
## IN THIS ISSUE



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## EPVC Mission

**Pharmaceutical Vigilance administration is the way through which the processes for authorizing, regulating, monitoring and evaluating the safety of any pharmaceutical product or medical device take place, in addition to disseminating any safety information for public health programs, healthcare professionals, and the Egyptian citizen.**

**The Pharmaceutical vigilance administration is an integral part of the Central Administration of Pharmaceutical Care that works on the enhancement of the pharmaceutical services to guarantee safe and effective use of medications in Egypt, under the patronage of the Egyptian Drug Authority.**

# Newsletter

# February 2024

**Volume 15** **Issue 2**

# Safety Notification ! Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE)

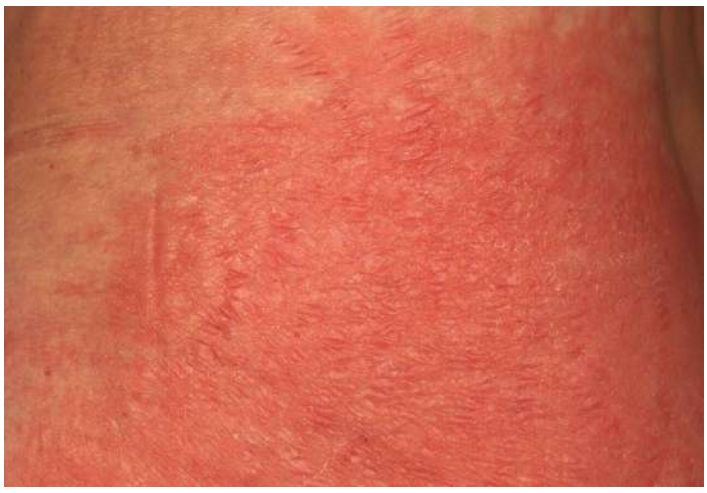
The Regulatory Authority in New Zealand has published the following safety notification:

## Key messages

- Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is a drug induced erythematous (red) rash involving the skin folds.
- Many medicines may cause SDRIFE, with beta-lactam antibiotics being the most commonly reported.
- SDRIFE is self-limiting and should resolve when the suspect medicine is withdrawn.

## What is SDRIFE?

Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is a druginduced rash involving the skin folds. SDRIFE presents as a well-defined symmetrical V-shaped erythematous (red) rash of the gluteal region or groin, hence its original name of 'baboon syndrome'. There is often involvement of at least one other skin fold or flexural area, such as the armpit and behind the knees. The lack of systemic symptoms is a key characteristic of SDRIFE. Aside from the rash, the person is generally well with no other symptoms.



## Which medicines are associated with SDRIFE?

SDRIFE is a type IV delayed hypersensitivity reaction to a systemic medicine, appearing a few hours to a few days after medicine exposure. The most common medicines associated with SDRIFE are beta-lactam antibiotics (e.g., penicillin, cephalosporins), which are implicated in about 50 percent of SDRIFE cases. There are many other medicines associated with SDRIFE, including non-beta-lactam antibiotics, analgesics, antifungals and iodine-containing contrast agents.

## How is SDRIFE treated?

SDRIFE is self-limiting and should resolve when the suspect medicine is withdrawn. Re-exposure to the suspect medicine usually causes SDRIFE to recur. Topical steroids may help to resolve the rash more quickly.

***References:***

***MedSafe :*** *(Click Here)*

## Safety Notification ! : Precautions for all Hemodialysis and hemofiltration machines

The medical authority in UK had issued a device Safety information entitled "Haemodialysis and hemofiltration machines: Actions to take following pressure-related alarms to avoid unintentional alteration of alarm limits".

**Background**:

All Haemodialysis and haemofiltration machines have the potential to incorrectly change venous and arterial pressure limitations after acknowledging an alert. The machine might not sound another alarm to notify the user of a persistent issue if the cause of the first alarm is not fixed.

