In the clinical practice setting, be it in a hospital or a primary care facility, nurses are faced with the challenging task of managing drug preparations and treatment on a daily basis. This entails a wide variety of activities, which include, but are not limited to the following:

- Evaluating and interpreting prescriptions, liaising with prescribing practitioners and other members of the multidisciplinary health care team, and implementing and co-ordinating their prescribed treatment regimens.
- Ordering, receiving, storing, issuing and reordering drug supplies (e.g. ward stock).
- Preparing and administering prescribed medication to patients in their care.
- Monitoring these patients for the effects of such medicines, as well as possible adverse reactions to the prescribed treatment.
- In settings where the prescribed treatment is not administered directly to the patient, there may be a need to monitor the patient for compliance (adherence) to the prescribed treatment regimen at regular intervals (see Box 1).
- Participating in the conduct of clinical drug trials (discussed further down).¹
Box I. Notes on patient adherence, or compliance with prescribed drug therapy*

Consider the following example, used for illustrative purposes only: Patient XYZ is a 31-year-old woman who is HIV positive and currently receiving an antiretroviral (ARV) treatment regimen, which consists of the following drugs:

- A fixed-dose combination tablet, which contains zidovudine (AZT) 300 mg, in combination with lamivudine (3TC) 150 mg, with one tablet to be taken orally every 12 hours.
- Nevirapine (NVP) 200 mg, one tablet to be taken orally every 12 hours.

She visits her local clinic for a routine follow-up and the resupply of her prescription every 12 weeks. She received a new 12-week supply of medication on 11 October, 2010. She has to start taking medication from the new supply on the same evening and complete the new supply on the morning of her next follow-up visit. She was subsequently asked to return to the clinic on 3 January, 2011.

At her follow-up visit, the prescribing practitioner decided to check her compliance to the prescription and asked her about her treatment and whether she was taking her medication regularly and as prescribed. She was very positive about her treatment and claimed that she felt a lot better. However, she also mentioned that she still had nine (9) of her “combination pills” and twelve (12) of her “nevirapine pills” left over, after she had taken one of each this morning. She stated that she finds it a little difficult remembering to take her medication every single day, and she also dropped one of her “combination pills” down the kitchen sink drain by accident a few days ago.

Calculating her compliance with the prescribed treatment:

Patient XYZ received 168 tables of each drug (i.e. a 12-week supply of each, since she needs to take one tablet of each drug twice daily) (12 weeks x 7 days x 2 tablets per day = 168 tablets).

She started taking her medication on the evening of 11 October, 2010. Therefore, she should have taken the 168th tablet of each drug on the morning of 3 January, 2011, requiring an urgent resupply on 3 January, 2011.

However, she had some tablets left over on the morning of 3 January, 2011.

Therefore, she did not take all of her medication as prescribed. From 11 October, 2010, to 3 January, 2011, she only took 158 tablets of the fixed-dose combination treatment, since she dropped one tablet down the drain and had nine tablets left over, and 156 tablets of nevirapine, since she has 12 tablets left over.

Thus, her compliance for the fixed-dose combination was (158/168) x 100) = 94%, and for the nevirapine it was (156/168) x 100) = 93%.

There are numerous factors that may influence the degree of compliance that patients will have with their prescribed treatment, including, but not limited to the following:

- The ease of taking the medication, the ability to swallow the tablets or capsules, or to be injected, for example.
- The taste of oral formulations, or other unpleasant or bothersome obstacles, such as topical preparations that stain the skin or clothing, or medication that discoursely bodily secretions.
- Adverse effects that make it difficult to tolerate the medication, such as nausea, headache, dizziness, drowsiness and other side-effects that make patients feel “bad”, cause discomfort, or interfere with their daily living.
- Financial considerations, socio-cultural and religious influences, and possible stigmatisation.
- Restrictions on dietary intake, smoking or the use of alcohol.
- Complexities such as having to specially prepare or self-inject medication.
- Complicated dosing regimens that make compliance difficult, for example, if a patient in full-time employment has to take tablets every four hours.
- How well the patient has been educated and informed about the treatment regimen, and what the prescribing practitioner hopes to achieve with the treatment, as well as what the realistic expectations are. Also the patient’s ability to understand the instructions and to remember to adhere to the treatment regimen. Various tools or aids may be used to assist patients in this regard.
- The (perceived) benefits that patients may obtain from their treatment.

