

PHARMACY BULLETIN

VOLUME 13, ISSUE 1

2012

WARNING ON COMBINATION OF ALISKIREN WITH ACEI OR ARB

On 22nd December 2011, European Medicines (EMA) issued a warning on prescribing Aliskiren combined with ACE inhibitors or ARBs. This warning was made following the decision by the manufacturer of Aliskiren, Novartis Europharm Ltd to terminate their **ALTITUDE** (Aliskiren Trial in Type 2 Diabetes Using Cardiovascular and Renal Disease Endpoints) study early due to potential risks of cardiovascular and renal adverse events in patients with type 2 diabetes and renal impairment and/or cardiovascular disease treated with Aliskiren.

The 4-year multinational randomised, double-blind, placebo controlled study was designed to evaluate the potential benefits of Aliskiren in reducing the risk of cardiovascular and renal events in more than 8,606 patients. The purpose of the study which was commenced in October 2007 was to determine whether Aliskiren at a target dose of 300mg once daily (compared to placebo), reduces death and disease caused by the heart, the circulatory system and the kidney. The primary outcome measures were looking into cardiovascular death, resuscitated death, non-fatal myocardial infarction, non-fatal stroke, onset of end stage renal disease and doubling of baseline serum creatinine concentration to above the upper limit of normal, sustained for at least one month.

Based on the preliminary interim analyses, the Data Safety and Monitoring Board (DSMB) noted that the active-treatment group experienced an increased incidence of nonfatal stroke, renal complications, hyperkalemia and hypotension over 18 to 24 months of follow-up. The committee concluded that patients were unlikely to benefit from Aliskiren on top of standard antihypertensive and hence has prompted the committee to recommend its termination. Additional analysis from

ALTITUDE are ongoing, however in the meantime as precautionary measure, the following is advised :

- Healthcare professionals should stop Aliskiren-containing treatment in patients who are diabetic and also taking ACE inhibitor or an ARB. Alternative antihypertensive treatment should be considered if necessary.
- Aliskiren-containing products should not be initiated in diabetic patients who are also taking either an ACE inhibitor or ARB.
- Patients should not stop any treatment before discussing with a healthcare professional.

Note :

- Aliskiren is available in Malaysia and PPUKM as follows : Rasilez 150mg & 300mg Film-coated Tablet, Razilez HCT 150/12.5mg, 150/25mg and 300/25mg Film coated tablet.
- It is approved for treatment of hypertension and indicated in patients whose blood pressure is not adequately controlled on Aliskiren or HCT monotherapy. It can also be used as replacement therapy in patients already receiving both Aliskiren and HCT from separate tablets at the same dose levels.
- In PPUKM, Aliskiren is a List A* item (**Prescriber: Cardiologists, Nephrologists and Endocrinologists ONLY**) and **approved for these indications :**
 - 1) Third line therapy for treatment of hypertension.
 - 2) Uncontrolled hypertension on triple antihypertensive medications including ARB and ACEI
 - 3) Patients with proteinuria already on ARB & ACE
- **Action taken by Pharmacy Department :** Patients who came to Outpatient Pharmacy for medication refill will be referred to their respective prescribers if found to have Aliskiren- ARB/ACEI combination. Cardiologists will de-

References :

1. <http://clinicaltrials.gov>
2. <http://www.theheart.org>
3. Novartis Malaysia Press Release

INCREASED UTERINE RUPTURE WITH **MISOPROSTOL** FOR THE INDUCTION OF LABOUR



THE NEWS

Tablet Misoprostol 200mg has been approved by the National Pharmaceutical Control Bureau (NPCB) for the indication of **healing duodenal ulcer and gastric ulcers**. The **off-label** use of misoprostol for the management of **stable first trimester miscarriages < 13 weeks** has been approved in the meetings of Panel review on the List of Medicines KKM chaired by the Head of the Ministry of Health (MOH).

NPCB has been informed that there were **off-label** use of misoprostol **for the induction of labour**, and this usage has been associated with **uterine rupture with previous caesarian section**. Therefore, the *Jawatankuasa Kerja Ubat-ubatan O&G*, Ministry Of Health has issued a letter to remind all O&G practitioners to consider this risk when prescribing misoprostol to induce labour to patients with history of c-section.

THE FINDINGS

1. One RCT comparing misoprostol (25ug vaginally every 6hours) with oxytocin for induction of labour in women who had undergone one prior cesarean delivery **was terminated after uterine scars were disrupted** in 2 women in the misoprostol group. (Alaistair et al, 2001, Misoprostol and Pregnancy, NEJM Vol 344, No 1)
2. In another case control study of uterine rupture in 89 women attempting vaginal delivery after caesarean section, **5.6% (n= 5) of the women in the misoprostol group had symptomatic uterine rupture**, as compared to 0.2% of the women undergoing a trial of labor without the administration of misoprostol ($P<0.001$). Notably uterine rupture did not occur in any of the women who had undergone a prior cesarean delivery after labor had begun spontaneously. (Plaut et al, 1999).
3. A retrospective study was conducted to review the incidence of uterine rupture in patients undergoing labor with a history of previous cesarean delivery which labor was induced with misoprostol. It was found that uterine rupture occurred in 4 of 41 patients. This showed that **the rate of uterine rupture (9.7%) was significantly higher in patients with previous c-sect delivery** ($P<0.001$). No uterine rupture occurred in 50 patients without uterine scarring. (Aslan et al, 2004)

RECOMMENDATIONS

1. The RCOG does not recommend misoprostol for the induction of labour.
2. WHO panel recommends a method with low risk of uterine hyperstimulation (balloon catheter) may be preferred in women with a scarred uterus.
3. If delivery is indicated, women who had a previous c-sect may be offered induction of labour with vaginal PGE₂ eg dinoprostone (NHS NICE Clinical Guideline 2008).



ANNOUNCEMENT : JKTU 1/2012

The first Drugs and Therapeutics Committee Meeting in 2012 was scheduled to be held on 24th February 2012, Friday at 3pm but has been postponed till further notice. For 2012, JKTU Committee have decided to limit submission of new drug to ONE new drug per department except for MEDICAL & SURGERY Department (1 NEW drug per UNIT). This is because the drug budget has been slashed from RM90 million to RM88.5 million. This will be reviewed yearly.

Dates for next meeting :

2/2012 : 15th June 2012

3/2012 : 14th September 2012

A publication of :

DRUG INFORMATION CENTRE
Pharmacy Department
UKM Medical Centre

Izyan Diyana Ibrahim
Ext 5415
izyandi@ppukm.ukm.my

Michelle Tan Hwee Pheng
Ext 5401
hptan@ppukm.ukm.my