Severe allergic reaction following consumption of a food supplement

ANSES received a report of life-threatening anaphylaxis after consumption of the food supplement Actirub® by a woman with an allergic predisposition. Causality of the product was deemed to be very likely in this case. Given the severity of the adverse effect described, ANSES is bringing this case to the attention of the general public and healthcare professionals. It warns people with allergies of the risk of severe allergic reactions from consuming purple coneflower and green chiretta. In addition, if adverse effects do occur, they should be reported to the national nutrivigilance scheme.

As part of the nutrivigilance scheme it has been running since 2009, ANSES received a report of anaphylaxis[1] potentially associated with consumption of the food supplement Actirub® marketed by Santé Verte. This product is presented as helping to support the immune system.

The alert

The report concerned a 49-year-old woman with an allergic predisposition, mainly skin allergies, with a diagnosis of sensitisation to cat and dog hair.

In January 2022, after waking up in the morning and on an empty stomach, she took a tablet of the food supplement Actirub® because of rhinitis.

Immediately afterwards, she suffered heartburn followed by itching hands. She also experienced sweats and hot flashes. After vomiting intentionally, she experienced hot and cold temperature swings. This was followed by generalised urticaria with facial oedema and difficulty swallowing, without respiratory discomfort.

When the emergency services arrived, she had major hypotension with a systolic reading of 60 mmHg (normal: 100–145 mmHg) and a temperature of 34.5°C. She was taken into care and lost consciousness in the ambulance.

The biological test results showed an elevated histamine level[2] (more than 100 µg/l, whereas normal levels are below 50 µg/l).

The other test results were normal. Grade 3[3] anaphylaxis was diagnosed.

Subsequently, on an unspecified date, a prick test[4] carried out with an Actirub® tablet crushed in water for injection was positive, with a 5 mm wheal and 9 mm rash showing sensitisation of the patient to one or more ingredients of Actirub®.

The consumer had previously taken the same product in 2019, without any associated food intake, and had immediately experienced a grade 1 reaction with rash and oedema of the hands, which resolved after she took an antihistamine.

What is the link with use of the food supplement?

The causality of the food supplement in the occurrence of the anaphylaxis was assessed using the method developed for the nutrivigilance scheme [1].

Causality takes four components into account: the onset time, the outcome after discontinuing the product, whether or not the effect reappears upon reintroduction, and the absence of any other possible explanation for the observed adverse effect. For the food supplement Actirub®, the time to onset of the effect was considered "compatible". The outcome was described as "suggestive". The reintroduction was considered "positive" due to the first episode in 2019.

1.Anaphylaxis is an acute, life-threatening, IgE-mediated allergic reaction that occurs in a previously sensitised patient when re-exposed to the sensitising antigen.
2.Histamine is a chemical compound whose levels increase in the event of an allergy.
3.Anaphylaxis severity grades range from 1 (low severity) to 4 (cardiac arrest) according to the Ring classification (Ring and Behrendt, 1999).
4.The prick test is used to explore an allergic reaction involving immunoglobulin E (Hayamizu et al.). It is an epidermal micro-puncture performed with a lancet or needle through an allergenic extract or suspect product.

The aetiological investigation led to the food supplement being formally incriminated, since a prick test was carried out with this product and proved positive. The Actirub® product was therefore deemed very likely responsible for the occurrence of the anaphylaxis, i.e. I4 on a scale ranging from I0 (excluded) to I4 (very likely).

Have similar cases been described in the scientific literature?

The literature search focused on possible human cases of anaphylaxis associated with the active ingredients of the food supplement Actirub®, which according to the manufacturer's website are purple coneflower (*Echinacea purpurea,* 300 mg/tablet), green chiretta (*Andrographis paniculata,* 150 mg/tablet), astragalus (*Astragalus propinquus,* 150 mg/tablet), white willow (*Salix alba,* 20 mg/tablet), N-acetyl-L-cysteine (118 mg/tablet), vitamin C (ascorbic acid, 80 mg/tablet), common mullein (*Verbascum thapsus* L., 75 mg/tablet.), common thyme (*Thymus vulgaris,* 70 mg/tablet), feverfew (*Tanacetum parthenium* L., 16.5 mg/tablet), black elder (*Sambucus nigra,* 10 mg/tablet), essential oil of narrow-leaved peppermint (*Eucalyptus radiata*, 5 mg /tablet) and zinc (5 mg/tablet).

This search showed that according to the literature, several ingredients, including purple coneflower and green chiretta, have been associated with the occurrence of anaphylaxis. White willow and astragalus may also play a role in the onset of this effect.

The scientific literature therefore showed that the observed anaphylaxis may have been due to several of the ingredients in the food supplement Actirub®, acting through a combination of mechanisms, some of which are dependent on immunoglobulin E (or IgE[5]). The combination of purple coneflower and green chiretta in the product may have increased the intensity of the allergic reaction.

Moreover, in the event of respiratory sensitisation to Asteraceae pollen, an allergic reaction to purple coneflower is possible from the very first ingestion.

Have similar cases been reported to the nutrivigilance scheme?

While no other cases of grade 3 anaphylaxis have been notified to the nutrivigilance scheme for the food supplement Actirub®, three cases of immediate hypersensitivity reactions following consumption of this food supplement have been reported: one case of grade 2 anaphylaxis, one case of palpebral angioedema (swelling of the eyelid) and one case of angioedema of the face and lips. The causality of Actirub® was deemed possible for these three cases.

There have also been reports of cases of immediate hypersensitivity reactions[6] with other products containing the same ingredients as Actirub®, mainly purple coneflower, green chiretta, black elder, common mullein or common thyme. In five of these, the causality of the product was either possible or likely. However, some of the products involved contained other known allergenic ingredients such as honey or propolis.

Conclusions and recommendations

The causality of the food supplement Actirub® in the occurrence of anaphylaxis in an allergic individual was deemed to be very likely. This product contains several ingredients, including purple coneflower and green chiretta, whose link with the occurrence of anaphylaxis has been documented in the literature.

ANSES recommends informing people with allergies about the risk of severe allergic reaction associated with the consumption of these two plants. They should carefully read the composition of the food supplements they plan to take, and ask their pharmacist for advice if they are in any doubt about one or more ingredients.

In addition, people with allergies should be particularly wary of products with multiple ingredients, because this increases the risk of cross-reaction with other allergens previously encountered (including by other routes of exposure, such as airborne pollen via the respiratory tract), and the risk of stronger allergic reactions occurring due to the simultaneous triggering of different mechanisms (allergic, mechanical or sensitisation).

5.IgE are the main antibodies responsible for immediate hypersensitivity reactions
6.Reaction occurring within a few minutes and a few hours of consumption.

In general, ANSES recommends that consumers of food supplements:

- notify a healthcare professional of any adverse effect occurring after consumption of a food supplement;
- comply with the conditions of use specified by the manufacturer;
- avoid taking food supplements on a multiple, prolonged or repeated basis throughout the year without having sought the advice of a healthcare professional (doctor, pharmacist, etc.);
- be wary of products claiming "miracle" properties;
- avoid the purchase of products sold through alternative channels (internet) and without personalised advice from a healthcare professional.

ANSES also reminds healthcare professionals that they must report to its nutrivigilance scheme any cases of adverse effects they suspect are associated with the consumption of food supplements. The analysis of these reports helps identify products or ingredients posing a risk, thereby protecting consumer health.

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TO FIND OUT MORE

ANSES OPINION on a case of grade 3 anaphylaxis associated with consumption of the food supplement Actirub