Are Drug Safety Measures Harmonized?  
A Real-World Data From Three Regulatory Authorities

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Presentation Outline

01 Introduction and Literature Review
02 Study Aims and Objectives
03 Study Methods
04 Study Results
05 Conclusion
Introduction and Literature Review
The Drug Cycle

Risk Minimization Measures (RMMs)

New Medicine

Clinical trial cycle

- Phase 1
- Phase 2
- Phase 3

Real World (Pharmacovigilance) cycle

- Periodic safety update
- Medicine marketed

Pre-clinical phase

Clinical development phase

Drug marketing phase
**What are RMMs?**

- Risk minimization measures (RMMs) are interventions intended to decrease or prevent the occurrence of adverse events associated with medications.
- Regulatory authorities, including SFDA, FDA, and EMA list risk minimization measures in their websites for specific medications.
# Published Literature on Differences Between Regulators

**FDA vs. EMA**

A study conducted in 2012 showed differences in RMMs, including:

- Differences in type of medications with risk measures
- Differences in documents/information across some medications

Study investigators suggested to update this comparison but no such update has been done.

**SFDA vs FDA and EMA**

- No study evaluated the differences between the published RMMs

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Saudi Food and Drug Authority (SFDA)

Food and Drug Administration (FDA)

European Medicines Agency (EMA)
Significance of The Study

- It is essential to have a consistent risk and benefit minimization measures across regulatory authorities.
- Differences in risk measures can impact medication use especially post-marketing.
- Unified RMMs data will facilitate the exchange of information between the regulators.
Study Aims and Objectives
Overall Study Aim

To compare the differences in RMMs between the SFDA, FDA, and EMA, in order to investigate whether there is a variability in measures done to optimize the risk and benefit of chemical entities and biologics.

Study Objectives

1. To describe the medication lists with RMMs across different regulatory authorities.
2. To compare the details of RMMs across regulatory authorities.

Risk Minimization Measures (RMMs)
Saudi Food and Drug Authority (SFDA)
Food and Drug Administration (FDA)
European Medicines Agency (EMA)
Study Methods
Study Design, and Source of Data

- Observational study
- Electronic search was done to retrieve publicly available information and documents of RMMs from the SFDA, FDA, and EMA websites
- All data are freely available online in regulators websites.
  - These medication data, do not include any patient information, therefore no IRB approval was needed for this study

Data Collection Process

Collect medication lists with RMMs data

Regulators websites were accessed to determine list of medications with RMMs

RMMs lists extraction

Medications with the same trade name were matched, then details of medication risks and RMMs content were extracted from each medication with RMMs in each regulatory authority

Content comparison

All risks and types of RMMs were compared

Risk Minimization Measures (RMMs)
Saudi Food and Drug Authority (SFDA)
Food and Drug Administration (FDA)
European Medicines Agency (EMA)
Study Results
Medications with RMMs in the SFDA’s (n=318)

Therapeutic classes of SFDA’s list

- Immunosuppressant: 19.9%
- Antihypertension: 11.4%
- Anticancer: 8.8%
- Antibiotic: 6.4%
- Antipsychotic: 5.7%
- Antidiabetic: 4.0%
- Antiviral: 4.4%
- Analgesic: 5.4%
- Anticoagulant: 4.0%
- Antiinflammation: 3.4%
- Others: 26.6%
318 medications with RMMs on SFDA website, 32 were group based and 28 were duplicated.

258 RMMs for unique products on SFDA website.

151 medications with RMMs also approved by the FDA.

95 medications with RMMs also approved by the EMA.

9 medications with RMMs comparable between SFDA and FDA.

71 medications with RMMs comparable between SFDA and EMA.

7 medications with RMMs comparable between SFDA, FDA, and EMA for the same products.
The 7 Matched Medications with RMMs Between Regulators

<table>
<thead>
<tr>
<th>Trade name (Scientific name)</th>
<th>Manufacturer name</th>
<th>RMM comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blincyto® (Blinatumomab)</td>
<td>Amgen</td>
<td>Similar</td>
</tr>
<tr>
<td>Kymriah® (Tisagenlecleucel)</td>
<td>Novartis</td>
<td>Similar</td>
</tr>
<tr>
<td>Lemtrada® (Alemtuzumab)</td>
<td>Sanofi</td>
<td>Similar</td>
</tr>
<tr>
<td>Tracleer® (Bosentan)</td>
<td>Janssen-Cilag</td>
<td>Different</td>
</tr>
<tr>
<td>Revlimid® (Lenalidomide)</td>
<td>Bristol-Myers Squibb Pharma</td>
<td>Similar</td>
</tr>
<tr>
<td>Prolia® (Denosumab)</td>
<td>Amgen</td>
<td>Different</td>
</tr>
<tr>
<td>Tysabri® (Natalizumab)</td>
<td>Biogen</td>
<td>Different</td>
</tr>
</tbody>
</table>
## Selected Examples for RMMs Content Comparison

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Risk</th>
<th>SFDA</th>
<th>FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprelsa® (vandetanib)</td>
<td>QT prolongation, Torsades de pointes, and sudden death</td>
<td>No RMM</td>
<td>Patient Brochure, Pharmacy Enrollment Form, Prescriber Enrollment Form</td>
</tr>
<tr>
<td>Remsima® (Infliximab)</td>
<td>Risk of Serious infections and HBV reactivation</td>
<td>HCP checklist, HCP guide, Patient card</td>
<td>No RMM</td>
</tr>
</tbody>
</table>

**Health care provider (HCP)**

**Hepatitis B virus (HBV)**
## Selected Examples for RMMs Content Comparison

<table>
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<tr>
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<th>EMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ozurdex®</strong> (dexamethasone)</td>
<td>Increased intraocular pressure, Glaucoma, Endophthalmitis, and Ocular hypertension</td>
<td>No RMM</td>
<td>Patient guide</td>
</tr>
<tr>
<td><strong>Revolade®</strong> (Eltrombopag)</td>
<td>Hepatotoxicity, Thrombotic/thromboembolic complications, Bone marrow reticulin formation and fibrosis, Haematological malignancies, and Post therapy thrombocytopenia</td>
<td>Patient support booklet, HCP safety guide</td>
<td>No RMM</td>
</tr>
</tbody>
</table>
This study shows substantial differences among the regulatory authorities regarding RMMs. Harmony in published risk measures can have a significant impact on medication safety.
Thanks

Feel free to ask

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