Pharmacovigilance Newsletter

Quarter 3,Issue 3

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Establishment of Pharmacovigilance stakeholders Forum

A multi-stakeholder platform is essential for coordinating national efforts to improve the implementation of pharmacovigilance activities. It is a partnership for implementing Pharmacovigilance activities under the leadership of EFDA. The platform plays a central role in the country-level process to develop, implement and monitor national safety montoring strategies and in facilitating collaborative action through strong coordination mechanisms and transparent decision-making at all stages of the planning and monitoring of PV strategies, as appropriate.

EFDA established a multistakeholder coordination and collaboration platform for pharmacovigilance on January 12,2023. The platform has its own Terms of reference/TOR that listed the different activities of the committee.

Welcoming of participants was conducted by Mrs. Asnakech Alemu , Director of Product safety directorate. She highlighted the importance of monitoring medicines and vaccine's safety after they are already in the market and being used by the public. Establishing a strong system that enables early detection of medicine safety related problems, timely investigating and taking appropriate action will preventing the public from unnecessary harm related to medicines and vaccines. This objective can be attained if only all stakeholders can work together and coordinate the tasks, they perform related to medicines safety.

Participants of the forum establishment meeting and members of the committee were composed of stakeholders who were identified as important stakeholders of Pharmacovigilance i.e.; Public Health programmes of FMOH (PMED, NTD, NTP, HIV, Malaria); Regional regulatory bodies; Regional health bureaus; Teaching institutions; NGO's (GAVI, WHO, UNICEF, USP/PQM+, GHSC-PSM, Ohio state university, JSI, Tony Blair Institute, CDC-Africa); Research institutions; Professional Associations; Drug importers and distributers' Associations; Drug Manufacturer's Associations; Private health sector associations; Market Authorization Holders; Consumer/Patient associations and the Media. *(Below are some pictures of the event)*

This newsletter is prepared and shared quarterly by EFDA with the objective of providing Medicine safety information and sharing the activities of the pharmacovigilance center at EFDA to healthcare providers working at both the public and private sectors.

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Activities Performed by the Pharmacovigilance center

Investigation conducted on case reports of Bupivacaine injection

The Pharmacovigilance team at the EFDA has previously investigated on various medicines safety and quality issues and regulatory measures were taken after the reports of the cases were presented to the pharmacovigilance advisory committee and recommendations were obtained. Hence after reports were obtained on the Use of Bupivacaine injection and the possible complications that could arise after the issues around the route of administrations. It was deemed necessary to investigate further and collect the necessary information that could enable decision making and regulatory measure. The objective of the investigation was to conduct a rapid assessment on the use of Bupivacaine injection at governmental and private health facilities.

Facilities that were expected to use anesthesia for various procedures were conveniently selected for the assessment and the data collection was conducted from January 2-6/2023 using a checklist developed for the purpose.

A total of 7 health facilities (four private and three governmental hospitals) were assessed, and anesthetists and pharmacy heads were interviewed for possible answers with respect to the use and procurement of the anesthesia.

The result of the rapid assessment showed that at all assessed hospitals the health care providers are using bupivacaine 5 mg/5ml solution for injection for different procedures as local anesthesia. Four private hospitals and one government hospital were using bupivacaine 5mg/5ml injection as recommended by manufacturer. While two of the government hospitals were using epidural anesthesia for spinal anesthesia procedure. There is also information that other governmental institutions also use the routes of administrations not as per the recommendation in the label. In addition, as observed during the assessment, the availability of the required type of route of administration and quantity of Bupivacaine has also been found to be critical at the health facilities.

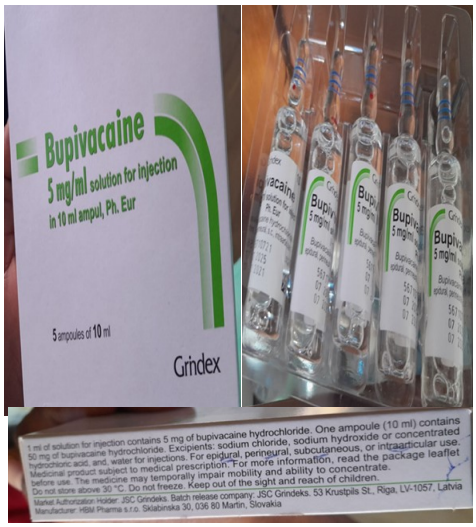
Hence, based on the obtained findings, it was concluded that there is a use of the injectable that is not in according to the labelling of the manufacturer and this has resulted (though not verified) in putting patients' life at risk.

