dsm-firmenich

DSM Nutritional Products LLC
45 Waterview Boulevard
Parsippany, NJ 07054-1298, USA
+1 201.400.9376
Carl.d-ruiz@dsm-firmenich.com

4 September 2025

CDR Trang Tran, PharmD, MBA, BCPS, Senior Regulatory Project Manager
Shannon Liu, DPT, Regulatory Project Manager
Division of Regulatory Operations for Nonprescription Drugs I
Office of Regulatory Operations
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993

Subject: **MGF 400105 – Response to IR #21 [3929]**

Dear Trang and Shannon,

We acknowledge receipt of FDA's Information Request (IR) letter dated August 25, 2025, and appreciate the continued review of our submission, including our August 21, 2025, response to IR #20 issued on August 14, 2025. That response included a global market survey of products containing bemotrizinol (BEMT) in combination with skin protectant active ingredients.

As a follow-up, FDA has requested an analysis of adverse events associated with these products to further support the inclusion of sunscreen-skin protectant combinations containing BEMT.

The requested information is provided below and submitted by the extended due date of September 4, 2025.

Further reference is also made to our submissions received on September 23, 27, and 30, 2024, in support of a Tier 1 Over-the-Counter (OTC) Monograph Order Request (OMOR) for a Generally Recognized as Safe and Effective (GRASE) determination for BEMT 6% as a new sunscreen active ingredient under FDA's OTC Monograph M020: Sunscreen Drug Products for OTC Human Use.

Bemotrizinol (BEMT)

DSM Response:

As detailed in our responses to IR #5 (2828) dated November 12, 2024, and IR #12 (3297) dated January 31, 2025, our review of TGA's Adverse Event Notifications (2020–2023), along with other public surveillance databases and literature sources, found no confirmed causal links to BEMT across sunscreen and skin protectant products.

Below is a further summary of currently available surveillance data and safety findings related to bemotrizinol (BEMT) from countries where it is approved, based on regulatory databases and public literature sources.

1. **Canada – Health Canada (Canada Vigilance Adverse Reaction Database)**

Health Canada maintains the Canada Vigilance Adverse Reaction Online Database, which includes reports of suspected adverse reactions to health products, including sunscreens. As of April 2025, there are no confirmed causal links between BEMT and serious adverse events reported in this database. While adverse reaction reports are collected from consumers, healthcare professionals, and manufacturers, the data do not indicate any specific safety concerns associated with BEMT-containing products. Adverse Reaction Database - Canada.ca

2. **Australia - TGA (Database of Adverse Event Notifications - DAEN)**

Australia's Therapeutic Goods Administration (TGA) operates the DAEN, which tracks adverse events related to medicines and medical devices. As highlighted in detail in our responses to IR #5 (2828) dated November 12, 2024 and IR#12 (3297) dated January 31, 2025, our review of TGA's Adverse Event Notifications (2020–2023) found no confirmed causal links to BEMT across 36 sunscreen and skin protectant products. The TGA uses this data to monitor unusual patterns, and BEMT has not triggered any safety alerts or regulatory actions. Database of Adverse Event Notifications (DAEN) | Therapeutic Goods Administration (TGA)

In our response to IR#20, we provided a market survey of products containing BEMT and the skin protectant active ingredients we support. We understand the IR# 21 question regards the combination of BEMT with other sunscreen protectant combinations and the adverse events associated with these combinations. To address this request, we have reviewed the TGA DAEN product case reports listed in IR#12, Attachment 2, submitted on January 31, 2025. The file, titled "Attach 2_DAEN Product Case Reports w MedDRA Reaction Terms_30-Jan-2025_025526," summarizes adverse reactions reported for sunscreen–skin protectant products containing BEMT and other active skin protectant substances sold in Australia.

Bemotrizinol (BEMT)

The reported adverse reactions and the associated sunscreen products' ingredients were copied into ChatGPT 4 on 3 and 4 September 2025, at chatgpt.com. The results were collected in a response document (https://chatgpt.com/c/68b86c64-1768-8322-af76-b0c4b595dbcc) and selected output is presented in this response document.

The adverse events listed in IR#12, Attachment 2 are associated with products containing 18 unique combinations of UV filters, summarized as follows.

