Safe Drugs Save Lives

NATIONAL DRUG AUTHORITY

Inside this Issue

ADVERSE DRUG REACTION REPORTING FOR QUARTER THREE

1.0 Background

This report provides a summary of individual case reports submitted to NDA by healthcare professionals from various health facilities in the country. The report presents frequencies of drug – reaction pairs and highlights some reactions that may need extra monitoring during patient care.

1.1 Adverse drug Reaction (ADR) Reporting Rates

A total of 115 case reports were received, with 30% reported to be serious. Kampala district reported highest (53%. n=61) followed by Lyantonde (9%; n=10) and Wakiso (9%, n=10). Infectious Diseases Institute (IDI) submitted the highest number of reports (n=29) followed by Mulago referral hospital (n=17) and TASO Entebbe (n=13) as presented in figure 1 below.

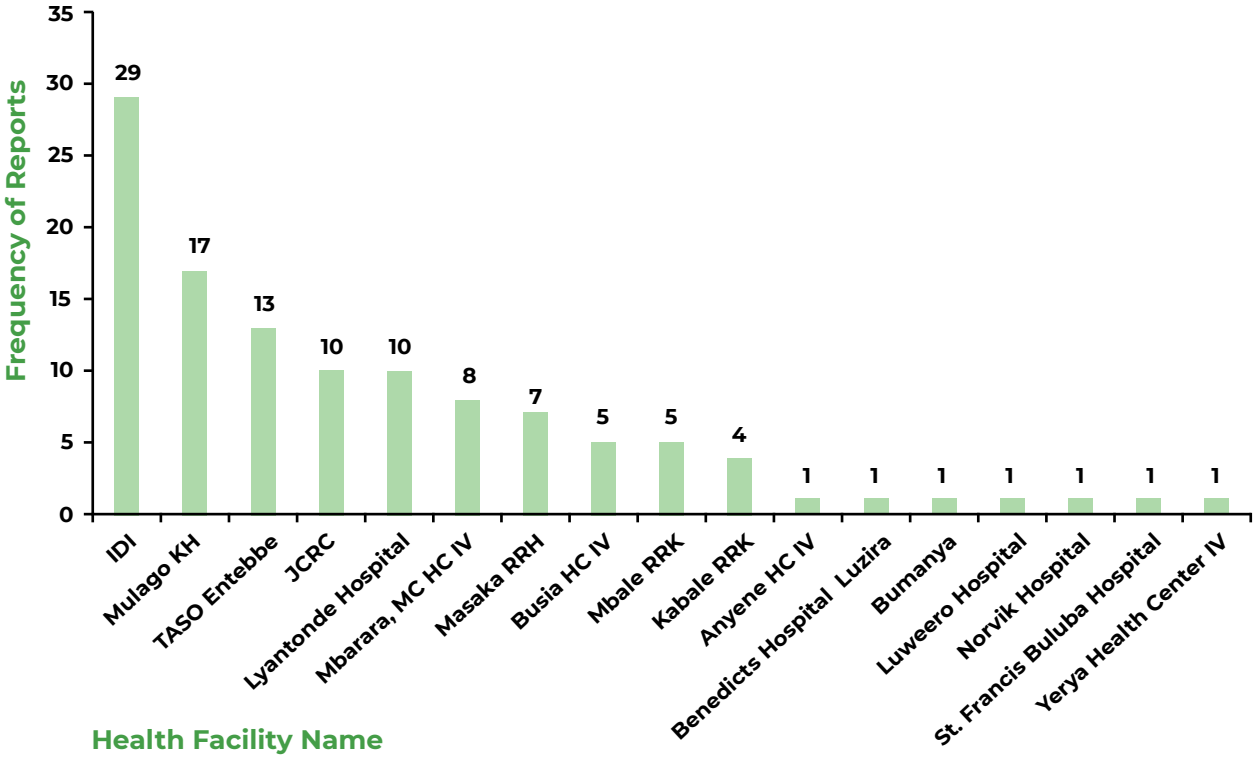

Figure 1.Number of ADR reports submitted by health facilities

Overall, Pharmacists submitted most reports (n=51, 44%) followed by Clinical Officers (n=19, 17%), Pharmacy Technicians (n=9, 8%), Medical Officers (n=7, 6%), nurses (n=4, 3%), and Physicians (n=3, 3%) respectively; while 22 reports (16%) were submitted by other health care professionals. The top 10 drug reaction pairs reported are presented in table 1 below.

