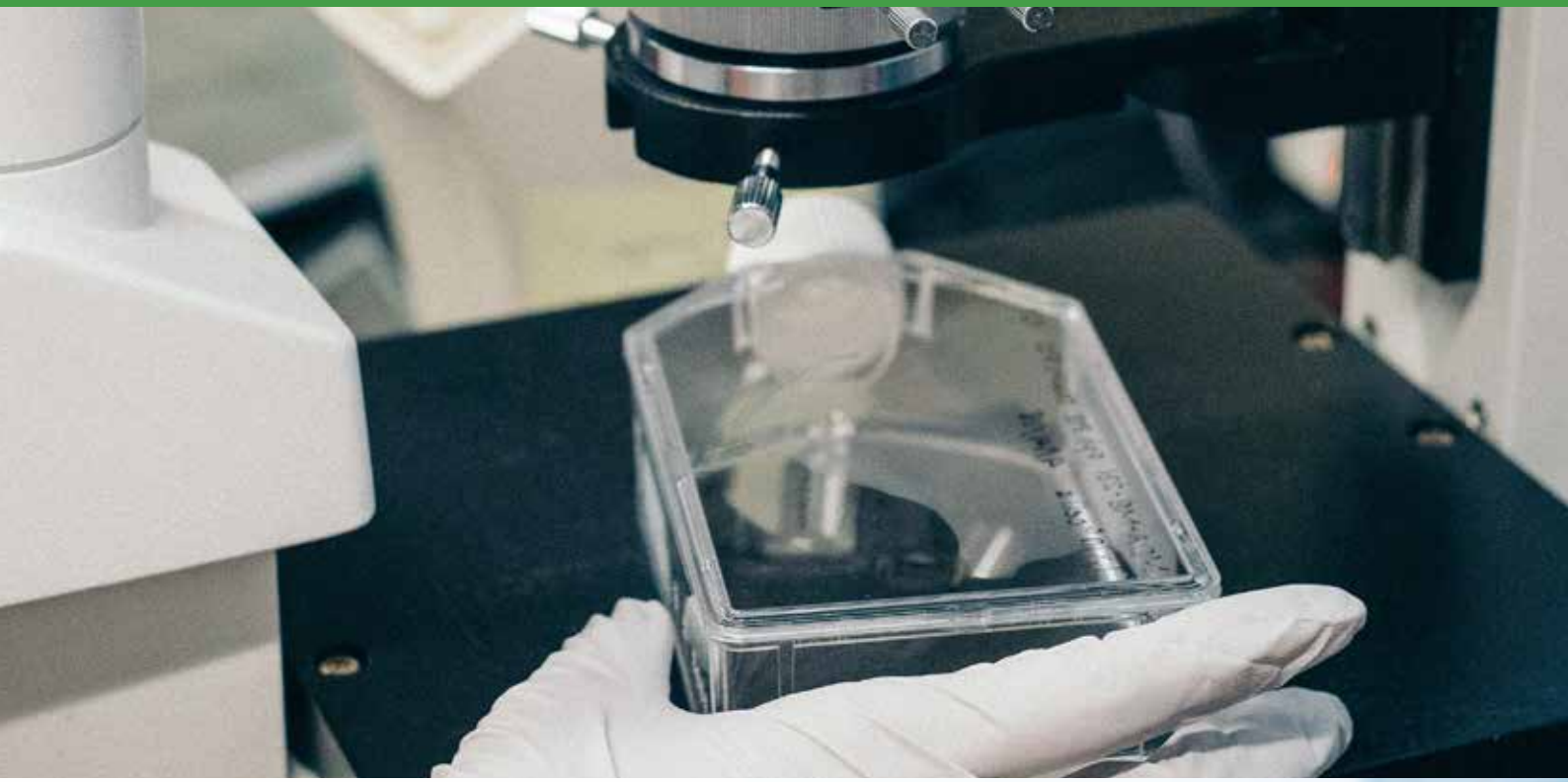
Safe Drugs Save Lives

NATIONAL DRUG AUTHORITY



Inside this Issue

LOCAL SIGNALS FOR CONTINUED VIGILANCE

Case report: Worsening hyperglycemia associated with Dolutegravir

Case presentation

E.B is a 53-year-old woman who presents to hospital in Uganda with complaints of worsening hyperglycemia, anxiety, insomnia, itching and headache. She is a known type- II diabetic, hypertensive and ISS patient for 16 years. She is managed with TDF/3TC/ DTG, Metformin, Glimepiride, Losartan and Hydrochlorothiazide. She states that her HAART medication was changed a month back from TDF/3TC/ LPV/r and that the symptoms started a week after this change was made. She was managed with Lantus, Epirax and sertr aline for the symptoms. A dechallenge for Dolutegravir was done and patient was monitored for a week