Set ID	And UV Filter Ingredients
1.	**4-methylbenzylidene camphor; bemotrizinol; butyl methoxydibenzoylmethane; octocrylene** (common in many Banana Boat products, also Cancer Council Active Dry Touch, etc.)
2.	**bemotrizinol; butyl methoxydibenzoylmethane; octocrylene; octyl methoxycinnamate; phenylbenzimidazole sulfonic acid** (all the "Ultra UV Protective Daily Moisturiser" / "Ultimate UV" range)
3.	**bemotrizinol; butyl methoxydibenzoylmethane; ethylhexyl triazone; homosalate; octocrylene; octyl salicylate** (Banana Boat Sport, Dry Balance)
4.	**bemotrizinol; butyl methoxydibenzoylmethane; homosalate; octocrylene; octyl salicylate** (Nivea Protect & Moisture, Nivea Ultra Sport, Nivea Ultra Beach)
5.	**bemotrizinol; butyl methoxydibenzoylmethane; drometrizole trisiloxane; ecamsule; ethylhexyl triazone; octocrylene; titanium dioxide** (La Roche-Posay Anthelios XL Tinted Fluid)
6.	**bemotrizinol; butyl methoxydibenzoylmethane; diethylamino hydroxybenzoyl hexyl benzoate; octocrylene; octyl methoxycinnamate; octyl salicylate** (SunActive SPF 50+ Face Cream)
7.	**bemotrizinol; butyl methoxydibenzoylmethane; homosalate; methylene bis-benzotriazolyl tetramethylbutylphenol; octocrylene; octyl salicylate; titanium dioxide; zinc oxide** (B3-T Superfluid Sunscreen)
8.	**bemotrizinol; diethylamino hydroxybenzoyl hexyl benzoate; octyl methoxycinnamate** (Ego Sunsense Anti-Ageing Face)
9.	**4-methylbenzylidene camphor; bemotrizinol; methylene bis-benzotriazolyl tetramethylbutylphenol; zinc oxide** (Nivea Kids Roll-On, Cancer Council Kids)

Bemotrizinol (BEMT)

10. **bemotrizinol; butyl methoxydibenzoylmethane; ethylhexyl triazone; homosalate; octyl salicylate; phenylbenzimidazole sulfonic acid**
    (DermaVeen Ultra Light Day Lotion)
11. **bemotrizinol; butyl methoxydibenzoylmethane; diethylamino hydroxybenzoyl hexyl benzoate; octocrylene; octyl methoxycinnamate; titanium dioxide**
    (Sunsense Performance SPF50+)
12. **bemotrizinol; butyl methoxydibenzoylmethane; drometrizole trisiloxane; ecamsule; ethylhexyl triazone; homosalate; octocrylene; octyl salicylate; titanium dioxide**
    (La Roche-Posay Anthelios XL Dry Touch Gel-Cream)
13. **butyl methoxydibenzoylmethane; homosalate; octocrylene; octyl salicylate; oxybenzone**
    (Neutrogena Ultra Sheer Body Mist SPF30)
14. **bemotrizinol; butyl methoxydibenzoylmethane; ethylhexyl triazone; homosalate; octocrylene**
    (Neutrogena Ultra Sheer Body Mist Spray – other variant)
15. **bemotrizinol; drometrizole trisiloxane; ecamsule; ethylhexyl triazone; octyl salicylate**
    (La Roche-Posay Anthelios Ultra Comfort Non-Perfumed Cream)
16. **bemotrizinol; butyl methoxydibenzoylmethane; drometrizole trisiloxane; ecamsule; ethylhexyl triazone; octyl salicylate**
    (La Roche-Posay Anthelios Ultra Tinted BB Cream)
17. **bemotrizinol; butyl methoxydibenzoylmethane; drometrizole trisiloxane; ethylhexyl triazone; homosalate; octyl salicylate**
    (La Roche-Posay Anthelios XL Wet Skin Kids Gel Cream)
18. **bemotrizinol; diethylamino hydroxybenzoyl hexyl benzoate; octyl methoxycinnamate; octyl salicylate; titanium dioxide**
    (Sunsense Junior)

Summary of Adverse Event Data (IR#12, Attachment 2)

- **Total Unique Ingredient Sets:** 18
- **Total Product Entries Reported:** 65

Distribution Overview:

- **Set 1 – Banana Boat family:** 22 products
- **Set 2 – Ultra UV Protective Daily Moisturizers:** 12 products
- **Set 4 – Nivea Protect & Moisture / Ultra ranges:** 11 products
- **All Other Sets:** Appear only 1–3 times each

Notable Brand-Specific Complexity:

- **La Roche-Posay:** Uses multiple distinct and complex ingredient sets (Sets 5, 12, 15, 16, and 17)

Summary of Adverse Reactions:

The table below summarizes the approximately 100 MedDRA adverse reaction terms found, grouped into six categories.