**Safety issue:**

The MHRA is aware of venous and arterial line disconnections causing excessive blood loss. All haemodialysis machines alarm when pressure falls below set limits. Some machines automatically re-center alarm limits around current pressure, leading to dangerous situations. The MHRA is aware of serious events, including fatal ones, where lower pressure limits were too low. Consideration should also be given to the potential for misreading the alarm type. High venous pressure alarms occur very frequently, for example due to patient movement, and may be dismissed as nuisance alarms. It is therefore possible that a low venous pressure alarm may be misinterpreted as a high venous pressure alarm and silenced without resolving the underlying problem.

**Actions:**

• Review the alarm section in the instructions for use of machines used in your facility.

• Identify how your machines react to user input following an alarm and share this information with all staff involved in acting on alarms.

• If the guidance in the instructions for use is not clear, contact the manufacturer for clarification.

• If a pressure related alarm is activated

o check the condition of the patient

o identify whether a high or low- pressure event has occurred

o check the integrity of the blood lines

- if high pressure, check for kinks and clots in the line
- if low pressure, check for loose connections, disconnections, leaks or needle dislodgement
- If the lines are covered by clothes, blankets or similar, lift these to ensure that a problem is not missed.

o Once the cause of the alarm is resolved, restart the therapy, and once the pumps are running again, verify that the updated pressure reading is acceptable. Do not continue the treatment if the pressure reading is lower than expected, as this may indicate that the blood leak is still present.

o Be aware that in some machines the alarm limits may re-centre around the current venous or arterial pressure when therapy is restarted. If the cause of the problem is not resolved, the venous pressure remains low and the new alarm limits may not be appropriate. In this case, the alarm will not reactivate if the problem remains until the venous or arterial pressure drops to the new low level.

o the lower venous or arterial pressure alarm limit should not be below levels which would detect blood loss as this effectively disables the alarm.

## Safety Notification ! : Precautions for all Hemodialysis and hemofiltration machines

• Be aware of user desensitization due to frequent alarms and do not repeatedly cancel or reset alarms without identifying and resolving the cause. Always respond to and act on pressure related alarms while protecting the patient as per local clinical protocol and clinical competencies.
• Risk assess your patients for secure fixing of needles and bloodlines. Unit dialysis patients should have their circuit visible during the whole dialysis process. Where this could conflict with maintaining patient dignity, such as patients with femoral lines, a risk assessment should be carried out and all mitigations recorded and enacted. Be aware that sleeping, agitated or confused patients and patients in side rooms or in difficult to observe areas may be more at risk.
• Only staff whose training and competence with the equipment (inclusive of correct management of alarms) has been established and recorded should be permitted to carry out treatment. They should receive education and continued support with regular reassessment of clinical competencies.
• Contact patients using these devices at home to ensure these patients understand the steps to take in response to an alarm and provide refresher training where necessary within the shortest possible timeframe.
• It is also recommended that all existing in-unit patients should be reminded not to silence alarms.

**EDA Recommendations:**

* EDA aware Health care professionals to follow the MHRA Actions listed above
* Report any Incident occurred from this device or any medical device

***References:***

***MHRA:*** *(Click Here)*

# Four Cases of Keratitis and Corneal Melt Associated with Local Anaesthetic Eye Drops Use

The Regional Center in Sohag received four reports regarding four male patients who had been using Oxybuprocaine hydrochloride (Benoxinate hydrochloride) ophthalmic solution without a prescription – as a self-medication- for an extended period ranging from 8 to 25 years. They were using it to alleviate eye discomfort caused by exposure to metal foreign bodies, which was due to their occupations as blacksmiths and welders.

One patient, using the drops since 2013, experienced severe eye pain, pressure, redness, and blurred vision. Despite hospital admission and treatment with various eye drops and ointments, his right eye still lacks vision till the moment. Another patient, using the drops for 25 years, faced eye irritation, pain, and frequent hospitalizations due to excessive usage. A third patient, with blurred vision, was diagnosed with bilateral corneal ulcers. The fourth patient experienced severe eye irritation and bilateral corneal ulcer, his right eye improved, but the left one is still recovering. Unfortunately, none of the patients have fully recovered.

