

**Drug Regulatory Authority (DRA), Ministry of Health, Bhutan – Newsletters  
dated 12 March, 2008**

DRA is pleased to share the following information on drugs as per the WHO Pharmaceutical News Letter, issue no. 6, 2007:

1. **Mycophenolate mofetil**(CellCept):Revised as category D drug, to reflect risk of fetal harm
2. **Rosiglitazone**: Revised prescribing information due to adverse cardiac events

**Mycophenolate mofetil:**

The US FDA is advising that there is now definite post marketing evidence of increase risk of first trimester pregnancy loss and congenital malformations, especially external ear malformations facial abnormalities including cleft lip and palate, anomalies of the distal limbs, heart, oesophagus, and kidney associated with the use of this drug during pregnancy.

The pregnancy category for this product has now been changed from category C (risk of fetal harm cannot be ruled out) to category D (positive evidence of fetal risk). In addition, women of childbearing potential (including pubertal girls and peri-menopausal women) taking this product must receive contraceptives counseling and use effective contraception.

**Rosiglitazone:**

According to the new restrictions:

- Rosiglitazone is no longer approved as monotherapy for type 2 diabetes except when metformin use is contraindicated or not tolerated.
- Rosiglitazone is no longer approved for use in combination with a sulfonylurea, except when metformin is contraindicated or not tolerated.
- Treatment with all Rosiglitazone products is now contraindicated in patients with any stage of heart failure.

Health professionals are also reminded that:

- Rosiglitazone is not indicated for use with insulin. This combination is associated with an increase risk of heart failure.
- Rosiglitazone is not indicated for triple therapy (that is, therapy with Rosiglitazone in combination with both metformin and a sulfonylurea). Increase in congestive heart and other fluid retention-related events have been reported in patients receiving rosiglitazone as a part of triple therapy.

DRA is pleased to share with you the following information on drugs as per the WHO Pharmaceutical News Letter, issue no. 6, 2007:

**Clozapine:** Constipation could be fatal

*“Clozapine-induced constipation may be associated with serious effects such as intestinal obstruction, bowel perforation and toxic megacolon. The four deaths reported to Intensive Medicines Monitoring Programme (IMMP), New Zealand demonstrate that these effects can be fatal. The authors note that although many anticholinergic drugs are known to cause dysmotility, clozapine has a much more potent effect through its interaction with multiple receptors, (including anticholinergic and serotonergic receptors) effecting gastrointestinal activity. This action is exacerbated by co-prescription of anticholinergic agents such as benztropine and tricyclic antidepressants. The IMMP reminds health professionals that the gastrointestinal effects of clozapine are potentially serious.*

*Awareness of this issue may prevent life-threatening complications. Patients should be asked about bowel function and dietary advice should be provided if needed’.*

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