Corby Clinical Commissioning Group

Nene Clinical Commissioning Group

Why is co-proxamol not recommended for prescribing?

Co-proxamol is an analgesic, containing paracetamol 325mg and dextropropoxyphene 32.5mg. It was used very widely for the treatment of mild-to-moderate pain, but its use has now declined due to concerns about the efficacy and toxicity of the product.

Recommendations

- No new patients should be started on co-proxamol
- Co-proxamol should not be used for any acute pain indication.
- Co-proxamol should not be used in patients under 18 years of age.
- Co-proxamol is contra-indicated in particular groups of people and so should not be prescribed for:
  - Patients who are alcohol-dependent or who are likely to consume alcohol whilst taking co-proxamol.
  - Patients who are suicidal or have history of addiction.
- Carry out a review of patients still being prescribed co-proxamol with a view to switch them to an alternative pain management regime.
- Document clinical reason(s) for continuing to prescribe co-proxamol and efforts made to switch to suitable alternatives.
- Highlight co-proxamols potential for serious cardiac side-effects, even at therapeutic doses, and make patient aware of the symptoms and what to do if they experience any of them

Background

The license for co-proxamol was withdrawn on the advice of the Committee on Safety of Medicines amid serious safety concerns in January 2005[1]. The withdrawal was phased over two years to allow prescribers and patients time to discuss alternative pain management regimes. The interim prescribing advice for co-proxamol pending its full withdrawal was that it could be used for milk to moderate pain in adults where first line analgesics have proved ineffective or are inappropriate.

Clinical Evidence

There is no robust evidence that co-proxamol is more effective than full strength paracetamol used alone in either acute or chronic use. No patient group was identified in which the risk:benefit of co-proxamol was positive[2].

Clinical data shows that dextropropoxyphene, even at normal therapeutic doses, has serious effects on the electrical activity of the heart resulting in prolongation of the P-R and Q-T intervals and widening QRS complexes[3].

The license was withdrawn due to concerns about the high incidence of suicide with the drug. In England and Wales in 1997–1999, 18% of drug-related suicides involved co-proxamol; these constituted 5% of all suicides. The toxic effects of dextropropoxyphene on respiration or cardiac function are usually the cause of death. Death from co-proxamol overdose may occur rapidly, the lethal dose can be relatively low, and the effects are potentiated by alcohol and other CNS depressants. The majority of co-proxamol overdose deaths occur before hospital treatment can be received. The risk can extend to others in the household of the person for whom the drug is prescribed. The risk of dying after co-proxamol overdose was

2.3 times greater than for tricyclic antidepressants and 28.1 times greater than for paracetamol.

Treatment of dextropropoxyphene overdose is not straightforward. Dextropropoxyphene has a very long duration of action so, like methadone, patients need to be monitored for a long periods following overdoses. This can also mean that additional doses of naloxone, which reverses its opioid effects, may be needed.

Since the withdrawal of the license, the number of deaths associated with co- proxamol has fallen dramatically from 388 in 1999 to 18 deaths in 2011 in England and Wales.

A six-year follow-up study to the withdrawal of co-proxamol reported in 2012 that there has been a significant reduction in poisoning deaths involving co-proxamol without a significant increase in deaths involving other analgesics, even though prescribing of other analgesics rose[4]. However, the results of this study were limited as it only considered deaths mentioning one substance. If deaths mentioning more than one substance are also considered, the number of deaths involving some analgesics has increased. Tramadol death rates are of particular note as they have risen between 2008 and 2012. There is also evidence that tramadol recreational use has also increased. Therefore prescribers should take care when considering alternative analgesics to co- proxamol.

Co-proxamol is now unlicensed and is only available on a 'named patient' basis. As an unlicensed drug, responsibility for the use of the drug rests solely on the prescriber.

Rationale for switching from co-proxamol to an alternative pain medicine

No patient group has been identified in which the risk:benefit ratio of using co-proxamol is positive.

Acknowledgement
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Switching options

Consider switch from co-proxamol to paracetamol 500mg tablets or capsules at a dose of 1g four times a day. If paracetamol on its own is ineffective, the addition of codeine phosphate might be beneficial. The BNF recommends a dose of 30-60 mg every four hours when necessary, to a maximum of 240 mg daily for mild to moderate pain. This dose will need to be reduced in patients with hepatic or renal impairment. It also warns that codeine is too constipating for long-term use.

Alternatively, and if safe and appropriate, consider a switch from co-proxamol to co-codamol 8mg/500mg tablets. Bear in mind that the elderly are more susceptible to the side-effects of opioids.

Summary

No new patients should be started on co-proxamol. Prescribers should actively review all patients being prescribed this unlicensed medicine and renew efforts to identify and prescribe an effective alternative analgesic.

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[1] MHRA Safety warnings, alerts and recalls for medicines: Co-proxamol. Accessed 05/02/13. http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON1004254

[2] The withdrawal of co-proxamol: alternative analgesics for milk to moderate pain. MeRec Bulletin, 2006; 16 (4) 5.

[3] (Dextro)propoxyphene: new studies confirm cardiac risks. Drug SafetyUpdate 2011; 4 (6): H1 Accessed 20/02/13. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON105759

[4] Hawton K, Bergen H, Simkin S, et al. Six-year follow-up of impact of co-proxamol withdrawal in England and Wales on prescribing and deaths: Time-series study. PLoS Med 2012; 9 (5): e1001213. Accessed 05/02/13 http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001213

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