The use of Generic Substitution in Immunosuppressive drugs for Organ Transplantation

The Kidney Alliance has become aware that....

Tacrolimus and ciclosporin:

Both tacrolimus and ciclosporin are widely used in organ transplantation and autoimmune conditions including membranous nephropathy. The safety and efficacy of tacrolimus and ciclosporin relies on maintaining blood levels within a narrow therapeutic range. High levels increase the risk of side-effects including damage to the kidneys (both native and transplanted). Low levels increase the risk of disease relapse or transplant rejection. Bioequivalence studies used to license generic products are not sufficiently robust to allow regular interchange between generic versions of these drugs:

Limitations of bioequivalence studies:

- They are carried out in health volunteers and do not reflect the unique absorption profiles of patients with chronic kidney disease and other co-morbidities.

- They are usually single dose studies which do not reflect steady state pharmacokinetics after repeated dosing

- They do not consider the effects age, ethnicity, gender, concurrent disease, drug-interactions

- Therapeutic equivalence is assumed based on bioavailability and does not reflect differences in overall exposure of the drug.

Changing patients from one brand to another or one generic equivalent to another would require additional monitoring, clinic visits and dose titration. Switching brands on a regular basis would render measured blood levels meaningless, putting the patient at risk. The risk of switching may be manageable where patients receive their immunosuppression in the hospital setting, but becomes totally unmanageable in primary care where there is less control over which brand the patient receives.

It is our view that all tacrolimus and ciclosporin products should be prescribed by brand name only. If any generic substitution is carried out it should be done in a controlled manner under close supervision of the specialist clinical team.

KA Secretariat: 26 Oriental Road, Woking, Surrey GU22 7AW   01483 724472

www.kidneyalliance.org   www.worldkidneyday.co.uk