As a result of these observation, EFDA Pharmacovigilance center has issued a letter of recommendation which was sent to all health bureau's so that they could notify their health facilities to use the medicine as per the direction provided.

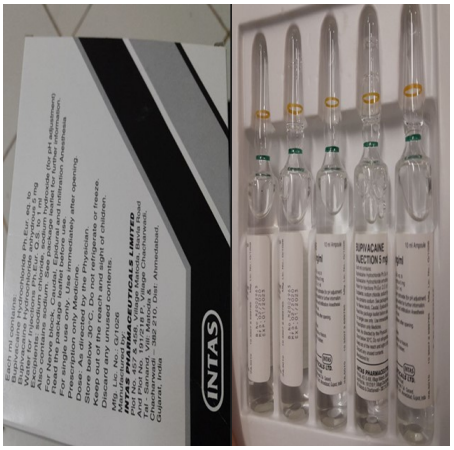
Pictures of the different brands of Bupivacaine obtained during the rapid convenience assessment (Saktar, Grindex and Intas) are attached below.

1. Brand type 1

2. Brand type 2



3. Brand type 3



Activities performed in the Pharmacovigilance center

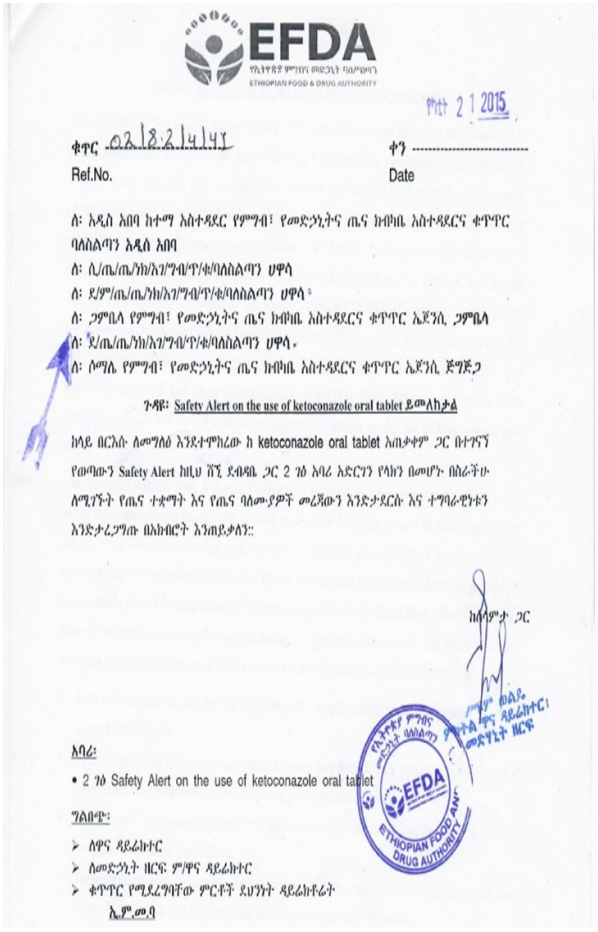
SAFETY ALERT on the use of Ketoconazole oral tablet

Since its introduction into the market in July 1981, ketoconazole oral tablet has been indicated to treat serious infections caused by fungi including blastomycosis, candidiasis, coccidiomycosis, tinea pityriasis versicolor and histoplasmosis. Moreover, it has also been in use for the treatment of cutaneous leishmaniasis, Cushing's syndrome and as an adjuvant therapy for prostate cancer in many other countries. However, many countries have limited its therapeutic indications due to safety concerns such as risk of liver injury and adrenal gland problems. Ex. France, UK, EMA, Australia, US and Rwanda had passed different regulatory restrictions on the use of ketoconazole oral tablet.

The Ethiopia Food and Drug Authority (EFDA) has received no safety report so far related to the use of ketoconazole oral tablet in the clinical practices in Ethiopia. As lack of safety report does not guarantee safety of the product, based on the currently available evidences from other countries regulatory authorities and published data, EFDA recommends (see the below letter) prescribers to limit the use of oral ketoconazole tablet for the treatment of systemic fungal infections. Since more effective and safer alternative systemic antifungal drugs (including itraconazole, fluconazole, and terbinafine) are available on Ethiopian market, EFDA's advice for health professionals include:

