



## South African Renal Society

[www.sa-renalsociety.org](http://www.sa-renalsociety.org)

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### SARS Statement on use of generic immunosuppressant drugs

#### A. Use of generics in solid organ transplantation

- a. There is insufficient scientific evidence to conclude that use of generic immunosuppressants in solid organ transplant is safe.
  - i. We support the opinion published in the British Medical Journal review which concludes: *“High quality data showing bioequivalence and clinical efficacy of generic immunosuppressive drugs in patients with transplants are lacking. There is insufficient evidence to provide reassurance that generics are equivalent to innovator immunosuppressants, but there are also no data to firmly suggest that generics are not equivalent and therefore unsafe. Given the serious consequences of rejection and allograft failure, well designed studies on bioequivalence and safety of generic immunosuppression in transplant recipients are needed.”* *Generic immunosuppression in solid organ transplantation: systematic review and meta-analysis. The BMJ | BMJ 2015;350:h3163 | doi: 10.1136/bmj.h3163*
- b. It is now well understood that a large proportion of later graft loss is through insidious antibody mediated rejection, and a role of generic drug substitution has not been established yet.
- c. The following South African specific factors add additional weight against the use of alternative drugs:
  - i. Low transplantation rates in SA with waiting periods lasting many years and even lower re-transplantation rates in case of an organ loss.
  - ii. Patient education issues: many transplant patients come from low socio-economic situations and have difficulties grasping complex polypharmacy prescriptions. Drug substitution-related patient error can lead to unintentional under- or over-dose with grave consequences.
  - iii. Pharmacist Education: in first world countries, our colleagues are facing challenges with substitution of one generic drug with another by uninformed pharmacists. With multiple generic drugs present in the SA market, such incidents will be inevitable. Bioequivalence varies among different generic formulations carrying additional risks.
- d. Consequences and risks of generic drug use:
  - i. In both de novo transplant recipients and later drug switches – risk of rejection leading to partial or complete loss of a transplanted organ. Need for additional physician visits for counselling and education (escalation of cost and work load).
  - ii. Need for additional therapeutic drug level monitoring (repeated laboratory tests at short intervals with significant cost escalation).
  - iii. Need for organ biopsy including cost of hospital admission, radiology, pathology, and possibly theatre.
  - iv. Potential need for use of higher maintenance generic drug doses.
  - v. Potential side effects leading to drug intolerance or discontinuation.
  - vi. Potential need for anti-rejection therapy (high cost therapy requiring hospital admission and organ biopsy).
  - vii. Risk for reinstitution of dialysis (catastrophic health and social event for a patient with major cost escalation).

### Recommendations

- Based on the above we do not support the use of generic immunosuppressant drugs in solid organ transplant recipients.
- Generic drug substitution must only be done in consultation with the attending physician and after obtaining patients' informed consent by the funder.
- When use of generic formulations is imposed by the funders and/or administrators, the following measures should be ensured:
  - Funder/administrator should provide an educational letter to patients explaining the risks of such decision and steps to minimise health risks.
  - Patient and Pharmacists Education/Communication letter issued.
  - No switching between various brands of generics should be allowed.
  - Additional funding should be pre-authorised for
    - Attending specialist consultations
    - Laboratory tests for drug levels and organ function monitoring
    - Organ Biopsy and pathology
    - Hospital admission
    - Antirejection therapy

### B. Use of generics in Autoimmune Kidney Diseases

- a. The large variety of autoimmune glomerular diseases, immunosuppressive protocols, and sparse amount of publications using generic drug formulations means that such decisions can only be opinion/consensus based.
- b. The role of oral immunosuppressants such as calcineurin inhibitors and anti-metabolites is less dramatic when compared to solid organ transplant recipients.
  - i. These drugs are mainly used as a maintenance therapy to sustain remission after high dose induction treatment.
  - ii. Therapeutic drug level monitoring is not well defined and is mainly aimed at avoiding toxicity.
  - iii. Patients requiring steroid sparing agents in remission are less likely to develop partial or complete loss of organ function.

### Recommendations

- Based on the above, with a larger cohort of patients (compared to transplants), and the need to provide sustainable affordable healthcare, we support the use of generic immunosuppressants in such patients except in high risk patients such as paediatric patients.
- We support prescription of generic immunosuppressants by physicians for autoimmune glomerular diseases.
- We support initiation of therapy with generic formulation, rather than later drug switches. When the original formulation is prescribed, no switching should be allowed without discussion with the attending physician and undertaking steps described above for solid organ transplant recipients.
- Switching between various brands of generics should be avoided.
- Additional funding should be available in case of disease flare/relapse or side effects leading to drug discontinuation or intolerance.

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