The evolution of medical opinion on the use of emetics

We take the safety of our products very seriously. Nearly 30 years ago, we requested that the FAO/WHO mandate the inclusion of an emetic in all paraquat formulations. Today, all Syngenta paraquat-containing products include the emetic PP796, a potent pharmaceutical that creates an urge to vomit, with the intent that any paraquat ingested is ejected.

Like all science, medical views on the use of emetics have evolved over the years. The science surrounding the use of emetic is complex, and the issue of the concentration of emetic in a product is more complicated than presented by Jon Heylings in his allegations against Syngenta. More emetic does not necessarily equal a safer product. In fact, some recent medical opinion has suggested the use of emetic could be counter-productive in the treatment of ingestion. Decisions linked to the level of emetic in our products are based on the best available science.

Emetics are widely used in the treatment of patients drinking chemical substances to expel the toxin from the body. PP796 is the emetic used in paraquat formulations. Its emetic properties were first discovered in the early 1970s when it was undergoing clinical trials to treat asthma. It has been included in paraquat formulations since being first introduced in 1977. Syngenta continues to follow scientific evidence and medical advice regarding the use of emetics as it evolves with time.

Data from the UK National Poisons Information Service in the 1980's verified that formulations containing PP796 at a concentration of 0.05% resulted in more frequent and earlier vomiting than those without emetic. PP796 is used in all our paraquat formulations at or above 0.05%.

In the early 2000s we developed a new formulation (Inteon) that we believed, based on our lab studies and modelling, would provide a step change in safety following ingestion. This included a gelling agent, purgative and an increased level of emetic. Disappointingly, two major studies to evaluate the performance in Sri Lanka which were published in 2008 and 2011, demonstrated that the new formulation did not meet expected levels of human safety benefit when it came to elimination of accidental fatalities, or reduction of deaths from intentional self-harm. In the absence of its ability to meet these goals, and lack of support for the formulation from regulators, the product was considered not viable and was withdrawn.

Since the 1980's there has been continued debate about the benefit of the use of emetics in the treatment of chemical poisoning. Concerns revolve around three areas:

1. Continued vomiting from emetics prevents the administration of activated charcoal. For substances that are bound to activated charcoal, its use is superior to emesis. Paraquat is adsorbed by and binds to activated charcoal.
2. Inducing emesis following the ingestion of a corrosive, such as paraquat, re-exposes the oesophagus to the chemical.
3. Poisoned patients may have a decreased level of consciousness. Emesis in these patients may cause aspiration and pulmonary injury.

Inclusion of the emetic remains mandatory (FAO Specification), however any further increases in the level of emetic could increase the risk of oesophageal or pulmonary injury, and the inability to administer activated charcoal.

A recent review of the pre-clinical and clinical data on PP796 by Dr. Jeff Brent, a medical toxicologist from the University of Colorado, suggests that there is no added clinical benefit from increasing the emetic level above that which Syngenta uses in its formulations. He also stated that increasing the emetic dose in paraquat formulations would require validation in a human clinical trial, and that currently there is insufficient data to justify that such a trial be undertaken.

In setting emetic levels, Syngenta's guiding principle has been to take the appropriate clinical medical judgements and decisions, based on all the available information. The only motivation Syngenta and its predecessors have had is to find the most appropriate level of emetic to best address the ingestion risk. Syngenta's primary focus is always to develop and steward products which are the most safe and effective. To that end, Syngenta has, over the lifetime of the existence of paraquat, invested hundreds of millions of dollars in developing and commercializing ever safer formulations and delivery systems.

For more information, please contact **media.relations@syngenta.com**.

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