Discussion

Diabetes Mellitus type II is an important cause of morbidity and mortality among people living with HIV1. The initial evaluations showed that the patient had uncontrolled hyperglycemia even though she was adhering to her antidiabetic medication.

She was managed with Insulin mixtard and later, Dolutegravir was substituted with Al- luvia. After one week, it was noted that the plasma glucose levels of the patient were controlled.

Several clinical trials have been conducted to demonstrate the efficacy of Dolutegravir. However, hyperglycemia has been reported in 3 of these as a potential side effect1. Therefore, there is need for healthcare professionals to closely monitor plasma glucose levels for HIV infected diabetic patients who are on Dolutegravir regimens.

Conclusion

There is a potential signal of hyperglycemia associated with Dolutegravir regimens in patients with HIV and Diabetes.

Reference

Milena M, Walsh S, Shannon G (2018). 'Dolutegravir induced hyperglycemia in a pa- tient living with HIV' Journal of Antimicrobial Chemotherapy, 73(1), 258-260.

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Case report: Aggression and disorientation associated with Hydroxyurea

NDA received a case report concerning a 3 year old female child who has been on hydroxyurea medication since she was two years for management of sickle cell crisis and developed aggressive tendencies. The report indicates that the child became aggressive by climbing windows and one time wanting to bite her finger off after taking the drug. Whenever the mother would discontinue the drug the child would stabilize. This happened on several occasions, when the drug was re-administered and the mother's option (as instructed by the physician) was always to stop the drug. Hydroxyurea for this patient has been suspended and given Glutamate powder as a substitute.

Hydroxyurea is indicated for the treatment of patients with: chronic myeloid leukemia, thrombocytopenia, or polycythemia as well as for the prevention of recurrent painful vaso-occlusive crises in adults, adolescents and children older than 2 years suffering from symptomatic Sickle Cell Syndrome

Labeled information:

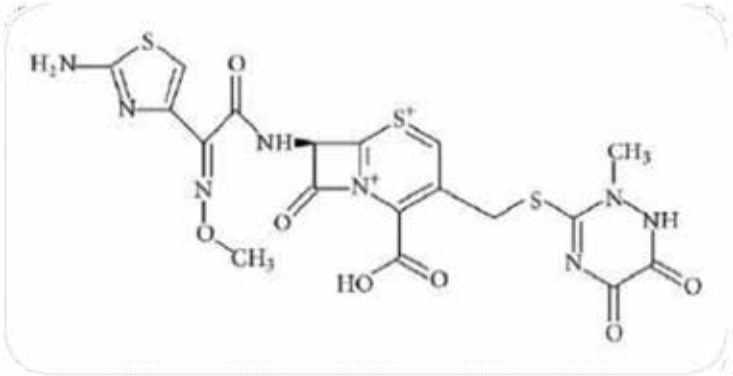
The summary of product characteristic (SmPC) for Hydroxyurea reports neurological disturbances including disorientation to be of rare occurrence with the drug. According to the WHO global database, aggression has been reported in 6 cases, while other psychiatric events are reported in 224 cases mainly in adults taking the drug.

Recommendation

Given the recent policy for use of hydroxyurea in management of sickle cell patients, there is need for healthcare professionals to be aware of the possible occurrence of disorientation especially in children who may not express or report such reactions when given hydroxyurea.

FOREIGN SAFETY UPDATES

Ceftriaxone: Risk of convulsions and involuntary movements



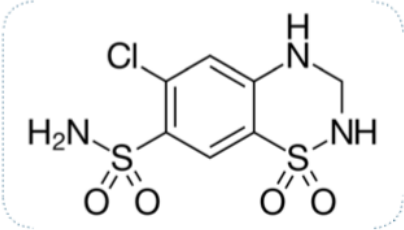
PMDA have announced that the package insert for ceftriaxone should be revised to include neuropsy- chiatric symptoms such as convulsions and involuntary movements as adverse reactions.

