

9 February 2010



Dear Healthcare Professional

Withdrawal of dextropropoxyphene-containing medicines

In December 2009 the Medicines Adverse Reactions Committee (MARC) reviewed the benefits and risk of dextropropoxyphene-containing medicines.¹ The MARC assessed the published literature; adverse reactions reported in New Zealand (NZ) and internationally; NZ Poisons Centre data, the results of a Paradex utilisation study conducted in New Zealand in 2007. The MARC also considered reviews conducted by other medicine regulators.

After analysis and discussion of the available data the MARC concluded there is evidence that:²

- These medicines are no more effective than maximum recommended doses of paracetamol alone.
- These medicines have the potential to cause more adverse reactions than paracetamol used at recommended doses.
- These medicines are more dangerous than other simple analgesics in overdose, particularly when combined with alcohol. Deaths have occurred in association with dextropropoxyphene use in NZ.³
- Deaths related to dextropropoxyphene overdose have occurred within 1 hour of ingestion and before medical intervention could be obtained.
- Prescribing restrictions introduced in 2006 have failed to ensure that these medicines were only used in patients for whom the benefits are likely to outweigh the risks.
- Overall the risks of these medicines **exceed** their benefits.

Therefore, in the interests of public safety, the MARC has recommended that Capadex and Paradex be withdrawn from New Zealand.⁴

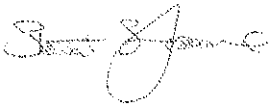
Medsafe supports the MARC's conclusions and is currently implementing their recommendation. In recognition of the significant number of patients currently taking dextropropoxyphene-containing medicines, the withdrawal will not be immediate to allow sufficient time for patients to be transferred to alternative medications.

In the interim, Medsafe advises the following:

- Do not start any new patients on Paradex or Capadex.
- Analgesic requirements of patients currently taking Paradex or Capadex should be reviewed at the earliest opportunity.
- In the UK where this medicine has already been withdrawn there is evidence to show that the majority of patients were successfully transitioned to full dose paracetamol alone, codeine alone or paracetamol/codeine combination products.⁵
- As dextropropoxyphene is an opiate similar adverse effects may be seen to those observed with other opiates and it may therefore not be appropriate to abruptly stop this medicine for some patients.

Further information will be provided as it becomes available. It is likely that a final date for withdrawal will be known within the next month.

Yours sincerely



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Footnotes

1. Capadex and Paradex are the only dextropropoxyphene-containing medicines available in New Zealand.
2. A summary of the MARC's discussion on dextropropoxyphene is included in the minutes of the December 2009 meeting, available on the Medsafe website <http://www.medsafe.govt.nz/profs/adverse.asp>.
3. Reith D et al. 2005. Opioid poisoning deaths in New Zealand (2001-2002). NZMJ 118(1209): U1293.
4. Dextropropoxyphene containing medicines have already been withdrawn from the UK and Sweden. Medicines regulators in Europe and Singapore have also announced that they will be withdrawing these medicines.
5. Hawton K et al. 2009. Effect of withdrawal of co-proxamol on prescribing and deaths from drug poisoning in England and Wales: time series analysis. BMJ 338: 62270.

Additional information

- More information is available as a "Question and Answer" document at:
www.medsafe.govt.nz/hot/media/2010/QandACapadexandParadex.asp
In addition, Medsafe's review of the benefits and risks of dextropropoxyphene-containing medicines is available at:
www.medsafe.govt.nz/hot/media/2010/MedsafeReviewDextropropoxyphene.pdf
- In 2009, 78,000 patients were estimated to be taking dextropropoxyphene-containing medicines in New Zealand.
- The Medicines Adverse Reactions Committee (MARC) is an independent expert advisory committee that advises the Minister of Health on medicines safety issues. A summary of the Committee's discussion on dextropropoxyphene is included in the minutes of the December 2009 meeting, available on the Medsafe website <http://www.medsafe.govt.nz/profs/adverse.asp>.
- The MARC first reviewed the use of Capadex and Paradex in 2005 and considered the balance of benefits and risks to be unfavourable for the majority of patients. After consultation with healthcare professionals, the MARC accepted that there was a clinical need for these products in a select group of patients. Medsafe introduced prescribing restrictions to limit use of these medicines to patients for whom healthcare professionals had indicated there was a clinical need. The MARC also requested that a medicines utilisation study be conducted to monitor the effect of the new restrictions. A study conducted for Paradex, showed that less than half of the prescriptions issued were in accordance with the new restrictions. A significant number of prescriptions were also issued to children. The MARC noted that New Zealanders were therefore, still being exposed to a medicine previously considered to have an unfavourable benefit risk balance. Therefore, a statutory review of the benefits and risks of these medicines was initiated under section 36 of the Medicines Act 1981.
- Section 36 of the Medicines Act 1981 gives the Director General of Health the power to require a medicine sponsor to supply information to support the efficacy and safety of that medicine. If a review of these data is unfavourable the Minister of Health may take action, including prohibiting the supply of medicine or removing the medicine from the market.
- The data sheet is a summary of the known effects of a medicine, and includes information on the approved uses of the medicine (indications) and is supplied and maintained by the pharmaceutical company. Data sheets for Capadex and Paradex are published on the Medsafe website <http://www.medsafe.govt.nz/profs/Datasheet/dsform.asp>. However, please note that during the MARC review it was highlighted that the product information for similar products in the US had recently been updated making the New Zealand data sheets out of date.
- Medsafe is the New Zealand Medicines and Medical Devices Safety Authority, and is part of the Ministry of Health.