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College of Pharmacy Research Day

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King Saud University

Off-label Medication Use Patterns:

Retrospective Study in a Tertiary Hospital in Saudi Arabia

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Outlines:

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1. Introduction
2. Aim and objectives
3. Method
4. Results
5. Summary and conclusion

Introduction:

Off-label medication use (OLMU) refers to any intentional use of authorized products for unapproved:

A. Clinical indication

B. Route of administration

C. Dosing frequency or duration

D. Age group

Stafford RS. Regulating Off-Label Drug Use — Rethinking the Role of the FDA. *N Engl J Med*. 2008;358(14):1427-1429. doi:10.1056/nejmp0802107

Introduction:

Common reasons for prescribing medications for off-label use:

- The **advances in clinical trials** are improving faster than the FDA's ability to approve medications for new uses.
- The **cost** to get a medication approved for a different use may not be worth it for the manufacturer.
- **Clinical trials do not always include certain populations**, such as children, and pregnant women.

Goločorbin Kon S, Iliković I, Mikov M. Reasons for and frequency of off-label drug use. *Med Pregl*. 2015;68(1-2):35-40. doi:10.2298/MPNS1502035G.

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Aim:

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Evaluate the extent of off-label medication use in King Khalid University Hospital (KKUH).

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Objectives:

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- To describe **the frequency and the pattern of accepted** off-label medication forms.
- To describe **the frequency and the reason for rejected** off-label medication forms.
- To classify the **most common off-label medications** prescribed.

Methods:

A retrospective analysis of filled '**Form B**' was submitted between the period of **January 2017 to December 2020** at **KKUH**.

Methods:

Form B:

Pharmacy Department
King Saud University Medical City

REQUEST FOR UNLISCENCED/UNAPPROVED USE OF MEDICATION
SINGLE PATIENT REQUEST

FORM B

Please read carefully:
This Form shall be filled along with on order or prescription to request the use of a formulary medication for AN UNLICENSED/UNAPPROVED: INDICATION; DOSE; ROUTE; DURATION OR AGE GROUP as per the [Unlicensed/Unapproved Use of Medications IPP] for treatment of a patient who has failed/ contraindication/intolerant to existing approved therapeutic alternative. Approval for the use of this medication is under the jurisdiction of the Department Chairman or Section Head of the medical department involved in the request.

The initial request must be accompanied by evidence based supporting literature.

Patient/guardian must be informed regarding the risk/benefits of the use of this medication by the treating physician and documentation in the medical record must be made.

Forms to be submitted electronically when available.

****When completed & signed/approved by the Section Head/Department Chairman, please forward manual form to the appropriate pharmacy area, or submit electronic form to Pharmacy Department.*****

Generic Name of medication:

Brand Name:

SPECIFIC DETAILS OF PATIENT:

Name: _____ **Medical Record No.** _____

Age: _____ **Weight:** _____ **Sex:** _____ **Allergies:** _____

Present Medical Problem(s):

Review of Systems *(Pertinent information only):*

Pertinent Laboratory Data:

Present Medications:

Pharmacy Department
King Saud University Medical City

Past Medical History /Drug History:

Rationale for Using this Drug for this Patient *(please include information on previous treatment modalities which have failed):*

The use of medication has been discussed with patient/Guardian: **Yes** ☐ **No** ☐

DRUG PROTOCOL
Please provide specific Information on how this drug will be used in this patient.
The information should include the following:

1. Dosage regimen & duration of therapy:

2. Therapeutic monitoring parameters:

3. Adverse effects, their management:

4. Criteria for discontinuing therapy:

5. Special precautions for the patient *(if any):*

6. Special nursing/pharmacy Instructions:

APPROVAL SIGNATORY SECTION: **Date:** _____

Requesting Consultant /Fellow's:

Name: _____ Signatures: _____

ID#: _____ Pager/Mobile Number: _____

If form is completed by Senior Registrar or Resident:

Name: _____ Signatures: _____

ID#: _____ Pager/Mobile Number: _____

Methods:

Data collection:

From each form B, patients' pertinent data, off-label medication use data, and the department of the prescribing physicians were collected.