Ceftriaxone is a cephalosporin antibiotic active against several microorganisms including: Strepto- coccus, Pneumococcus, and Escherichia coli. It is indicated for the treatment of bacterial infections such as sepsis, pharyngitis, tonsillitis and acute bronchitis. A total of 19 cases of neuropsychiatric symptoms were reported in Japan in the previous three years, and a causal relationship with ceftriaxone could not be excluded for 11 cases. Other cases of neuropsychiatric symptoms have been reported in patients treated with ceftriaxone in other regions.

Reference

WHO Pharmaceuticals Newsletter issue 5 2018

Hydrochlorothiazide Association with Non-Melanoma Skin Cancer (NMSC)



Hydrocholorothiazide(HCTZ) is a diuretic drug used in the treatment of high blood pressure, usually in combination with other anti-hypertensive drugs. Emerging safety information has indicated an increased risk of non-melanoma skin cancer (NMSC), Basal cell carcinoma(BCC), and squamous cell carcinoma (SCC) associated with increasing cumulative dose (long term use) of HCTZ exposure. Photosensitising actions of HCTZ (known adverse effect of HCTZ) could act as possible mechanism for NMSC. There is however no similar risk associated with other diuretics and other anti-hypertensives like calcium channel blockers, Angiotensin converting enzyme inhibitors (ACE inhibitors), or Angiotensin II receptor blockers (ARBs).medicines.

Recomendations

- Patients taking HCTZ should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies.

- Possible preventive measures such as limited exposure to sunlight and adequate protection when exposed to sunlight should be advised to patients in order to minimise the risk of skin cancer.
- The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC.

MEDICINE USE: PRESCRIBING ERRORS

Compiled by **David Walusimbi**

Prescribing medicines is the primary tool used by all healthcare systems to treat dis- ease, alleviate symptoms and prevent future illness. It requires knowledge of conditions as well as the medicines used to treat them. Most drugs are prescribed according to their availability and tolerability in that com- munity.

In this country, the Uganda Clinical guide- lines is a resource that is often used to pro- vide guidance when making prescriptions. The prescriber needs to do a risk benefit assessment as well as pay attention to detail in order to optimize therapy for a particular patient.

Prescribing can improve health, but also has potential hazards. Studies have found that prescribing is the most challenging area for new healthcare graduates, and that unintended errors are common both among trainees and professionals. Although the majority of prescriptions are suitable, many studies from around the world have drawn attention to the significant rates of prescribing errors and avoidable adverse drug reactions.

In Uganda, 1 in 5 HCPs disclosed that they had committed potentially harmful MEs, while 2 in 5 reported that they had seen other HCPs make MEs that had the potential to harm patients1. These errors not only harm patients but present unnecessary costs attributable to therapeutic failure and pro- longed hospitalization.

Prescribers have to select the right medicine, dose, route and frequency of administration while taking into account predicted individual variability in medicine handling and response as a result of comorbidity, genetics, and interacting medicines. Newly graduated doctors write a large proportion of hospital prescriptions, and it is therefore unsurprising that widespread evidence exists to show that prescribing by this group is frequently sub-optimum. However, senior doctors also make errors, and concerns regarding prescribing skills among all prescribers have been expressed internationally2.

Most public facilities in Uganda have a general prescription form but this may not always be used. The form 5 is more frequently used in it's place for prescribing. Clinical history often takes precedence on a form 5 and prescribing information is usually written at the end where it may not get adequate space which can potentially result in incompleteness.

Prescribers often work under very high-pressured circumstances, full of distractions. It is therefore not surprising that errors do occur. They have a heavy burden of administration and require continuous multi-tasking which results in them being more error-prone.

The number, age, and vulnerability of hospital patients have also progressively increased, as well as the complexity of the treatment regimens for common disorders2.

In view of this situation, it might be expected that trainees and new graduates would be well prepared to begin prescribing in these demanding work environ-

ments. However, a clear theme from many studies is that students and new graduates often do not feel adequately prepared to carry out their role in prescribing, a concern echoed by their supervisors2.