Skin Reactions	Eye Reactions	Systemic / General Symptoms	Product-Related Issues	Ineffectiveness / Sunburn	Other / Rare Events
Rash	Eye pain	Headache	General complaint	Sunburn	Renal failure
Erythema	Eye swelling	Nausea	Quality issue	Therapeutic product ineffective	Anuria
Blister	Eye pruritus	Asthenia	Physical consistency issue	Drug ineffective	Skin cancer
Dermatitis (incl. allergic/contact)	Eyelid infection	Feeling abnormal	Container issue	Condition aggravated	Concomitant disease aggravated
Urticaria	Periorbital swelling	Pain	Expiration issue		
Rosacea		Facial/peripheral swelling	Recalled product		
Acne		Paraesthesia			
Pruritus					
Burning sensation					
Exfoliation					
Lesion					

Bemotrizinol (BEMT)

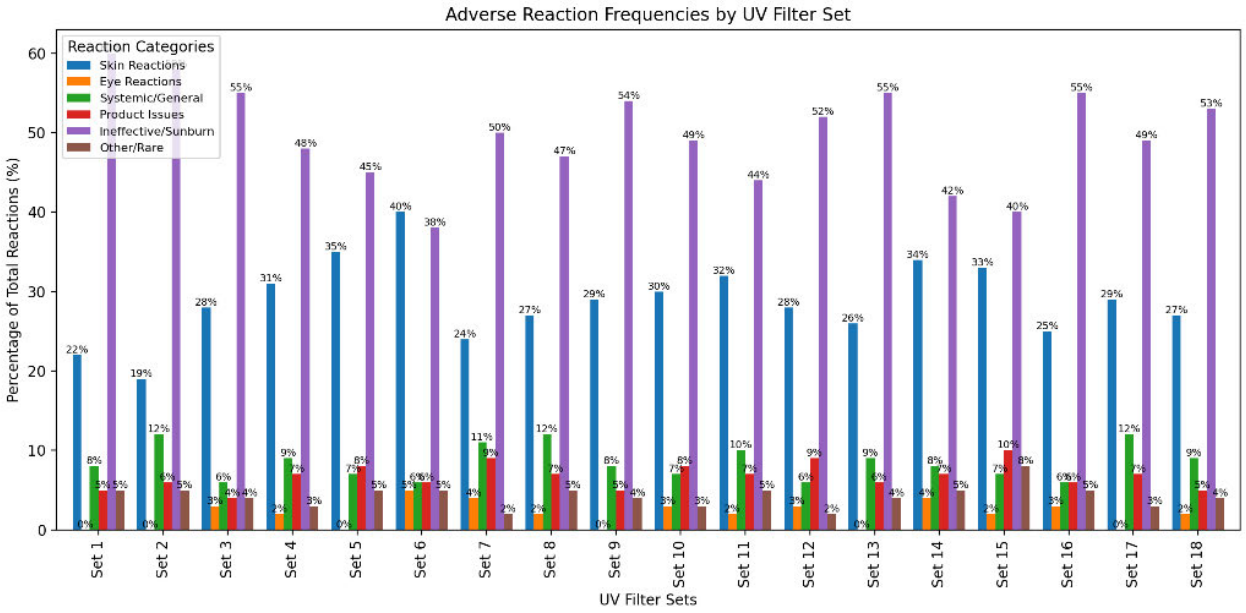
Skin Reactions	Eye Reactions	Systemic / General Symptoms	Product-Related Issues	Ineffectiveness / Sunburn	Other / Rare Events
Burns (chemical, thermal, third-degree)					
Application site irritation/hypersensitivity					

The table below summarizes observed patterns in adverse reactions by category and UV filter set:

Category	Typical Frequency	Notable Sets / Observations
Ineffectiveness / Sunburn	40–60%	Dominant across all 18 sets
Skin Reactions	20–35%	Higher in Set 5 and Set 6 (up to 35–40%)
Eye Reactions	0–5%	Notable in Set 6 and Set 7
Product Issues	5–10%	Present in every set
Systemic / General Reactions	6–12%	Stable across sets
Other / Rare Events	<8%	Infrequent, serious events

The distribution of these adverse reactions by the UV filter Sets are shown in the figure below.