- **Patients' pertinent data:**
  - Demographic data
  - Present medical history.
  - Past medical/medication history.
  - Discussing use of medication with patient/guardian.

- **Off-label medication use data:**
  - Generic name of the off-labeled medication prescribed.
  - Medication protocol (dosage regimen, monitoring parameters, adverse effects…etc.)

Methods:

Data analysis:

To facilitate the accuracy of classification, classification systems were used.

- **Classification of medication:**

  The ***Anatomical Therapeutic Chemical (ATC) classification system*** that developed by World Health Organization (WHO) was used to group all medications into categories according to the organ or system on which they act and their therapeutic.

- **Classification of indication:**

  The ***International Classification of Diseases (ICD-11)*** that developed by WHO was used to group the indications.

- **Determine the pattern of use:**

  Lexicomp was used as the standard reference for KKUH to determine the pattern of off-label medications.

- **WHOCC - ATC/DDD Index .WHO. Updated December 14, 2021. Accessed December 22, 2021. https://www.whocc.no/atc_ddd_index/**
- **ICD-11 for Mortality and Morbidity Statistics. WHO. Updated January 2022. Accessed January 5, 2022. https://icd.who.int/browse11/l-m/en**

Methods:

Statistical analysis:

- **A <u>descriptive analysis</u> of data collected from Form B was performed.**
- **All categorical variables were calculated as:**

  Frequency and **percentage** using Microsoft Excel®.
- **All Numerical variables were calculated as:**

  Frequency, **percentage**, **mean** and **median** using Microsoft Excel®.

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Results:

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- **Out of 512 reviewed forms**, (**92%**, n= 471) were **accepted** and (**8%**, n= 41) were **rejected**.
- **Out of 41 rejected forms,** (**70%**, n= 28) were **rejected due to stock unavailability.**
- **23% of the forms were supported by the evidence** provided by physicians/pharmacists, while 77% had no evidence to support its use.
- **Surgical department (50%),** dermatology department (16%), and neurology department (13%) were the **most common departments prescribing off-label medications.**

Table 1: Demographic characteristics

Characteristics	n	%	Mean	Median
Gender:				
Male	224	44	N/A	N/A
Female	288	56		
Age:				
>28 days- 23 months	10	2		
2-11 years	42	8		
12-17 years	31	6	40	39
18-65 years	372	73		
>65 years	57	11		
Body Mass Index (BMI):				
Underweight	47	9		
Normal weight	113	22	29	29
Overweight	115	22		
Obesity	226	45		
Missing	11	2		

Results:

Table 2: Prescribed class of medications

Prescribed class of medications (with examples)	n	%
Anti-infective agents: Vancomycin Vancomycin and Gentamicin	**262**	**51**
Immunomodulating agents: Rituximab Infliximab Methotrexate	**175**	**34**
Other agents: Respiratory system agents Cardiovascular system agents	**75**	**15**

Table 3: The most common indications for off-label prescription

Indications per anatomical groups (with examples)	n	%
Diseases of the musculoskeletal system or connective tissue Osteoarthritis Total knee replacement	**97**	**19**
Diseases of the skin Bechet disease Alopecia	**95**	**19**
Diseases of the nervous system Multiple sclerosis Epilepsy	**70**	**14**
Diseases of the respiratory system Interstitial lung disease Bronchiectasis exacerbation Asthma	**17**	**3**

Results:

- **Example of the specific indications are:**
  - Bechet disease.
  - Cytokine storm.
  - Hodgkin lymphoma.
  - Alopecia Universalis.
- **Example of patient special circumstances:**
  - Living away from Riyadh.
  - Unable to attend regularly to the hospital.