Table 1: Top 10 Reaction- Drug pairs reported

S/N	Reactions and associated drug(s)	Frequency of Reaction
1	**JOINT/MUSCLE PAINS**	**15**
	Pyrazinamide	7
	Tenofovir	3
	Dolutegravir	2
	Perfloxacin	1
	Kanamycin	1
	Isoniazid	1
2	**Headache, nausea, vomitng, general body weakness**	**13**
	TDF/3TC/EFV	5
	Dolutegravir	4
	Ethionamide	2
	Kanamycin	1
	Gentamycin	1
3	**Skin reaction**	**10**
	TDF/3TC/DTG	5
	Carbamazepine	2
	Isoniazid	1
	TDF/3TC/EFV	1
	Neverapine	1
4	**Hypergylcemia, Hypersensitivity, general body weakness**	**7**
	Dolutegravir	6
	Carbamazepine	1
5	**Severe headache**	**5**
	Gentamycin	2
	NIFEDIPINE	2
	Dolutegravir	1
6	**Dizziness,, general body weakness, lower limb pain**	**5**
	Dolutegravir	3
	TDF/3TC/EFV	1
	Isoniazid	1
7	**Increased blood pressure/creatinine**	**4**
	Dolutegravir	3
	Tenofovir/lamivudine	1
8	**Deep jaundice**	**3**
	Isoniazid	2
	Efavirenz	1
9	**Insomia, Dizziness, weakness**	**3**
	Dolutegravir	3
10	**Hearing loss**	**3**
	Kanamycin	3

1.2 Reactions that require extra monitoring

a) Previously unknown incidents of tinnitus, increased appetite/weight gain with Dolutegravir

In this reporting period, NDA received three (3) reports of tinnitus in patients taking Dolutegravir. The events involved 2 females and one male, all above 45 years of age. They all reported tinnitus on the day the drug was initiated. Tinnitus is not a labelled reaction and is not included on the product label for Dolutegravir. However, a search in Vigibase (WHO ADR database) indicates some cases of Tinnitus with patients taking DTG. At the moment, there is a lot of missing information with the case reports and additional monitoring and reporting of this reaction is needed in order to strengthen evidence for the association of this reaction with DTG.

There were 4 cases of increased appetite and weight gain occurring within the a few days of initiation of DTG all in patients aged 45 years and above. Some observational studies have showed results suggestive of an association between integrase inhibitors and weight gain particularly among women. Additional evidence will be necessary through monitoring of patients in randomised clinical trials to strengthen the potential association. It's therefore imperative for health workers to document and report any significant changes (>5% weight gain) changes in body weight and other cardiovascular markers in patients on Dolutegravir.

b) Joint pain/ arthralgia in concomitant use of pyrazinamide and fluoroquinolones

Joint pain associated with pyrazinamide is a known ADR common among TB patients. Usually symptoms of arthralgia generally diminish over time even without intervention. They can also be managed by giving patients NSAIDs like ibuprofen, indomethacin or Aspirin. In light of emerging evidence of disabling joint and tendon disorders with fluoroquinolones use, the potential worsening or causative effect of fluoroquinolones when used concomitantly should be considered. For patients on MDR TB treatment, persistent arthralgia and other tendon disorders including gait should be carefully evaluated and Fluoroquinolones should be considered as an alternate possible cause for heightened tendon disorders especially when in combination with Pyrazinamide.