Advice to HCPs

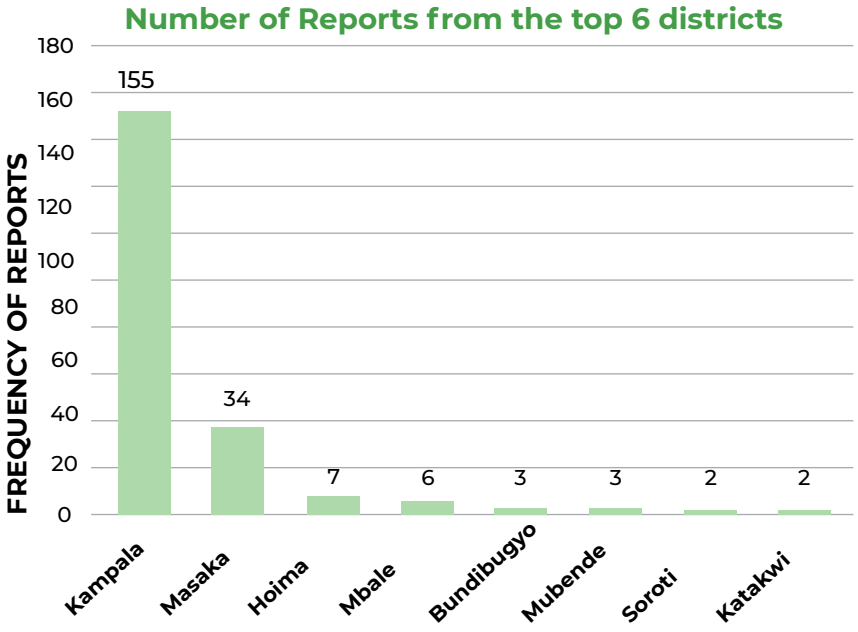
- Conduct continuous training to promote better prescribing skills in healthcare.
- Incorporate prescription safety assessment programs in MTCs in order to bridge the gap between theoretical pharmacology education and practical application of that knowledge to patient care
- Report any occurring MEs to NDA so that common occurrences can be communi- cated and overcome.
- Report ADRs due to MEs to NDA. This way, there is information that can be used to guide all other HCPs on what they might expect during an ME with a specific drug.
- It is important to note that MEs are majorly unintended and they may happen at pre- scriber level or patient level.

References

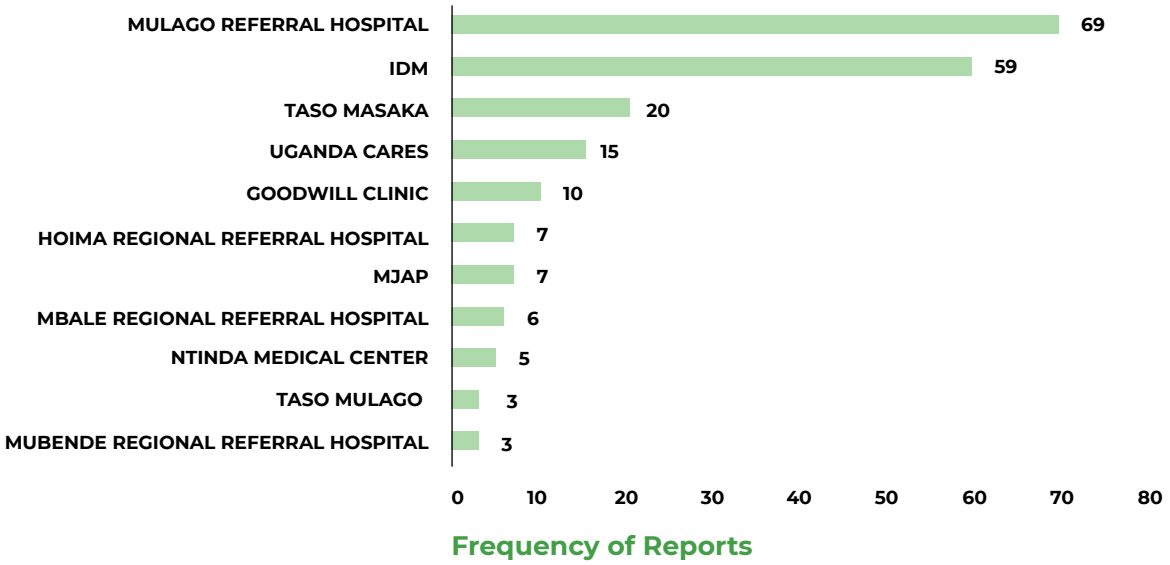
1. Kiguba R, Waako P, Ndagije H.B, Karamagi C (2015). 'Medication Error Disclosure and Attitudes to Reporting by Healthcare Professionals in a Sub-Saharan Afri- can Setting: A Survey in Uganda' Drug Real World Outcomes, 2015 Sep; 2(3): 273–287.
2. WHO Drug Information Vol. 32, No. 2, 2018

