HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Ibuprofen-containing medicines – Potential risk of Acute Generalised Exanthematous Pustulosis

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID), commonly used for the reduction of pain, inflammation and fever. While its safety profile is generally well established, ibuprofen, like other medicines is subject to ongoing monitoring nationally and at EU level.

Through routine safety monitoring, a possible relationship between ibuprofen and Acute Exanthematous Pustulosis (AGEP) was identified. AGEP, also known as 'pustular drug eruption', 'pustular drug rash' or 'toxic pustuloderma' is an uncommon skin eruption characterised by superficial pustules. AGEP is a rare, but well recognised severe cutaneous adverse reaction (SCAR), which is attributable to medicines in the majority (>90%) of cases. It is characterised by a sudden onset of fever and pustulosis with leukocytosis, generally occurring within 48 hours of administration of the suspected medication and in most cases results in a single episode that resolves spontaneously. However, in severe cases, there may be mucous membrane and systemic organ involvement.

The product information for ibuprofen-containing medicines already listed other SCARs such as Toxic Epidermal Necrolysis (TEN), Stevens-Johnson Syndrome (SJS) and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) as rare side effects. The product information for ibuprofen-containing medicines has now been updated to also include AGEP as a side effect, with the frequency currently unknown. Ibuprofen should be discontinued at the first appearance of signs and symptoms of a severe skin reaction, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Please note that the product information for ibuprofen/pseudoephedrine-containing medicines was previously updated to add AGEP as an established side effect.

As AGEP is currently understood to be a T-cell mediated neutrophil-rich type IVd hypersensitivity reaction based on drug-specific immune components, a biological mechanism for ibuprofen to cause this reaction was considered plausible. Studies also indicate that innate cells might be involved in the pathogenesis of AGEP.

Advice to Healthcare Professionals

- Severe skin reactions including AGEP may occur with ibuprofen-containing products. The frequency of AGEP is currently unknown.
- Ibuprofen should be discontinued at the first appearance of signs and symptoms of a severe skin reaction, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.
- The product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) for ibuprofen-containing products has been updated to reflect this information.

Key Message

Acute Generalised Exanthematous Pustulosis (AGEP) has been reported in relation to ibuprofen-containing products.

Ibuprofen should be discontinued at the first appearance of signs and symptoms of a severe skin reaction, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

All reports of suspected adverse reactions should be reported to the HPRA via the available methods (www.hpra.ie/report).

Further details on ibuprofen-containing medicines are available at www.hpra.ie and www.ema.europa.eu.