1. Oral ketoconazole should not be prescribed for fungal infections unless there is no other alternative available.
2. Prescribers should review patients who are taking this medicine for fungal infections, with a view to stopping treatment or choosing an appropriate alternative.
3. Pharmacists should not dispense ketoconazole oral tablets without prescription.
4. Topical ketoconazole formulations (such as creams, ointments, and shampoos) have very low systemic absorption and may continue to be used as currently approved.
5. Close safety monitoring particularly for liver function should be done for patients taking ketoconazole oral tablets.
6. Patients' awareness on signs and symptoms of ketoconazole adverse events should be raised to report them on time.
7. Health professionals should be vigilant on the safety of ketoconazole oral tablets and report any adverse events encountered to EFDA using the yellow form, free toll no, (8482) , e-reporting and MedSafety app,

Finally, the Ethiopian Food and Drug Authority kindly requests all health institutions (public or private), and all health professionals to discharge their responsibilities in implementing this regulatory decision to protect the public from preventable adverse drug events.



EFDA
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ETHIOPIAN FOOD & DRUG AUTHORITY

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ጉዳዩ፡ Safety Alert on the use of ketoconazole oral tablet ይመለከታል

ከላይ በርእሱ ለመግለፅ እንደተሞከረው ከ ketoconazole oral tablet አጠቃቀም ጋር በተገናኘ የወጣውን Safety Alert ከዚህ ሸኚ ደብዳቤ ጋር 2 ገፅ አባሪ አድርገን የላክን በመሆኑ በስራችሁ ለሚገኙት የጤና ተቋማት እና የጤና ባለሙያዎች መረጃውን እንድታደርሱ እና ተግባራዊነቱን እንድታረጋግጡ በአክብሮት እንጠይቃለን::

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• 2 ገፅ Safety Alert on the use of ketoconazole oral tablet

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International Safety update reports

Signal obtained from WHO/UMC

Methotrexate and muscle spasm

Rosa María Papale, Argentina and Mónica Tarapués, Ecuador

Methotrexate was granted US FDA approval in December 1953. Since then, it has been used via oral, intramuscular, intravenous, subcutaneous, intrapleural, and intrathecal routes of administration. Methotrexate acts by inhibiting enzymes responsible for nucleotide synthesis.

It is used for the treatment of several neoplasmic conditions, such as acute leukaemia, lymphomas, osteosarcoma, breast cancer, and in autoimmune diseases, such as rheumatoid arthritis and psoriasis. In addition, it is used to treat gestational choriocarcinoma, chorioadenoma, hydatiform mole, and advanced mycosis fungoides.

Muscle spasm covers several overlapping concepts of true spasm and cramps. Spasms are involuntary muscle contractions. When these are prolonged and painful, they are often referred to as cramps.

A screening of VigiBase, the WHO global database of individual case safety reports (ICSRs), identified the association of the MedDRA Preferred Term (PT) 'muscle spasm' with methotrexate. A qualitative analysis of 47 cases was undertaken with a completeness score of over 0.70. The similarity of characteristics with respect to time to onset, the biological plausibility, the improvement after drug withdrawal, all provide evidence of this association.

As of May 2020, there were 397 reports for the MedDRA Preferred Term 'muscle spasms' associated with methotrexate. Due to the large number of cases, a completeness score over 0.7 was set for this analysis so as to identify the causality patterns that strengthen the signal. In the present case series, 47 cases were evaluated.

The reports came from 18 countries, most of them in Europe but also from the Americas, Africa, and Asia. There were 30 females and 17 males. The age was recorded for 45 patients, ranged from 13 to 87 years (median 57); 31 were adults. Thirty-six cases (76%) were reported by health professionals (20 by physicians and 16 by pharmacists). Sixteen cases were considered serious, mainly under the criterion of other medically important condition (10 cases)

Muscle spasms or muscle cramps are not currently mentioned in the SPC for methotrexate, and this ADR could have an impact on the quality of life of patients undergoing treatment with methotrexate. Patients, as well as physicians, should be aware of these ADRs to avoid a reaction.

Prescribers and patients need to be aware that muscle spasms could be present with the use of methotrexate. This adverse reaction could impair the patients' quality of life, especially long-term users with chronic diseases. For this reason, it is reasonable to consider an in-depth clinical analysis when the patient mentions these complaints, especially patients on low doses. *Source- WHO Pharmaceuticals Newsletter No. 1, 2022*

Please use any of the adverse drug event reporting tools and report any adverse drug reactions ,medication errors and product quality defects that you may encounter in your healthcare practice!

For our previous editions of the Pharmacovigilance newsletters