

**Appendix to CMDh position**

*Divergent position to CMDh position*

**Article 31 of Directive 2001/83/EC resulting from pharmacovigilance data**

Procedure No: EMEA/H/A-31/1344

Diclofenac-containing medicinal products (systemic use)

The following CMDh Member supports the divergent position appended to the PRAC recommendation on diclofenac-containing medicinal products dated 13 June 2013, as stated below:

**CMDh member expressing a divergent position:**

Žydrūnas Martinėnas (LT)	26 June 2013	Signature: .....
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**Divergent statement**

Restriction of dose and duration in those with established cardiovascular disease is a more appropriate current option than to totally contraindicate at all doses and durations in those patients.

The evidence of hazard is best shown by the CPT systematic review [Lancet, 2013] with indirect comparisons. It shows that high-dose diclofenac is as hazardous as Cox-2 inhibitors and ibuprofen in terms of cardiac problems. This translates to a low absolute risk, on average of 3 extra major vascular events (one fatal) per thousand patients treated for a year. While the evidence that the risk is markedly less at lower doses it seems likely to be so, and the absolute risk is clearly duration-related.

The best evidence from the CPT review suggests that ibuprofen at high dose is as cardio-toxic and more gastro-toxic than diclofenac. In addition, ibuprofen, but not diclofenac, has been known for some years to reduce the efficacy of low-dose aspirin in preventing cardiac disease. In this context, a much stronger restriction for diclofenac is currently unjustified.