tr>
<tr>
<td>Oral hypoglycaemic agents</td>
<td>10.7%</td>
<td>51.8%</td>
</tr>
<tr>
<td>Opioids</td>
<td>4.8%</td>
<td>32.4%</td>
</tr>
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</table>

**Figure 1. Total expenditure per individual on CDL programme**

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