These are examples of factors to evaluate and consider whenever patients are found not to be complying or adhering to their prescribed treatment. These factors determine how well patients will tolerate their treatment, and the better they are able to tolerate it, the more likely they will be comply or adhere thereto.

(*Adapted from: Schellack, G. Pharmacology in clinical practice: application made easy for nurses and allied health professionals. 2nd ed. Claremont: Juta & Co, Ltd; 2010.)
It follows from the abovementioned activities that there is an important interaction between prescribers, dispensers and patients, and that nursing practitioners play an integral part in the success of this therapeutic interaction. Key aspects pertaining to this interaction are illustrated in Figure I. These aspects will be discussed in more detail below.

**Prescriber, Dispenser and Patient, and the Role of the Nurse**

**Figure I.** The role of the nurse in the interaction between prescriber, dispenser and patient. Refer to the accompanying text for a discussion on the numbered labels, 1-7.

(From: Schellack, G. Pharmacology in clinical practice: application made easy for nurses and allied health professionals. 2nd ed. Claremont: Juta & Co Ltd, 2010.)
1. **Prescribing practitioner:** An authorised prescriber will diagnose an illness or clinical condition, set attainable treatment goals, and prescribe appropriate medication, if indicated. Such a prescription may aim to relieve some, or all of the patient’s symptoms, assist in diagnosing the full extent of the patient’s condition, prevent further deterioration of the condition, address and modify the actual disease process, or aim to achieve a combination of these therapeutic goals. Typically, the prescriber would be a medical practitioner or a dentist. Under certain, specified circumstances, however, registered nurses may also act as prescribing practitioners.1,2

2. **Prescription:** A valid (legal) prescription is required for any Schedule 3, 4, 5 or 6 substance to be used as part of the patient’s pharmacotherapy. Schedule 1 and 2 substances may be purchased as over-the-counter (OTC) medicines from a pharmacy, while Schedule 0 substances may be sold in an open shop (e.g. a supermarket or the front shop of a pharmacy). Refer to Box 2 for more information on the requirements for a prescription and to Figure 2 for additional information on the scheduling of medicines. However, a prescriber may add Schedule 0, 1 and 2 items to the prescription as well. Note that without a prescription, nurses who are not authorised prescribers may not administer any medication, irrespective of the scheduling status thereof to patients in their care (unless specific, legally acceptable provisions have been made in their scope of practice or otherwise).1-5

**Box II. Regulatory requirements for a prescription**

Regulation 28 of the General Regulations (R.510) made in terms of the Medicines and Related Substances Act (1965, as amended) clearly states the requirements for a legal prescription for medicine.3 The prescription should be written in legible and indelible print, or be typewritten or computer-generated, and be signed by the medical practitioner, dentist, veterinarian, or authorised prescribing practitioner (e.g. the nurse). It should at least state the following:

- The name, qualifications, practice number and address of the prescribing practitioner.
- The name and address of the patient.
- The date of issue of the prescription.
- The approved generic name or the proprietary name of the medicine.
- The dosage form.
- The strength of the active ingredient(s) contained in the dosage form, as necessary, and the quantity of the medicine to be supplied.
- The instructions for the administration of the specified dosage form and the frequency of the administration.
- The age and sex of the patient (especially important in the case of children and the elderly). Also note that the patient’s body weight and/or body mass index (BMI) may be desirable for accurate dosage calculations to be made.
- The number of times that the prescription may be repeated (if applicable and allowed).

Furthermore, take note of the following:

- The signature of the prescribing practitioner must be handwritten.
- In the case of substances with a high potential for abuse, and where the likelihood exists that prescriptions may be altered to exaggerate the quantities or dosage strengths to be supplied (e.g. Schedule 5 and 6 substances), the quantities should preferably be written in both symbols and words.