After being admitted to the hospital, all four cases were diagnosed as keratitis complicated with corneal melt, they were cultured and found to be infected with secondary bacterial infections.

These cases were extremely serious, resulting in prolonged hospitalization and no other medications were used concurrently.

## Background:

**Keratitis** is the inflammation of the cornea and is characterized by corneal edema, infiltration of inflammatory cells, and ciliary congestion. It is associated with both infectious and non-infectious diseases, which may be systemic or localized to the ocular surface, noninfectious keratitis can be caused by a relatively minor injury, such as from wearing your contact lenses too long or getting a foreign body in the eye while Infectious keratitis can be caused by bacteria, viruses, fungi and parasites. With prompt attention, mild to moderate cases of keratitis can usually be effectively treated without loss of vision. If left untreated, or if an infection is severe, keratitis can lead to serious complications that may permanently damage your vision. (1,2)

**Corneal melt,** also referred to as corneal melting, is a condition characterized by the loss of the corneal epithelium and the thinning of the corneal stroma. It is associated with various factors, including infections, sterile inflammation, and damage to the cornea due to surgery or exposure to chemicals. Collectively, these factors represent a significant cause of blindness. Corneal melt often serves as an early stage in the development of corneal perforation, a severe eye condition. The significance of corneal melt lies in its clinical consequences, which include eye-related health issues such as vision loss given the limited availability of effective treatments as current treatment options are either insufficiently potent or act too slowly to prevent corneal perforation. (3)

**Oxybuprocaine hydrochloride:** Oxybuprocaine (also known as Benoxinate) is a local anesthetic, which is used especially in ophthalmology and otolaryngology. Oxybuprocaine binds to sodium channels and reversibly stabilizes the neuronal membrane which decreases its permeability to sodium ions. (4)

Corneal stroma: A dense connective tissue of remarkable regularity. It makes up the vast majority of the cornea, and plays a pivotal role in normal visual function. Anatomically, it is located between the outer epithelium and the inner endothelium and is the thickest layer of the cornea. Keratocytes in the stroma produce a variety of cellular products, including growth factors/cytokines, extracellular matrix (ECM) components, and kinases. These products support normal corneal development and homeostasis. (5,6)

# " Four Cases of Keratitis and Corneal Melt Associated with Local Anaesthetic Eye Drops Use

**Labeled information: (7)**

According to Oxybuprocaine hydrochloride SPC, it is stated under section 4.1(Therapeutic indications) that" Oxybuprocaine is used as a topical ocular anaesthetic.

It is stated under section 4.1 (Special warnings and precautions for use) that "The cornea may be damaged by prolonged application of anaesthetic eye drops."

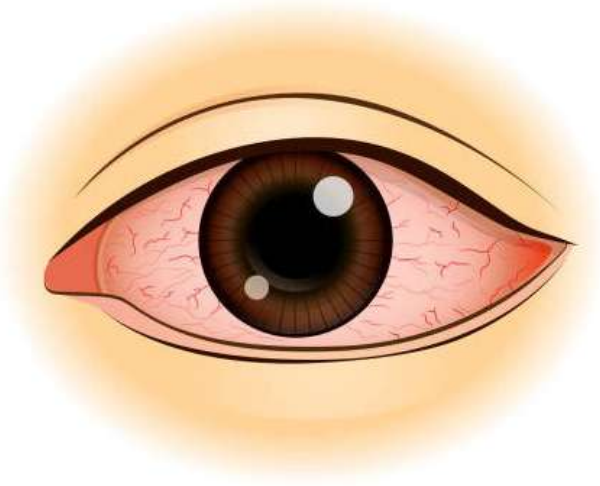
It is stated under section 4.8(Undesirable effects) that "In very rare cases, uncontrolled use, i.e. long-term and/or too frequent use, may result in keratopathy, hypopyon, or central corneal erosion including central scarring. Corneal perforation may also be possible.

Eye disorders : unknown frequency: Eye pain, eye irritation, blurred vision, keratopathy, hypopyon, corneal erosion, corneal perforation, eye allergy and allergic blepharitis."