Table 4: Reasons for prescribing off-label medications

Reason	n	%
Failing previous medication/therapy, need aggressive treatment	157	31
Pre/post operative	139	27
Not filled by physician	131	26
Specific indication	43	8
Other reasons Side effect/complication of previous medication and therapy Patient special circumstances	42	8

Results:

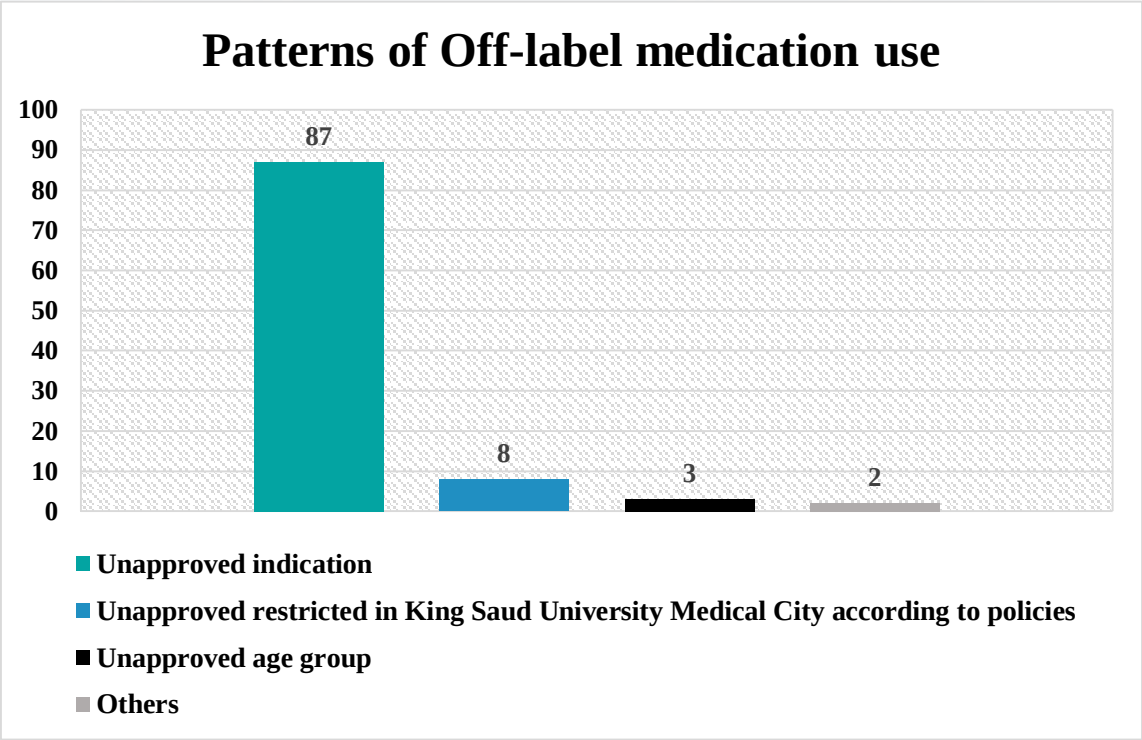

Figure 1: Pattern of off-label medication use

- To clarify, **8% of the total forms** filled by the physicians were **not considered an off-label medication** according to the definition, but since **prescribing some medications is restricted to certain departments due to King Saud University Medical City (KSUMC) policies,** physicians must fill the form if the medication prescribed not related to their specialties.

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Summary and Conclusion:

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- 92% of the forms were accepted. The most common class of medication prescribed were anti-infective agents and immunomodulating agents. Failing previous medication/therapy was common for prescribing off-label medication, while stock unavailability was the main reason for the rejected forms.

- Prescribing off-label medications is part of clinical practice where it's allowed, but negative consequences are possible. However, pharmacists can play a major role in preventing these consequences by reviewing off-label medication prescriptions and providing case-by-case evidence through a deep literature review.

- Our findings could form recommendations that would help in the revision of policies and regulations to improve OLMU in KKUH and other healthcare institutions in Saudi Arabia.

References:

- Stafford RS. Regulating Off-Label Drug Use — Rethinking the Role of the FDA. *N Engl J Med*. 2008;358(14):1427-1429. doi:10.1056/nejmp0802107
- Goločorbin Kon S, Iliković I, Mikov M. Reasons for and frequency of off-label drug use. *Med Pregl*. 2015;68(1-2):35-40. doi:10.2298/MPNS1502035G.
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Thank you

Do you have any question?