When a prescription is sent by fax, email, telephone or electronic transmission, the dispenser has to verify its authenticity. A permanent record must be made of the prescription. The original prescription must follow within seven working days. In the case of a verbal instruction (i.e. a telephonic prescription) the treatment period may not exceed seven days. However, in the case of a Schedule 5 or Schedule 6 substance, the verbal instruction may only be given for a maximum treatment period of 48 hours and must be signed by the prescribing practitioner within 72 hours.

The General Regulations do not provide any specific guidelines for receiving telephonic orders. Therefore, it is recommended that the following guideline be followed in the clinical practice setting:

A telephonic order must be written down upon receipt and then read back to the prescribing practitioner and signed by the person taking down the prescription. A second person should preferably be available to verify the process and co-sign the prescription. Healthcare institutions may also have specific guidelines or policy documents on the exact procedure to be followed.

(*Adapted from: Schellack, G. Pharmacology in clinical practice: application made easy for nurses and allied health professionals. 2nd ed. Claremont: Juta & Co, Ltd, 2010.)
General considerations:
- A prescription is only valid for a period of 30 days.
- For verbal instructions the authorised prescriber must be known to the dispenser.
- An authorised prescriber must keep a record of the diagnosis relevant to the prescription and indicate it on the prescription if the patient gives his/her consent.

**SCHEDULE 0**
- May be sold in an open shop.

**FIVE (5) BROAD CATEGORIES**
In accordance with Section 22A of the Medicines and Related Substances Act (No. 101 of 1965, as amended)

**SCHEDULE 1 and 2**
- May be sold without a prescription to persons who are apparently over the age of 14 years.
- May be repeated for a maximum of 6 months if indicated on the prescription.

*Schedule 1: A record of the prescribed particulars of the sale must be kept.
Schedule 2: The prescribed particulars of the sale must be recorded in a prescription book.

**Prescription only**

**SCHEDULE 3 and 4**
- A prescription is required.
- May be repeated for a maximum of 6 months if indicated on the prescription.
- Emergency resupply is possible.

*The prescribed particulars of the sale must be recorded in a prescription book.

**Emergency resupply:** In the case of an emergency, and to prevent treatment disruptions when the repeat period of 6 months has expired, the pharmacist may resupply on a non-recurring basis, in accordance with the original prescription, a supply for a maximum of 30 days.

**SCHEDULE 5 and 6**
- May be sold on prescription only.
- Emergency resupply is not allowed except for verbal instruction from an authorised prescriber (for a supply not to exceed a treatment period of 48 hours).

*The prescribed particulars of the sale must be recorded in a prescription book.

**Schedule 5:** Prescriptions may be repeated for a maximum of 6 months. Specific requirements apply to extended periods of treatment (> 6 months) for Schedule 5 analgesics, antidepressants, tranquilisers and anxiolytics, and a new prescription is required.

**Schedule 6:** Prescriptions may not be repeated. For periods of treatment of more than 30 days a new prescription is required.

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*Figure II.* Regulating how scheduled substances are made available to the public

(From: Schellack, G. Pharmacology in clinical practice: application made easy for nurses and allied health professionals. 2nd ed. Claremont: Juta & Co Ltd; 2010.)
3. **Dispenser**: The person who dispenses the prescribed medication (typically, a pharmacist) will interpret and evaluate the prescription, select, manipulate or compound the medicine, and label and supply the medicine in an appropriate container. Furthermore, instructions and information need to be given to the patient to ensure that the medicine will be used safely and effectively. In some situations, as is the case with a dispensing doctor, for example, the prescriber may also be the dispenser. Pharmacists are obliged by law to dispense interchangeable multi-source medicines, also referred to as generic substitution, in accordance with the stipulations of section 22F of the Medicines and Related Substances Act (No. 101 of 1965, as amended). In the case of a hospitalised patient, for example, the pharmacist will not dispense medication directly to the patient, but rather supply medicines that have been dispensed to individual patients and labelled accordingly to the nursing unit or ward.1-5

