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Authorisations of Caustinerf arsenical and Yranicid arsenical used in dental procedures revoked in the EU

On 25 April 2014, the European Medicines Agency recommended that the marketing authorisations for the dental pastes Caustinerf arsenical, Yranicid arsenical and associated names be revoked in the EU due to concerns over the risk of genotoxic effects (damage to the genetic material in cells) and cell death in tissues around the teeth. The dental pastes, which contain an arsenic-based compound, arsenic trioxide, have been used to remove the damaged nerves in the dental pulp (the inside of the tooth).

In a review conducted by the Agency's Committee for Medicinal Products for Human Use (CHMP), analyses of data from laboratory and population studies indicate that the arsenic contained in them may pose a risk of genotoxic effects that could increase the risk of cancer. In addition, there have been a small number of cases where arsenic is thought to have leaked into the areas around the teeth, causing parts of the tissue to die, including bone (osteonecrosis).

During the review, the CHMP considered measures to minimise the risks identified with these products but concluded that restrictions and additional guidance to dentists would not reduce the risks to an acceptable level.

Therefore, in the light of current standard of care available, the Committee concluded that the benefits of Caustinerf arsenical and Yranicid arsenical do not outweigh their risks and recommended that their marketing authorisations be revoked.

The review was initiated at the request of the French medicines agency (ANSM) after new data became available that raised concerns about the safety of these products.

The CHMP recommendation was sent to the European Commission and on 11 July 2014 the Commission issued a legally binding decision revoking the authorisations for Caustinerf arsenical, Yranicid arsenical and associated names throughout the EU.

Information to patients

- Caustinerf arsenical and Yranicid arsenical dental pastes will no longer be used for removing damaged nerves in teeth, because they may pose a risk of genotoxic effects (which can cause cancers) and cell death in tissues around the teeth which may be difficult to treat.
- If you require such treatment, your dentist will use other methods available which do not contain arsenic.

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- If you have any questions or concerns, speak to your dentist.

Information to healthcare professionals

The EMA has concluded that the benefits of Caustinerf arsenical, Yranicid arsenical and associated names do not outweigh their risks and has recommended that their marketing authorisations in the EU be revoked. Dentists should use other alternative methods available for removing dental pulp.

The EMA recommendations are based on a review of data indicating a potential genotoxic effect of the products due to the presence of arsenic trioxide (arsenous anhydride). *In vitro* studies with Caustinerf arsenical and Yranicid arsenical have confirmed a clastogenic/aneugenic potential and there are published data showing that arsenic compounds have a toxic effect on reproduction in animals. In addition, epidemiology studies have shown an association between arsenic and spontaneous abortions and stillbirths.

The risk of arsenic from the dental paste leaking into the general circulation and the tissues surrounding the teeth cannot be excluded.

Post-marketing surveillance of Caustinerf arsenical and Yranicid arsenical has identified a small number of cases of periodontal necrosis, including 12 cases of osteonecrosis. The majority of cases occurred within 7 days of using the pastes.

More about the medicine

Caustinerf arsenical, Yranicid arsenical and associated names are dental pastes that have been used in procedures to remove the damaged nerves in the dental pulp. They contain 3 active substances: ephedrine hydrochloride, lidocaine and arsenic trioxide (arsenous anhydride).

The dental pastes are applied to the tooth after the tooth has been opened surgically. Seven days later the tooth is re-opened and the infected pulp is surgically removed.

The products were authorised in Estonia, France, Italy, Latvia and Lithuania.

More about the procedure

The review of Caustinerf arsenical, Yranicid arsenical and associated names was initiated on 24 October 2013 at the request of the French medicines agency, under Article 31 of Directive 2001/83/EC.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted an opinion. The CHMP opinion was forwarded to the European Commission, which endorsed it and issued a final legally binding decision on 11 July 2014.

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