

Summary Safety Review - Clobazam-containing products - Assessing the Potential Risk of Drug Reaction with Eosinophilia and Systemic Symptoms

Product: Clobazam-containing products

Potential Safety Issue: Drug reaction with eosinophilia and systemic symptoms (DRESS), a serious, potentially life-threatening drug reaction that includes fever, rash, high white blood cell count, and affects one or more organs

Key Messages

- **Clobazam is authorized for sale in Canada as an add-on therapy in patients whose epilepsy is not well controlled on their current antiepileptic drugs.**
- **Health Canada reviewed the potential risk of DRESS with clobazam use after becoming aware of international case reports published in medical literature.**
- **Health Canada's review concluded that there may be a link between the use of clobazam and the potential risk of DRESS.**
- **Health Canada will work with the manufacturers to update the Canadian product safety information for clobazam-containing products to include the risk of DRESS.**

Overview

Health Canada reviewed the potential risk of drug reaction with eosinophilia and systemic symptoms (DRESS) with clobazam use after becoming aware of international case reports published in the medical literature.

DRESS is a rare, but serious, and potentially life-threatening drug reaction that includes fever, severe skin rash or peeling of the skin over large areas of the body, swollen face and high white blood cell count, affecting 1 or more organs. The symptoms of DRESS typically appear within 2 weeks to 2 months after starting a medication.

DRESS is also known as Drug Rash with Eosinophilia and Systemic Symptoms, Drug Induced Hypersensitivity Syndrome or DRESS syndrome.

Use in Canada

- Clobazam is a prescription drug authorized in Canada as add-on therapy in patients whose epilepsy is not well controlled on their current antiepileptic drugs.
- Clobazam has been marketed in Canada since 1991. It is currently available as 10 mg clobazam tablets.
- There were about 444,000 prescriptions filled for clobazam in 2019, 10% of which were for children.

Safety Review Findings

- Health Canada reviewed information provided by the manufacturers, data from clinical studies, information resulting from searches of the Canada Vigilance database^a, and the published literature.
- Health Canada's review focused on 2 Canadian cases and 18 international cases of DRESS in patients taking clobazam. From those cases, only 4 (international) met the criteria for further assessment to determine if there was a link between the use of clobazam and DRESS. Three of them were published in the medical literature and involved children.
- In all 4 cases, a link between clobazam use and DRESS could not be ruled out. Two cases were found to be probably linked to the use of clobazam. The 2 other cases were found to be possibly linked to clobazam use, however, these patients were also taking other medications that have been known to cause DRESS.
- There are no confirmed cases of DRESS in Canada associated with the use of Clobazam.

Conclusions and Actions

- Health Canada's review of the available information concluded that there may be a link between the use of clobazam and the potential risk of DRESS.
- Health Canada will work with the manufacturers to update the Canadian product safety information for clobazam-containing products to include the risk of DRESS.
- Health Canada encourages consumers and healthcare professionals to [report](#) any side effects related to the use of clobazam and other health products to the [Canada Vigilance Program](#).
- Health Canada will continue to monitor safety information involving clobazam-containing products, as it does for all health products on the Canadian market, to identify and assess potential harms. Health Canada will take appropriate and timely action should new health risks be identified.

Additional Information

The analysis that contributed to this safety review included scientific and medical literature, Canadian and international information and what is known about the use of clobazam both in Canada and internationally.

For additional information, [contact the Marketed Health Products Directorate](#).

References

1. Kardaun S.H. Sekula P. Valeyrie-Allanore L. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): An Original Multisystem Adverse Drug Reaction. Results from the Prospective RegiSCAR Study. *British Journal of Dermatology*. 2013; 169:1071-1080
 2. Manyas et al., 2020, Let A Drug Reaction With Eosinophilia and Systemic Symptoms Syndrome Associated With Clobazam, *Pediatric Emergency Care*:Volume 36, Number 3, March 2020, e75
 3. Marzec S, Solomon J, Nguyen N, Rajbhandari P. Red as a beet but not quite so sweet. *Hospital Medicine*. 2018 Apr 8-11; Orlando, Fla. Abstract 406
 4. Razanapinaritra et al., 2019. DRESS syndrome induced by clobazam in a child: A new case. *Revue française d'allergologie* 59 (2019) 346-9.
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a) Canadian reports can be accessed through the [Canada Vigilance Online Database](#).