4. **Medication**: With the exception of the novel biotechnology-derived agents, drugs are chemical substances that influence physiological (including biochemical) or mental processes in the body. When used with discretion and vigilance, drugs will display their beneficial biological effects in the presence of physical or mental illness. Some drugs may even be used to prevent or diagnose disease. The art and science of drug preparation and the design of dosage forms is known as pharmaceutics. Drugs that have been pharmaceutically prepared are called medicines. A medicine may therefore contain one, two or many different drugs, as active substances within a suitable base of pharmaceutically inactive substances known as excipients.6

Therefore, it is important to note that a certain medication may contain more than one drug as an active ingredient. The other important aspect pertaining to the medication is adequate information on its correct, safe and effective use in clinical practice. The importance of referring to the approved package insert cannot be overstated. The pharmacist also plays a vital role as a member of the multidisciplinary team and will be able to provide information on the classification and mechanisms of action of medicines, their required storage conditions, indications, preparation for, and routes of administration, safe and effective dosages, possible drug interactions, expected adverse effects, therapeutic drug monitoring (TDM) and other relevant aspects. In addition, a variety of other resources may be consulted. With regard to the interchangeable multi-source medicines (IMSMs), these are medicines that contain the same active ingredients (e.g. the same drugs), in the same dosage form, strength or concentration, and are meant to be administered via the same route, e.g. oral or parenteral. Registered IMSMs are considered to be therapeutically equivalent to the original product.1,5-6

5. **Patient**: Patients may self-medicate (e.g. use Schedule 0 medicines that they bought from a pharmacy or supermarket), or use OTC medication (Schedule 0, 1 or 2) from a pharmacy, or they may take prescribed medicines. Hospitalised or institutionalised patients may have their medication administered to them by nurses. For optimal effectiveness, patients need to comply with, or adhere to their prescribed treatment regimen (see Box 1).1

6. **Stock**: The management of pharmaceutical stock entails activities such as the ordering, receiving, storing and issuing of stock, reordering and inventory management, as well as storage conditions, shelf-life (expiry dates) and security issues. This may take place at various levels, including a depot, pharmacy, clinic, or at ward (nursing unit) level.1

7. **Nurse**: Nurses will administer prescribed medication to patients in their care as part of their scope of practice, which also includes preparing such medicines for administration and monitoring these patients for the effects of such medicines, as well as possible adverse reactions. Nursing practitioners need to ensure that they understand what the prescriber is aiming to achieve with the treatment, what the medication in question may be expected to do to the patient, and how it should be administered for optimal effect. Note that, under specified circumstances, the nurse may also be the prescriber.1,2,7

### The development of new drugs and the role of the nursing practitioner

Stringent regulations, international guidelines and ethical codes govern the way in which new drugs are being developed and brought to market. The drug development process ensures that new drugs are safe and effective, manufactured according to the highest standards and marketed in a responsible and scientifically sound manner.6

The new drug development process is a complex and highly regulated one involving many different role players. It requires significant resources, scientific research processes, complex and interlinked stages of development and enormous financial investment that need to be carefully managed to discover, design, test, develop and register a new drug for the global market.6

Strictly speaking, there is a clear distinction between drug discovery and drug development, although many authors use the concept of “new drug development” to include both of these major stages. The drug discovery stage encompasses the highly-evolved chemistry and...
biotechnological techniques used in the pharmaceutical industry today. However, these complex techniques, related processes and procedures do not fall within the scope of this text. On the other hand, many aspects of the drug development stage have a direct impact on clinical practice and warrant a more detailed explanation.6,8,9

During the testing and development of new drugs, the safety, tolerability, efficacy and usefulness of the drug in question must be determined in the following way:

- **Pre-clinical testing** (laboratory and animal testing) is used to determine the basic pharmacodynamic and pharmacokinetic properties of the drug and to detect acute, sub-acute and chronic toxicity. The aim is to detect any toxic effects that the drug may have on cells, tissues and organs, and also any carcinogenic (cancer-inducing), mutagenic (causing mutant genes) and teratogenic (leading to recognisable birth defects) effects. Pre-clinical testing also assists scientists in establishing the drug’s therapeutic index (i.e. the difference between the minimum plasma concentration at which the drug is effective and the minimum plasma concentration at which the drug becomes toxic).6,8,9