Bemotrizinol (BEMT)



Notably, sunburn and product ineffectiveness were the most frequently reported adverse reactions across the various UV filter combinations, accounting for approximately 40–60% of reports across all sets. Skin reactions—such as rash, erythema, blister, dermatitis, urticaria, rosacea, acne, pruritus, burning sensation, exfoliation, and others—were the second most common, occurring in 20–40% of the sets.

Conclusion:

An analysis of all skin protectant combinations in commercial sunscreen products found in Australia indicates that no specific adverse reaction can be linked to any individual UV filter, including BEMT or the combinations reported.

3. European Union

Adverse events must be reported under the Cosmetovigilance Serious Undesirable Effects (SUE) reporting system, as mandated by EU Regulation 1223/2009 on cosmetic products. This regulation defines undesirable effects as adverse reactions attributable to the normal or reasonably foreseeable use of a cosmetic product, and serious undesirable effects as those resulting in outcomes such as hospitalization, disability, or death. However, the SUE system is not publicly searchable by ingredient, and there is no publicly available evidence of serious undesirable effects associated with BEMT-containing products in the EU. This supports BEMT's continued use in sunscreen and skin protectant formulations under EU regulatory oversight.

4. Saudi Arabia – SFDA Surveillance and Regulatory Status of BEMT

Bemotrizinol (BEMT) is permitted for use in cosmetic products in Saudi Arabia under the regulations of the Saudi Food and Drug Authority (SFDA). All cosmetic products, including sunscreens containing BEMT, must be registered in the GHAD system prior to marketing, ensuring compliance with safety and quality standards (source: Cosmetics legislation and product registration in Saudi Arabia - CE.way.

The Saudi Vigilance System serves as SFDA's electronic post-market surveillance platform for reporting adverse events and product defects. Adverse events must be reported within defined timeframes:

- Within 2 days for severe public health threats
- Within 10 days for serious injury or death
- Within 30 days for other incidents

Reports must include investigation findings, technical documentation, and any safety corrective actions taken (source: Reporting Medical Device Incidents & Adverse Events to SFDA - PharmaKnowl). Although SFDA does not publicly release ingredient-specific adverse event summaries, there are currently no known safety alerts or recalls associated with BEMT-containing sunscreen products in Saudi Arabia.

5. Public Literature

A recent study evaluating sunscreen safety reported a few adverse effects, all of which were mild[1]. No serious adverse events (SAEs) were associated with BEMT use. This aligns with findings from other global pharmacovigilance systems, including the TGA (Australia) and EU Cosmetovigilance, which have not reported any confirmed SAEs linked to BEMT-containing products.

Safety Summary for Bemotrizinol (BEMT)

A comprehensive review of global pharmacovigilance systems - including those maintained by the EMA, Health Canada, TGA, SFDA, and EU Cosmetovigilance - along with clinical pharmacokinetic and safety studies, indicates that bemotrizinol (BEMT) is not associated with any serious adverse events (SAEs) when used in sunscreen and SPF skin protectant products.

---

[1] Turner CW, Torgerson L. Modernizing U.S. Sunscreen Regulations: How Newer Filters Can Improve Public Health. Photodermatol Photoimmunol Photomed. 2025 Sep;41(5):e70032. doi: 10.1111/phpp.70032. PMID: 40778531; PMCID: PMC12332967.

Bemotrizinol (BEMT)

BEMT exhibits low systemic absorption, no endocrine-disrupting activity, and minimal potential for dermal irritation or sensitization, supporting its safety for long-term topical use. These findings support the inclusion of BEMT in FDA-regulated skin protectant products that make SPF or sunscreen claims, in alignment with the safety standards outlined in the OTC Skin Protectant Monograph.

This response is being submitted electronically under Module 1 via FDA's NextGen portal.

Please contact me if there are any further questions.

Sincerely,

Carl D'Ruiz, MPH.
Senior NA Science, Advocacy and Business Development Manager, Beauty & Care