ADVERSE DRUG SUMMERIES FOR PERIOD OCTOBER - DECEMBER 2018

A total of 216 case reports were received, with 48.1 % reported to be serious. Kampala district reported highest (71.8%. n=155) followed by Masaka (15.7%; n=34), as shown in figure 1 below.



Mulago National Referral Hospital-TB Clinic (n=69) submitted the highest number of reports followed by Infectious Disease Institute (n=59) and TASO Masaka (n=20) as shown in the figure 2 below.



Over all, Pharmacists submitted most reports (n=125, 56.4%) followed by Pharmacy Technicians (n=33, 16.6%), Medical officers (n=31, 15%), clinical medical officers (n=21, 9.2%), nurses (n=5, 2.4%), and Physician (n=1, 0.5%).

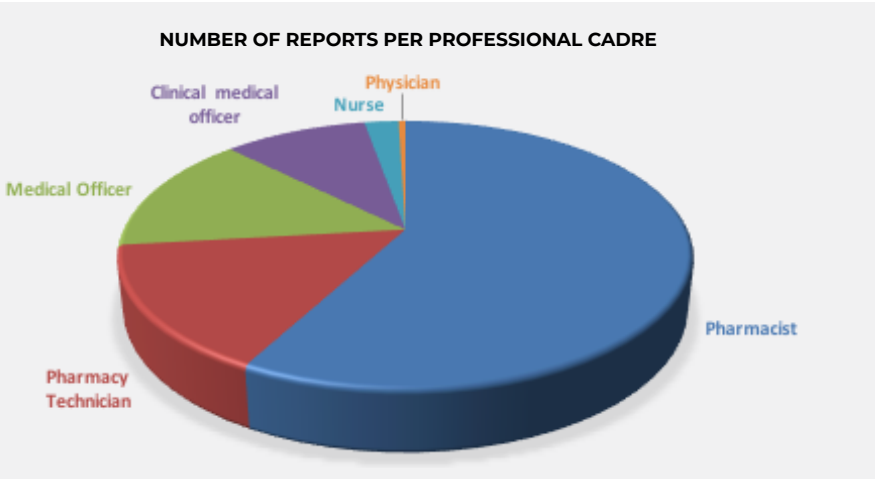


Table 1. Top 10 Reaction- Drug pairs reported

Reactions	Count of Reaction
Chest pain/Epigatric pain	**9**
Cycloserine	1
Ethionamide	1
Pyrazinamide	4
Levofloxacin	3
Headache	**6**
Dolutegravir	6
Severe headache /dizziness / blurred vision	**26**
Gentamycin	26
Hearing loss	**4**
Kanamycin	4
Insomnia	**5**
Dolutegravir	5
Itching skin rash	**11**
Abacavir	1
EFavirenz	3
Nevirapine	4
Pyrazinamide	3
Joint Pain	**35**
Dolutegravir	1
Pyrazinamide	27
Tenofovir	7
Nail discolouration	**4**
Zidovudine	4
Nausea	**8**
Cotrimoxazole	1
Levofloxacin	1
Moxifloxacin	1
Pyrazinamide	3
TDF/3TC/EFV	2
Renal Toxicity	**6**
Tenofovir	6
Grand Total	**114**

If you have any comments or feedback on any of the articles in this bulletin, we would be pleased to receive them at druginfo@nda.or.ug/ dps@nda.or.ug

To report Adverse Drug Reactions complete the Adverse Drug Reaction form and return it to any NDA office near you or send a direct online report at

https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationI D=UG

Fax: +256-414-655.60.80 E-mail: druginfo@nda.or.ug
or whatsapp on 0791415555

You can visit us at: **www.nda.or.ug**