- Subsequently, **clinical trials** (tests on human subjects) must establish whether cumbersome side-effects (which animals are incapable of complaining about) occur, what the ideal dosing schedule should be and how effective the new drug is compared to existing drug treatments, or in some instances to a placebo (“dummy” treatment). Clinical trials entail the testing of drugs on human subjects, where medical supervision is essential to conducting safe and ethical research.6,8,9

Drug metabolism differs significantly between animals and humans. Therefore, kinetic and dynamic principles, and the toxicity profile of a drug are also investigated further during clinical trials. These trials are conducted in four phases:

- **During Phase I** the drug is tested on a small number of healthy individuals, usually fewer than 100 healthy volunteers. These are so-called, first-in-human studies. In the case of antiretroviral agents and the antineoplastic drugs used to treat cancer, for example, the healthy volunteers are substituted with patients suffering from the specific condition. Human pharmacological profiling, safety and tolerability, with the possible inclusion of early efficacy measurements, form the basis of Phase I development, which is carried out under highly-controlled circumstances in specialised clinical research units.6,8-10

A more recent development was the introduction of the so-called **Phase 0 study** as a bridging strategy between the drug discovery stage and the drug development stage. It is aimed at limiting human exposure to drugs that may not be effective and therefore may not warrant further development (which then also carries a huge cost-saving benefit). During a Phase 0 study, a very limited number of patients are exposed to a really small, sub-therapeutic dosage of the drug for a limited period of time. This is referred to as micro-dosing and gives researchers the benefit of beginning with human pharmacological profiling of the drug early on (before Phase I commences), but with very limited exposure of the study participants to possible risks involved, as well as to make more informed decisions about future development strategies for the new compound at an exceedingly early stage in the development process.6,11

- **Phase II** introduces the drug to a selected number of diseased patients suffering from the actual condition that the drug is meant to treat (i.e. exploring the therapeutic benefits in targeted patients), usually a few hundred subjects. Efficacy now starts to form an important part of the study focus, together with safety, as well as the establishment of an optimal dosing regimen. For a number of practical reasons, this phase may be subdivided into Phase IIa and Phase IIIb.6,8-10

- Extensive trials, on a much larger scale and usually involving several hundred to several thousand subjects, are conducted during **Phase III**. The major focus during this phase of the drug’s clinical development is to establish and confirm its efficacy and therapeutic benefit. These trials are conducted over longer periods of time, utilising a broader range of defined patient populations and may include combination therapy with one or more existing drug treatments. It may also be necessary for the development programme to be continued once an application has been made for marketing authorisation, or for peri-approval studies to be conducted. For this purpose, **Phase IIIb** studies are utilised and are considered to be an extension of the Phase III development programme.6,8-10

- Once marketing of the drug has begun, **Phase IV**, or post-marketing surveillance, commences, and side-effects, additional indications, efficacy and tolerability may be investigated to the full. Data derived from these studies are gathered from the real-world utilisation of the drug in day-to-day clinical practice.6,8-10

Clinical trials must be carefully planned, well designed and properly controlled. Therefore, the randomised controlled trial (RCT) is most often used, especially during the later stages of the drug’s clinical development. However, a single RCT is usually inadequate for determining the new drug’s performance in comparison with standard treatments or placebo. This is because of limited resources and the small number of patients that are usually available for inclusion in a single trial. By combining the results of different randomised trials, which comply with set criteria as to the control, validity and reliability of each one, into one single overview of all available data (i.e. employing a
meta-analysis of the research findings), this problem may be overcome.6,12

Another recent advance in the drug development process, which challenges the traditional way of conducting RCTs, is the introduction of the concept of adaptive clinical trials that will help to shape the way in which clinical trials are designed, conducted and analysed into the future. One example that is already being used entails combining a Phase II and a Phase III trial into one “seamless” adaptive clinical trial.6,13

The various role-players within the pharmaceutical industry, who are responsible for, or involved in new drug development include:

