

# PRODUCT ADVISORY STATEMENT (PAS180328)

## GASTRO-INTESTINAL ADVERSE EVENTS

**OVERVIEW:** Very occasionally, adverse effects have been reported after ingestion of either fresh broccoli sprouts or supplements manufactured from fresh sprouts. These effects are typically gastro-intestinal in nature and include nausea, gastro-abdominal discomfort and diarrhoea.

The limited data available seem to indicate that such effects are generally limited to those with pre-existing gastro-intestinal conditions and in particular in those with dysbiosis.

It has been observed, however, that for those so affected, the dose can be managed in a manner whereby the symptoms disappear and may not recur even after the consumption of larger doses.

The information which follows is applicable to the following products:

### CELL-LOGIC range

- EnduraCell powder
- PomGenex
- EnduraCell BioActive capsules
- EnduraCell PLUS
- DefenCell
- CardiOS

### INTEGRA NUTRITIONALS range

- Geneactiv GFE
- Geneactiv GFP
- Geneactiv GFD
- Geneactiv GFC

## BACKGROUND TO PRODUCT MECHANISMS

**Cellular Defences:** The bioactive compound yielded in varying amounts by each of these products is Sulforaphane (SFN). The most-studied mechanism associated with SFN is its role in upregulating the defensive processes intrinsic to human cells. In this capacity, SFN is known to be the most potent naturally-occurring molecule.<sup>2</sup>

**Antibacterial:** In addition to this role, SFN is also known to exhibit antimicrobial effects on pathogens resident in the gastro-intestinal lumen. Several clinical trials have confirmed its effects on inhibiting the carcinogenic bacterium, *Helicobacter pylori*. Subsequent studies show its significant effect on inhibiting 48 strains of *H.pylori*. It has been shown to be equally effective against strains resistant to two antibiotics commonly used to treat human *H. pylori* infections.<sup>3-6</sup>

In its inhibitory effect on *H.pylori*, SFN has been shown to block the ability of *H.pylori* to produce *urease*, the enzyme responsible for the development of the gastric inflammation which leads to more insidious effects with time.

**Immune-enhancing:** Furthermore, SFN stimulates the gut epithelial cells to produce *beta-defensin*, an anti-bacterial compound that cells release to defend themselves against pathogens.<sup>7</sup> This specific immune-enhancing effect of SFN is supported by other beneficial effects on cellular defences in general and specifically in this case, on intestinal epithelial cells and their beneficial relationship with the gut microflora.

## CLINICAL RELEVANCE

**Intestinal Dysbiosis:** Intestinal dysbiosis is a condition defined by an imbalance between the desirable commensal organisms that inhabit the gut lumen and the undesirable species that may also reside there and which may be potentially pathogenic.

In individuals with either known or unknown dysbiosis, SFN may destroy pathogens or otherwise undesirable organisms. If the effect is significant, the resultant die-off effect is likely to increase the quantity of microbial degradation products in the gut lumen. Those products that are unable to be adequately detoxified by the intestinal epithelial cells will be carried by the portal circulation to the liver for its more intensive detoxification.<sup>8</sup> If the quantity of microbial degradation products being produced exceeds the body's ability to detoxify them, the individual may experience adverse symptoms; such symptoms may include gastro-abdominal discomfort, diarrhoea and nausea.

**Biofilm degradation:** *In vitro* studies have shown that SFN can degrade periodontal biofilms that typically prevent the resolution of infections.<sup>9</sup> In so doing, SFN exposes the microbes to attack by elements of both the innate and adaptive immune system. Mucosal biofilm communities are also known to inhabit the human intestinal tract, such that there is the potential for SFN to disrupt biofilms here and in so doing, release a significant population of microbes into the intestinal mucosa, thereby upregulating and potentially overloading detoxification pathways.<sup>7,10</sup> Such responses can be responsible for the unpleasant gut symptoms described above.

## THEORETICAL INTERPRETATION

Of the few reports we have received of adverse effects, seemingly following the ingestion of a SFN-yielding supplement, it is apparent that very few patients do experience these effects. The limited data available would seem to indicate that the patients most likely to be affected already have a gastro-intestinal condition, possibly dysbiosis.

It has also been observed that when those so affected are advised in the manner described below, the symptoms disappear and do not return, even after returning to the dose that initially appeared to trigger the adverse effects. This response would indicate that in susceptible individuals, a lower dose of SFN is more appropriate in the short term, with the intent to slow down the anti-microbial and detoxification processes.

## HOW TO ADDRESS THESE EFFECTS

Our experience indicates that the following approach provides a satisfactory resolution to the issue:

- Discontinue the source of the SFN.
- Assuming that this resolves the symptoms, resume the product at a much smaller dose. This dose may be as little as will fit on the tip of a sharp vegetable knife blade.
- Take one such dose daily for a few days to ensure that the gastrointestinal area remains comfortable.
- Gradually increase the dose by taking a second similar dose per day.
- Repeat the process by increasing a little each day, monitoring symptoms to determine daily dose.
- Typically, within 2 weeks, the standard recommended dose can be taken without ill effect.
- Those with known dysbiosis or other gastrointestinal symptoms will typically find that these symptoms have either partially or fully cleared.

## SPECIAL NOTE

**Safety:** SFN has been tested and found to be safe for doses higher than it is practical for humans to consume.<sup>11</sup> Its dose-response is linear at levels typical of oral ingestion by humans, so that the higher doses will exhibit more significant effects.

The **Sulforaphane Yield** per capsule of each product is:

EnduraCell powder	~ 20 mg per gram	DefenCell	~ 5 mg per capsule
EnduraCell BioActive	~ 16 mg per capsule	CardiOS	~ 2 mg per capsule
EnduraCell PLUS	~ 16 mg per capsule	PomGenex	~ 20 mg per scoop

## REFERENCES

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