**Literature information:(8)**

Topical ocular local anesthetics typically do not cause significant eye-related side effects when applied topically for short durations. However, their prolonged use can lead to severe and potentially permanent damage to the cornea, resulting in vision impairment. Local anesthetics function by slowing down the migration of corneal epithelial cells, disrupting certain cellular structures, and damaging the surface microvilli of the cornea. This disruption can result in lasting epithelial defects and the breakdown of the corneal tear film with continued use of the drugs.

Long-term use of local anesthetics can deprive the corneal epithelium, possibly leading to the formation of dense yellow-white rings within the corneal stroma. These rings may appear as early as 6 days or as late as 60 days after initial use. Fortunately, these corneal rings usually resolve once the local anaesthetic is discontinued. Studies have shown that local anesthetics can directly harm stromal keratocytes, and secondary infections are common consequences of the local anaesthetic chronic use. In some cases, topical chronic use of local anesthetics has led to conditions like Candida keratitis and infectious crystalline keratopathy.



Furthermore, prolonged use of these anesthetics can cause irreversible damage to endothelial cells, resulting in a loss of one-third to two-thirds of endothelial cells in the cornea. Various forms of uveitis – middle layer of the eye inflammation- have been reported. There have even been cases of ocular perforation requiring enucleation following their chronic use.

Topical ocular anesthetics can enhance the mydriatic (pupil-dilating) effects of mydriatic drugs. Additionally, oxybuprocaine has been shown to significantly increase corneal thickness in females but not in males

## " Four Cases of Keratitis and Corneal Melt Associated with Local Anaesthetic Eye Drops Use

**Recommendations to healthcare professionals: (9)**

EPVC Decided to disseminate the following educational material to healthcare professionals in order to address the problem for safer use of Benoxinate hydrochloride ophthalmic solution.

**Physicians shall:**

- Balance prescribing for specific diagnoses in addition to careful clinical monitoring of the effects of treatment to minimize the risks.
- keep patients aware of Benoxinate containing eye drops misuse dangers.
- Conduct a thorough history and physical condition of the patient.
- Educate the patient (especially solderer and blacksmith patients ) about the medication; explain the details of the treatment in lay terms or in terms that are easily understood by the patient.
- Monitor adverse events during treatment with Benoxinate.
- Consider potential consequences of adverse events prior to initiating Benoxinate. With concerns about Benoxinate used in solderer and blacksmith for long -term (for pain relief due to their exposure to foreign metallic objects).

**Pharmacists shall:**

- Control of OTC sales (shall be dispensed as a prescription only medication).
- keep patients aware of Benoxinate containing eye drops misuse dangers.

**Both Physicians and Pharmacists should instruct the patients to:**

- Protect their eyes from dust.
- Protect their anesthetized eye from dust particles, which could cause
- infections.
- Do not touch or rub their eyes while their eyes are numb as they may scratch the surface
- of the eye and damage it.
- Be careful of Driving or operating machinery until they know how Benoxinate HCL affects them.
- Blacksmiths and solderer should be counseled on the importance of using personal protective equipment, including safety glasses, welding helmets, and goggles, to safeguard their eyes and face and to prevent their eyes 'exposure to foreign metal bodies. (10)