Active monitoring efforts on the new drugs in Public Health Programs

The Ministry of Health is rolling out several new drugs particularly for HIV and TB programs. These new molecules like Dolutegravir and Bedaquiline are in the early post-marketing phase, a period of initial or first time use in settings different from clinical trials and where much larger populations might be exposed in a relatively short timeframe. This makes it imperative to actively monitor their use for emerging safety information not captured during clinical trials, to characterize known risks of a drug, important potential risks, and important missing information, including the potentially at-risk populations and situations where the product is likely to be used that have not been studied pre-approval.

The Ministry of Health and NDA have established a Pharmacovigilance technical working group to offer leadership in the planning and implementation of active drug monitoring for all new drugs in public health programs. The team has a multi-disciplinary membership drawn from various stakeholders, including; NDA, Pharmacy division, AIDS Control Program, National TB and Leprosy Program, Maternal and child Health Implementing partners, among others. The ongoing efforts will focus on enhancing capacity for active drug safety monitoring in target select facilities where the new drugs are in use. This initiative we believe will go a long way to improve ADR reporting with the overall aim of strengthening patient safety.

Figure 2: Part of the ADSM sub-committee during a planning meeting at Ministry of Health

Shaping a pharmacovigilance strategy for Uganda

The National Drug Authority is commissioned to coordinate the pharmacovigilance activities in the country. Consequently, it's responsible for setting the tone for all systems, activities, processes, and initiatives to identify, mitigate and or prevent drug mediated harm. Such efforts involve several stakeholders including, policy makers, and public health programs, NGOs, implementing partners, health professionals, the public and others.

NDA is currently developing National Pharmacovigilance Strategy to harmonize activities of all partners to reduce duplication, maximize available resources, and adequately leverage on existing structures while focusing on identified common goals. To maximize contributions from stakeholders and stimulate ownership of the strategic direction, we have conducted country wide stakeholder consultations which were closed with a national stakeholder meeting on 21ST March 2019 to gather input and feedback of the proposed strategy. We would like to thank all those that have contributed to these efforts towards giving direction to pharmacovigilance in Uganda.

Figure 3: National stakeholder meeting on the Pharmacovigilance strategy

World TB day- 21st March, 2019

A growing partnership with the National Tuberculosis and leprosy Program with a call to action to reduce the burden of Tuberculosis in Uganda.
Tuberculosis (TB) is an infectious airborne disease and is transmitted through air from a TB patient mainly through coughing. We present below simple facts that you need to know about TB and how you can act to reduce the burden.

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1. What are the symptoms of TB?

Tuberculosis (TB) is an infectious airborne disease and is transmitted from a TB patient mainly through coughing.

Early stages: May have no symptoms: As the TB disease develops individuals may experience some or all of the following: Cough, sometimes with sputum (spit) which can be blood stained; Fevers especially in the evening; Sweating, especially at night; Unexplained weight loss; low weight gain for children; History of TB contact for children under 5 years; Chest pain; Sometimes lumps (swollen lymph nodes) in the neck or armpits

2. TB and HIV

a)- TB is the leading cause of illness and death among people living with HIV; b)- Without proper treatment, approximately 90% of people living with HIV die within two to three months of contracting TB; c)- People living with HIV who have TB disease die sooner than those without TB--even if they are receiving antiretroviral treatment; d)- Globally, 12% of all TB deaths occur in people living with HIV

3. The following situations aid the spread of TB

a)-The TB germ is spread from one person to another through the air. b)-TB spreads in many ways e.g. coughing, talking, sneezing; c)- TB can be transmitted to every person irrespective of age, social status or place of residence. d)- Closeness to the patient; e)- Time spent together with the patient – the longer, the chances ; f)-Crowding; g)- Poor ventilation; h)-Low immunity of the individual - Immunity in the case of the person contracting the disease

4. Testing for TB

a) Anyone with suspicious signs and symptoms should be tested to see if they have TB
b) Attention should be given to the categories of people who are at higher risk of developing TB (e.g. HIV positive people, pregnant women, children, people with chronic diseases like diabetes, cancers. Health workers, prisoners, refugees, contacts of people with TB disease).

