

Safety warning: combination products containing codeine and ibuprofen

Overview of: European Medicines Agency Pharmacovigilance Risk Assessment Committee. Codeine with ibuprofen: PRAC adds warning for serious renal and gastrointestinal harms. September 2022.

Key learning points

- ▶ The European Medicines Agency (EMA) has warned of serious harms associated with medicines containing both codeine and ibuprofen.
- ▶ There have been reports of renal, gastrointestinal and metabolic toxicities from prolonged or high-dose use of combination products containing codeine and ibuprofen.
- ▶ The EMA has recommended adding new safety warnings for products available in the EU highlighting the risk of renal tubular acidosis and hypokalaemia.

The safety committee of the European Medicines Agency (EMA) has recommended adding new warnings for products available in the European Union (EU) that contain a combination of codeine and ibuprofen.¹

Overview

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended new safety measures for products containing a combination of codeine and ibuprofen.¹ The committee reviewed several cases of renal, gastrointestinal and metabolic toxicities associated with abuse of, and dependence on, codeine and ibuprofen combinations, some of which were fatal.

PRAC noted that regular use of codeine with ibuprofen may lead to dependence and abuse due to the codeine component.¹ The committee found that, when taken at higher than recommended doses or for a prolonged period, the combination of codeine and ibuprofen can cause damage to the kidneys in the form of renal tubular acidosis, in which the kidney cannot remove acids from the blood into the urine. Kidney damage also causes hypokalaemia, which can result in muscle weakness and light-headedness.

The PRAC recommended that information should be provided to healthcare professionals and to patients to inform them of signs of abuse and dependence, and

risks of serious harm.¹ Patients should be advised to consult their doctor if they wish to use codeine with ibuprofen for longer than recommended and/or at higher-than-recommended doses.

As products that contain both codeine and ibuprofen are available without prescription, PRAC has suggested that the safest way to mitigate these risks and prevent harm and dependence would be by changing the classification of such medicines to prescription-only status.¹

Context

In the UK, combination products containing codeine and ibuprofen are available as pharmacy medicines and can be purchased without a prescription. Typically, the combination product contains 12.8 mg of codeine phosphate and 200 mg of ibuprofen per tablet.² The combination is licensed for use by anyone aged over 12 years 'for the short-term treatment of acute moderate pain which is not considered to be relieved by other analgesics (eg, paracetamol, ibuprofen or aspirin) alone, such as: rheumatic and muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea'.² The recommended dose is one or two tablets every 4–6 hours with no more than six tablets to be taken in 24 hours. The product information advises that codeine with ibuprofen should not be taken for more than 3 days continuously

without medical review and 'the patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 3 days'.

The EMA's recommendations apply to countries and medicine regulatory agencies within the EU. It is not known if the UK Medicines and Healthcare products Regulatory Agency will review the legal status of combination products containing codeine and ibuprofen or will issue guidance to healthcare professionals in the UK highlighting these safety concerns.

Contributors DTB Team.

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References

- 1 European Medicines Agency. Codeine with ibuprofen: PRAC adds warning for serious renal and gastrointestinal harms. meeting highlights from the pharmacovigilance risk assessment Committee (PRAC) 26-29, 2022. Available: <https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-26-29-september-2022> [Accessed 12 Dec 2022].
- 2 Ibuprofen and codeine 200mg/12.8mg film-coated tablets. summary of product characteristics, UK. The Boots company PLC, February 2021.

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