



Centrum für Therapiesicherheit in der Chinesischen Arzneitherapie

Center for Safety of Chinese Herbal Medicine

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C T C A L e t t e r – A p r 2 0 2 4

Urgent Safety Concern!

Scandal Involving Kobayashi Pharmaceuticals – Suspected Severe Adverse Reactions Linked to Red Yeast Rice Batches

Dear therapists, pharmacists, and healthcare professionals,

We would like to draw your attention to a potentially serious health risk that may also affect European consumers.

The Japanese company **Kobayashi Pharmaceuticals** is currently under investigation in a scandal involving suspected severe adverse reactions associated with red yeast rice products marketed by the company. Red yeast rice (RYR) is produced by fermenting white rice with the mold *Monascus purpureus*. Traditionally, it has been used as a dietary supplement and as a food colouring agent.

In European countries, red yeast rice is primarily consumed as a dietary supplement for lowering cholesterol. Theoretically, red yeast rice may elicit the same adverse effects as lovastatin, since its active component, monacolin K, is largely chemically identical. Reported adverse effects of red yeast rice include elevated muscle serum creatine kinase, rhabdomyolysis and liver injury similar to those observed with lovastatin.

Recently, multiple hospitalisations in Japan were linked to red yeast rice consumption, with cases of renal injury and even fatalities. A death has also been reported in Taiwan. To date, 157 individuals in Japan have been hospitalised in connection with the Kobayashi product, while several hundred more are experiencing symptoms.

Kobayashi Pharmaceuticals supplies red yeast rice to approximately 50 companies in Japan and two companies in Taiwan. These in turn distribute the product to wholesalers, potentially affecting up to 1,800 dietary supplement manufacturers. Following the directive of Japanese authorities, the company recalled multiple red yeast rice products. The South Korean Ministry of Health has published a list of 182 Kobayashi products and issued a warning against their use.

The causal link between these products and the clinical cases is currently under investigation. Initial suspicion focused on contamination with the nephrotoxic mycotoxin citrinin, which can arise under improper storage conditions. However, citrinin was not detected.

Attention has since shifted to the potentially toxic compound **puberulic acid** (a natural compound of blue mold) which was detected in batches manufactured at the Osaka plant between April and October 2023. Although previously not known to exert nephrotoxic effects, its role in the present cases is under active discussion.

Red yeast rice supplements are available in Germany, Austria, and Switzerland. They are marketed as dietary supplements that naturally lower cholesterol and are available through retail outlets and via the internet. Claims of therapeutic or medicinal efficacy, however, violate pharmaceutical legislation, as such claims would require formal drug approval. Therefore, it cannot be excluded that batches already recalled in Japan are still being sold in Europe under various dietary supplement labels.

Given these reports, we recommend suspending the use of red yeast rice products until further information regarding the safety and non-toxicity of these products is available, or until affected batches have been removed from the market.

The CTCA (Center for Safety of Chinese Herbal Therapy, e.V.) will continue to monitor the situation and keep you informed as further details emerge.

References:

Ärzteblatt online 28.03.2024, <https://www.aerzteblatt.de/treffer?mode=s&wo=1041&typ=1&d=150343&s=cholesterinsenker&s=japan>

Ärzteblatt online 02.04.2024, <https://www.aerzteblatt.de/treffer?mode=s&wo=1041&typ=1&d=150382&s=cholesterinsenker&s=japan>

Pharmazeutische Zeitung online 02.04.2024, <https://www.pharmazeutische-zeitung.de/untersuchun-gen-nach-todesfaellen-in-japan-146514/>

The Japan Times online 29.03.2024, <https://www.japantimes.co.jp/news/2024/03/29/japan/science-health/kobayashi-pharma-apologizes-inpresser/>

Reuters online 30./31.03.2024, <https://www.reuters.com/world/asia-pacific/second-kobayashi-pharma-japan-factory-inspected-overdeaths-2024-03-31/>

<https://www.reuters.com/world/asia-pacific/kobayashi-factory-searched-over-deaths-possibly-linked-supplements-2024-03-30/>

<https://www.bfr.bund.de/cm/343/cholesterinsenkung-mit-folgen-nahrungsergaenzungsmittel-mitrotschimmelreis-nur-nach-aerztlicher-ruecksprache-einnehmen.pdf>

<https://www.bfarm.de/SharedDocs/Pressemitteilungen/DE/2016/pm3-2016.html?nn=468782>.

Stellungnahme der gemeinsamen Expertenkommission BVL/BfArM Einstufung von Rotschimmelreisprodukten (02/2016)