5. Treatment issues

a) TB disease can be cured, even in people living with HIV, diabetes and cancer.
b) Treatment takes a minimum of 6 months in Uganda, depending on disease type which can go up to 20 months.
c) TB patients may not spread the disease after 2 weeks of initiation on medicines (starting treatment); however patients still likely have the mycobacterial organisms which can become resistant if treatment is not continued.
d) TB should be diagnosed and treated as soon as possible. This helps to reduce the risk of transmission to other people
f) TB can be transmitted further if treatment support to the patient is not given and the patient copy treatment prematurely.
g) TB can become resistant if treatment usually 6 months treatment is not adhered to.
h) Proper treatment of TB to completion for cure can lead to prevention of transmission to any others around the patient so support TB patients to complete treatment.

6. Medication for tuberculosis

The anti-tubercular drugs are used in different combinations in different circumstances. For example some anti TB drugs, the first line drugs, are only used for the treatment of new patients who are very unlikely to have resistance to any of the TB drugs. There are other TB drugs, the second line drugs, that are only used for the treatment of drug resistant TB

Uganda uses fixed dose combination drugs for treating tuberculosis;

a) Adult patients with drug susceptible TB take a combination of **Rifampicin+Isoniazid+Pyrazinamide+Ethambutol** in a single tablet daily for 2 months followed by fixed dose combination of **Rifampicin +Isoniazid** for 4 months.
b) Children are given fixed dose combination of Rifampicin+Isoniazid+Pyrazinamide in a single dispersible tablet, this is taken for 2 months in conjunction with a single formulation of Ethambutol (non-dispersible). They afterwards continue with a fixed dose combination of Rifampicin +Isoniazid in a dispersible tablet.
c) The drug resistant patients take a regimen of single formulations for a longer period of 9-20 months. The drugs included are **Ethionamide 250mg tabs, Levofloxacin 250mg tabs, Moxifloxacin 400 mg tabs, Pyrazinamide 400mg tabs, Ethambutol 400mg tabs, Clofazimine100mg caps, Isoniazid 300mg tabs, Linezolid 600mg tab, Bedaquiline 100mg tabs, Cycloserine tabs and an aminoglycoside injectable**(where applicable)

7. Prevention and control of TB

Special precautions must be taken to avoid people contracting TB from patients

- Early diagnosis and treatment
- Observe proper cough habits - Cover mouth with handkerchief, any other piece of cloth or an arm/elbow when you cough or sneeze.
- Patients using masks
- Keeping the environment clean
- Proper architectural planning to allow proper ventilation
- Opening windows, doors including those of public transport vehicles like buses and taxis.
- Avoid crowding
- Using special lights that kill germs
- Persons in close contact of persons with TB should be checked for TB irrespective of having or not having TB symptoms.

8. What to do when one has TB symptoms

- Early treatment from a health facility, taking medicines as instructed by health providers
- Completion of the dose minimum of 6 months and could be more depending on the severity of the disease-

9. As healthcare providers, you are advised to do the following:

- Active screening of patients,
- Systematic evaluation of presumed cases,
- Immediate enrollment on treatment upon diagnosis and proper follow up of patients to ensure adherence to treatment.

10. NDA's contribution to reducing the burden of TB

- New and more superior medicines have been licensed to combat drug resistant TB.
- NDA continues to carry out routine post market surveillance, sampling and testing of drugs used in treatment of TB on the market through its WHO prequalified laboratory, using the latest analytical technology.
- Monitor the safety of Anti-TB medicines in Uganda in order to contribute evidence on the Benefit-risk balance of TB treatment

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

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

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