

PMDA Alert for Proper Use of Drugs

Pharmaceuticals and Medical Devices Agency

No. 9 April 2012

This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Early Detection of Drug-induced Serious Skin Disorders

Drugs may induce serious skin disorders. In particular, approximately 600 cases per year of oculomucocutaneous syndrome (Stevens-Johnson syndrome) or toxic epidermal necrolysis have been reported during the last 2 and a half years. Of these cases, approximately 10 percent has resulted in sequelae or deaths. **Early detection and treatment are important** for good prognosis.

For early detection of serious skin disorders

If patients are taking drugs known to cause serious skin disorders, please pay attention to the following points:

Explain to patients about serious skin disorders as follows:

- Adverse reactions including serious skin disorders may occur.
- If the following initial symptoms in addition to rash are observed, the patient should **consult a doctor or pharmacist immediately**.

Consider the possibility of serious skin disorders as well if the following initial symptoms with rash are observed.

<Initial symptoms>

Pyrexia ($\geq 38^{\circ}\text{C}$), ocular hyperaemia, eye discharge, swelling of eyelid, difficulty in opening eyes, lip/genital erosion, pharynx pain, etc.

*A photo from "Manual for Management of Individual Serious Adverse Drug Reactions (Stevens-Johnson syndrome)"



Mild erythema or erosion, etc. may lead to serious skin disorders, and some cases result in a serious condition such as death, blindness and corneal sequelae. It is important **to detect these disorders at an early stage and treat them appropriately**.

It is important to consult and refer patients to a dermatologist at an early stage.

- If rapidly spread erythema or prolonged symptoms are observed, the patient should **consult or be referred to a dermatologist immediately**.

Refer to "Manual for Management of Individual Serious Adverse Drug Reactions" as well for information about early detection and treatment of serious skin disorders including Stevens-Johnson syndrome and toxic epidermal necrolysis (http://www.info.pmda.go.jp/juutoku/juutoku_index.html). (Japanese text only)

Frequently-reported drugs

Serious skin disorders (Stevens-Johnson syndrome, toxic epidermal necrolysis) caused by the following drugs have been reported frequently.

*Derived from Pharmaceuticals and Medical Devices Safety Information No.290
(Reports during the last 2 and a half years)

Therapeutic categories
Antiepileptics
Antipyretics and analgesics, anti-inflammatory agents*
Antibiotics
Antipodagric
Antineoplastics
Common cold drugs*
Synthetic antibacterials etc.

Active Ingredients
Allopurinol
Lamotrigine
Carbamazepine
Acetaminophen
Loxoprofen sodium hydrate
Garenoxacin mesilate hydrate etc.



* Including over-the-counter drugs

Cases of serious skin disorders (Stevens-Johnson syndrome) due to delayed detection and treatment

A case for which there was a long time between the initial symptoms onset and the hospital visit

A male patient in his 70s. The patient started receiving diclofenac sodium 50 mg/day for the treatment of back pain and then experienced oral and genital erosion, generalised erythema, pyrexia of 39°C. He could not take meals due to oral pain. 2 days after the onset of symptoms, he still had pyrexia, skin eruption on the trunk, and genital pain and genital skin eruption. He visited the emergency outpatient 8 days after the onset of symptoms and was referred to the department of dermatology on the following day (9 days after the onset of symptoms). He was diagnosed with Stevens-Johnson syndrome and was prescribed corticosteroids. He recovered from Stevens-Johnson syndrome 23 days after the onset of symptoms.

A case for which there was a long time until the disorder was diagnosed

A female patient in her 70s. The patient started receiving allopurinol 50 mg/day for the treatment of hyperuricaemia. Day 10 of administration, she experienced redness of pharynx, pyrexia of around 38°C, ocular hyperaemia, eye discharge, and lip swelling. Day 11 of administration, she visited the department of general medicine and was diagnosed with pharyngitis and was prescribed a common cold drug. Subsequently, face oedema developed. Day 13 of administration, eyelid oedema and skin eruption on the trunk and palm developed, and she was admitted to the department of otorhinolaryngology for pharyngitis. Day 15 of administration, skin eruption, enanthema, and pharyngeal oedema progressed. The patient was diagnosed with Stevens-Johnson syndrome caused by allopurinol, and administration of allopurinol was discontinued. She was transferred to the department of dermatology. Steroid pulse therapy was started. Day 13 of discontinuation, she was discharged from the hospital. At the time of discharge, slight shallow erosion on the oral mucosa was noted. Day 26 of discontinuation, erosion was epithelialized and the patient recovered.

About this information

- * "PMDA Alert for Proper Use of Drugs" communicates to healthcare providers with clear information from the perspective of promoting the proper use of drugs. The information presented here includes such cases where the reporting frequencies of similar reports have not decreased despite relevant alerts provided in package inserts, among Adverse Drug Reaction/infection cases reported in accordance with the Pharmaceutical Affairs Law.
- * We have tried to ensure the accuracy of this information at the time of its compilation but do not guarantee its accuracy in the future.
- * This information is not intended to impose constraints on the discretion of healthcare professionals or to impose obligations and responsibilities on them, but is provided to promote the proper use of drugs.