- The pharmaceutical, biotechnology and biopharmaceutical companies who research and develop new drugs and medicines, pioneer groundbreaking new therapies and endeavour to address unmet medical needs. It is currently being estimated that the development of a single new drug could take as long as 10–15 years to complete and cost as much as US$1 billion or more. These drug companies usually have dedicated research and development staff and facilities, but may also collaborate with government organisations, academic institutions, other companies and various service providers to discover, develop, manufacture and promote new medicines.6,8,9,14

- Clinical research organisations that provide expert drug development services to the pharmaceutical industry and often participate in drug development programmes to varying degrees.6,14

- Clinical investigators and their investigative site staff, who may include sub-investigators, study coordinators, research nurses, pharmacists and other health professionals who recruit, screen, enrol, treat, monitor and follow up carefully-selected subjects (i.e. study participants or study patients) when approved clinical trials are conducted.6,14

- Regulatory authorities who have legislative oversight on all matters relating to the approval, conduct and inspection of clinical trials, as well as the investigational product (i.e. the study drug or study medication under investigation). Examples of such regulatory authorities include the United States Food and Drug Administration (FDA), the “competent authorities” of the Member States of the European Union (e.g. the MHRA in the United Kingdom and the BfArM in Germany), Agência Nacional de Vigilância Sanitária (ANVISA) in Brazil, and the South African Medicines Control Council (MCC). These authorities are usually also responsible for the subsequent registration of new medicines in their respective countries; however, a single application could also be made to the European Medicines Agency (EMA, formerly EMEA) for a marketing authorisation in the European Union (EU).6,14

- Central and local research ethics committees and institutional review boards who ensure that properly approved clinical trials are conducted according to local and international ethical standards and guidelines to protect the rights, safety and wellbeing of all subjects participating in such trials. The World Medical Association’s Declaration of Helsinki, the International Conference on Harmonisation (ICH), applicable EU Directives and the relevant parts of the FDA Code of Federal Regulations, provide ethical guidance, as well as rules and regulations where applicable.6,14

Nurses may participate in the conduct of clinical trials in a number of diverse roles, with varying degrees of responsibility. Such roles may include that of research coordinators, study nurses, clinical site monitors and drug safety monitors (the latter supporting pharmacovigilance, defined by the World Health Organisation as “…the science and activities relating to the detection, assessment, understanding and prevention of (the) adverse effects (of drugs) or any other drug-related problem”).15

Conclusion

The aforementioned overview aimed to provide the reader with a high-level introduction to a vast and complex topic, namely the role that nursing practitioners play in the management of drug preparations and treatment. It is quite evident from the discussion that this role is a complex and multi-faceted one, which ranges from that of primary caregiver having to prepare and administer medication to a patient and monitoring patient compliance, to the ordering, receiving and storing of drugs, prescribing medication (in certain situations) and participating in clinical drug trials. Some of these aspects will be expanded upon in future articles, which will aim to highlight some of the contemporary, practice-related aspects of pharmacology, drug therapy, and applied nursing pharmacology currently facing the nursing practitioner.

References


**MIGRAINE RESEARCH INSTITUTE**

**South African Police and Nurses receive 50% discount**

The Headache Clinic will be honoring all South African police personnel and registered nursing staff with a special “Salute to Heroes” treatment plan. Starting in February all “Heroes” will be treated at 50% of the usual cost of diagnosis and treatment.

Dr Elliot Shevel the chairman of the South African Headache Society and founder of The Headache Clinic explains: “It takes a very special type of person to become a nurse or police officer, someone that is willing to give and asks very little in return. It is common practice for police and nurses to work in highly pressurized environments and we as The Headache Clinic can’t afford to let their levels of service decrease due to incapacitating migraine. It takes considerable toll on police and nurse’s minds, bodies and spirits and they are frequently overworked and underpaid. This campaign is in recognition of the outstanding contribution they make to society”. To receive their ‘Salute to Heroes’ treatment plan, South African police personnel will have to present their SAPS badges and registered nursing staff will have to present an up-to-date SANC receipt on the day of their diagnosis.

The pain associated with migraine can seriously impact an individual’s quality of life both through pain and through feelings of isolation. Support and information is available free of charge by specialist migraine nursing staff on 0861 678 911 or on www.headacheclinic.co.za.

For more information please contact Mary-lee Cantor on +2711 484 0933.