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Phenylephrine: EU Manufacturers, Don't Panic, But May Be Time To Prepare

by David Ridley

European OTC manufacturers don't need to worry too much about the questions raised about oral phenylephrine's efficacy as a nasal decongestant in the US, advises industry physician James Walmsley. However, he said it may be an opportunity for companies to "ask themselves how they would respond to any future challenges on their core active ingredients."

European OTC manufacturers concerned about the US Food and Drug Administration's recent review of oral phenylephrine, which showed limited efficacy in nasal congestion, have "no need to panic," according to James Walmsley, industry physician and a former medical director at J&J Consumer.

European regulators are unlikely to review oral phenylephrine, given that there are no safety concerns and similar mechanisms to review efficacy don't exist.

But the US review should act as a "bit of a wakeup call" to European industry, Walmsley told HBW Insight.

"It's an opportunity for companies to ask themselves how they would respond to any future challenges on their core active ingredients, and whether they need to consider updating their clinical data," said Walmsley, who is managing director of specialist advertising review service AdverCheck.

EU Review 'Unlikely'

With regards to phenylephrine, the ingredient is available in oral form without a prescription in the majority of European countries. Walmsley said that an EU-wide efficacy review is "possible, but unlikely." There's little precedent for European regulators to routinely undertake a review of

a drug just on the grounds of efficacy, he pointed out.

JAMES WALMSLEY

Usually, in the EU, medicines are reviewed on safety grounds, for example in the case of pseudoephedrine – another widely used OTC nasal decongestant active ingredient. Earlier this year, reports of posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome triggered a EU-wide safety review. (Also see "*Pseudoephedrine Safety Review Initiated In EU Over Link To Neurological Problems*" - HBW Insight, 13 Feb, 2023.)

Over 400 products were affected by the review, including major brands such as Bayer's Aspirin Complex (pseudoephedrine hydrochloride/acetylsalicylic acid), Reckitt's Nurofen Cold & Flu (pseudoephedrine hydrochloride/ibuprofen) and Johnson & Johnson's Sudafed (pseudoephedrine hydrochloride).

"When there's a safety issue, regulators may revisit the overall balance of risks and benefits," Walmsley noted. "That's when companies may be asked to justify the efficacy of a medicine."

In the US, the efficacy review was prompted by a citizen petition submitted by University of Florida pharmaceutical researchers in 2015 asking the agency to remove phenylephrine from the final OTC CCABA monograph. The petition noted multiple studies showed clearly that phenylephrine "is no more effective than placebo in decreasing nasal congestion and increasing the dose fourfold did not provide additional benefit."

In September, an FDA advisory panel unanimously agreed that research doesn't support oral phenylephrine's efficacy for nasal decongestion at the 10mg dose set in the cold, cough, allergy, bronchodilator and anti-asthmatic OTC monograph for the ingredient. (Also see "*US Advisory Panel Leaves No Room For Doubt: Oral Phenylephrine Ineffective As Nasal Decongestant*" - HBW Insight, 12 Sep, 2023.)

OTC Doubts

Were the US to withdraw the oral phenylephrine monograph, which is not a certainty at this stage, Walmsley suggested that there may be some potential knock on effects in Europe.

Firstly, phenylephrine-containing products on the US market may have to be reformulated. This could result in some European products also being reformulated, given the international

footprint of certain OTC cough and cold brands.

Secondly, and potentially more seriously, doubts about oral phenylephrine's efficacy may spread to other OTC products, undermining the public's confidence in non-prescription medicines.

"It's possible that it might knock consumer confidence in the effectiveness of OTC medicines in general," Walmsley warned. "I think that would be a shame because phenylephrine is an exception to the rule."

It's important to remember, Walmsley pointed out, that the vast majority of active ingredients that companies have in their OTC portfolio are supported by robust clinical data conducted to modern standards.

This is particularly the case with ingredients that have been switched from prescription-only to OTC status in the last few decades, Walmsley said, such as sumatriptan, esomeprazole, and sildenafil.

"It's important that consumers have confidence in the effectiveness of OTC medicines," he added. "Otherwise we will have more doctor and hospital visits for non-serious self-limiting conditions, like coughs and colds."

Old OTCs

However, there may be other, older OTC ingredients that "could potentially have questions about the quality or age of the data," Walmsley conceded.

"My guess would be that we're largely talking about ingredients used in cough and cold," he said, adding that "many of these active ingredients go back a long time."

"Dextromethorphan and guaifenesin have both been speculated to be at risk of an efficacy challenge in the US," he added.

"Companies don't usually have much incentive to update their clinical trials because these are all generic ingredients. But they may want to proactively identify any key efficacy gaps at this stage," he advised.

Walmsley stressed that any questions regarding other OTC ingredients should be grounded, first and foremost, in the fact that these products have been licensed and authorized as safe and effective medicines by regulators across the world.

"I think that's hugely important," he insisted. "It's also crucial that if new concerns come up, they are grounded in science."