***References:***


***[1] Keratitis definition:*** *(Click Here)*

***[2] Keratitis*** *(Click Here)*

***[3] "Corneal melt definition :*** *(Click Here)*

***[4] Oxybuprocaine hydrochloride definition :*** *(Click Here)*

***[5] Corneal Stroma:*** *(Click Here)*

***[6] Corneal Stroma:*** *(Click Here)*

***[7] Oxybuprocaine hydrochloride SPC:*** *(Click Here)*

***[8] Drug-Induced Ocular Side Effects:*** *(Click Here)*

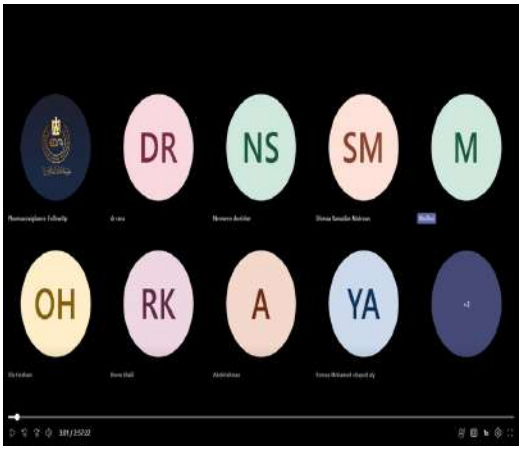
***[9] Recommendations to healthcare professionals :*** *(Click Here)*

***[10] Welding - Personal Protective Equipment and Clothing :*** *(Click Here)*

## Egyptian Pharmaceutical Vigilance Center (EPVC) Vigiflow expansion project Trainings for Raising Reporting Awareness

The Egyptian Pharmaceutical Vigilance Center (EPVC) is delighted to continue vigiflow expansion trainings to the advanced & well matured organisations in vigiflow Exapnasion Program in collaboration with SMC "Specialized Medical Centers" to the following organisations:

Almahalla cardic Center, Alzaytoun specialized Hospital, Banha Children hospital, Damnhour Oncology Center, Mansoura International Hospital, Nasser Institute, Qena Oncology Center.




This training aims to strengthen VigiFlow Expansion Program and ensure the reports quality.

While these training sessions are continued, EPVC is actively revising reports from the national database, revising them, and providing helpful feedback to the collaborting organizations. This deliberate approach is expected to result in a more robust and reliable method of tracking and managing medication safety risks.

EPVC would like to express its appreciation to the Egyptian Healthcare Authority and Giza Health Directorate -MoHP for their high quality Individual Case Safety Reports(ICSRs) on the national reporting

## "Together for Safe Medicine" Initiative News:

We are happy to announce the end of registration for the 4th wave of the EPVC initiative together for safe medicine. We can not wait to start the 4th wave activities to complete the journey after the success of the first three waves of the Initiative "Together for Safe Medicine "which achieved the Spread of pharmacovigilance science and activities between healthcare professionals and the public all over Egypt governments during the last two years.

EPVC Tips

On Pharmacovigilance

## Store Medicines Safely:

Where you store medicine can affect how well it works.

- Take care of medicine storage to keep it from getting damaged.
- Heat, air, light, and moisture may damage medicine.
- Store medicines in a cool, dry place.
- Always keep medicine in its original container.
- The cotton ball pulls moisture into the bottle.
- Always store medicine out of reach and out of sight of children.

***Visit EDA website to find all medicine- related news, updates and alerts*** *Click here*

***You will find all EPVC Newsletters and DHPCs*** here

***You will also find all alerts regarding counterfeited and falsified products released by Central Administration of Operations*** *here*

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

# One report counts

## A call for reporting

**Please remember that you can report safety information of medicines to EPVC using the following communication information:**

## What is Pharmacovigilance

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug- related problem.

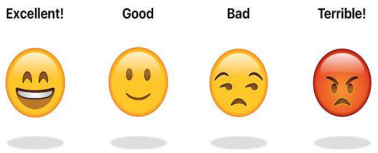
## What is the Egyptian Pharmaceutical Vigilance Center?

With the increasing demand for patient's safety which is becoming more stringent, . The Egyptian Pharmaceutical Vigilance Center was established to be responsible for the safety monitoring of the pharmaceutical products throughout its lifecycle and it is the regulatory authority regarding Pharmacovigilance and its applications .

EPVC monitors the safety of all types of pharmaceutical products, including human medicines, biological products, supplements, cosmetics, veterinary medicines, medical devices, Biocides and pesticides

**Participate with us**

We invite you to take a quick survey on how much our communication with you is effective
We value your feedback! Help us enhance our communication by taking a quick survey. Your insights are crucial in ensuring we meet your expectations.
Survey Link: (Click Here)




**Thank you for your valuable input**

## Communication information

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