Recent Regulatory Updates in Jordan FDA

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Senior Regulatory Pharmacist at Registration Department/JFDA

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27-30 January - DC – USA
About me

1. I am 43 pharmacist holding bachelor’s degree in Pharmacy from Jordan in 1999.


3. Senior Regulatory pharmacist in Jordan food and drug administration (JFDA) since 2008:
   - Secretary of the higher Drugs committee.
   - Head of the post approval changes committee.
   - Secretary of the technical committee for originator products.
   - Ideal employee for the year 2013.

4. Member board of the Jordan pharmacy association (JPA) since 2017.

5. The oldest sister (the mother) in my small family (father & 2 sister).
“Maintaining public health by offering preventive, treatment and health control services, as well as organizing and supervising health services offered by the public and private sectors.”

His Majesty King Abdullah II
Jordan Food and Drug Administration “JFDA”

- was established in April 2003, supported by legislation and guidelines. (previously was apart of MOH).
- The first independent authority model in our region so it become a model to follow in the region regarding setting the regulations.
- Achieves significant success on its role as regulatory agency by setting and implementing clear regulations in line with international guidance US-FDA, EMA, ICH,.... taking into consideration the need for world wide harmonization to ensure food and drug safety and efficacy.
Highest JFDA priorities

➢ To be recognized world wide.

➢ To maintain safety and efficacy of the drugs.

➢ To be always harmonized with the international guidance US-FDA, EMA, ICH,.... to ensure drug safety and efficacy.

➢ To be accredited as training centre at national, regional, international level, conducting training and building capacity to countries in region.

( many training sessions / Diploma were held )
Highest JFDA priorities

➢ to encourage local industries keeping applying GMP, competing, developing and expanding within the challenging regional market noting that recently Jordanian manufacturing companies are producing Biosimilars via contract manufacturing.
JFDA’s Organizational Structure
Drug Directorate: The only official body that is responsible for regulating all aspects related to medicines throughout the full lifecycle.

Scope of activities:
- Marketing Authorizations (Registration of Products)
- Sampling & Laboratory analysis.
- Lot release
- Post-marketing surveillance
- Monitoring and inspections
- Clinical trials monitoring
- Price regulation
- Raising public awareness.
- Rational drug use
Mission of Drug Directorate

JFDA

To maintain the safety and efficacy and good quality of products including infants milk formula and their special formula, medicinal plants, natural products, pharmaceutical preparations containing vitamins and minerals, and any other substances related to treatment or cure of human beings from diseases at affordable price.
Achievements of Drug Directorate in JFDA Registration Division

Registered in 2019

- Generic products: 176
- Origenator (NCE & BLG): 72
- Biosimilar product (BLS): 4
- Vaccine & Sera: 11
- Herbal drugs: 7
- Vitamins / Infant...: 96

Registered in 2019
Achievements of Drug Directorate in JFDA
Clinical Division

- Number of B.E studies approved in 2019: 160
- Number of Clinical trials approved in 2019: 43
Achievements of Drug Directorate in JFDA Inspection Division

To Accredit GMP

- Local Manufacturers being inspected in 2019: 92%
- International Manufacturers being inspected in 2019: 8%
In Biological & biosimilar application we have to Accredit both the API & FP manufacturing site:

- if the manufacturing site is not accredited, the site should be inspected to be accredited or as recommended by the committee, JFDA Director can replace the inspection in case of providing any of the following documents:

- CPP from the relevant authority in the USA or from the (EMA) or Japan or Canada or two CPP from the responsible authorities in two accredited countries from the following list: (United Kingdom, Germany, France, Belgium, Switzerland, the Netherlands, Sweden, Austria, Australia, Finland and Spain).

The CPP must be for the same product in case of biological & biosimilar.
Entrepreneurship & Global Harmonization

1- JFDA became a new ICH observer in 2019

2- Pre-accession member / pharmaceutical inspection cooperation scheme.
Entrepreneurship & Global Harmonization

3- Automating regulatory submission process by launching eCTD in 3/2019 in addition to the adoption of Drug Workflow System (eJDWS) for files and variations submissions, send inquiry to the applicant.

JFDA Drug Workflow System

Please use the username and password provided to you by the JFDA to access the eJDWS.

<table>
<thead>
<tr>
<th>JFDA adopted Drug Workflow System</th>
<th>Password</th>
</tr>
</thead>
</table>

Forgot Password? Sign In
1- JFDA adopted an accelerated approval on 20/2/2019 as follows:-

➢ Any originator products (NCE, biologics, Biosimilar, vaccine and sera) have both EMA and US FDA approval should be registered within 60 days from the date of submission.

➢ Any originator products (NCE, biologics, Biosimilar, vaccine and sera) have either EMA or US FDA approval should be registered within 90 days from the date of submission.

(This will speed marketing authorization and patient access to new drugs with positive benefit – risk balance and avoid duplication and use resource efficiently).

About 30 products were registered by the fast track line.
JFDA latest updates

❖ JFDA updated PAC guidelines in 2017 (harmonized) by changing the category of variation (about 28) from registration approval (RA) to Notification form (N1, N2) this reduce time line to get approval “On spot approval (PAC for vaccines & BLG were added

❖ New guidance for API supplier accreditation (after the saratns crisis) in 2019.


❖ New guidance for Value added medicine in 2018 (Leaders in the region)

❖ New legislation about vitamins and herbal product in 2018.

❖ 10- Updating the guidelines for the registration of radio active materials (under process).
JFDA Trend in Biosimilar
History for biosimilars guidelines

2004
Criteria for Registration & Re-registration of all drugs
Concept of biosimilars not mentioned

2008
Update manufacturing sites accreditation criteria of biologicals (to include API sites/ per product)

2009
Draft guidance for biologicals & biosimilars/ CTD format for all drugs
Apply EMA guidelines

2012
First biosimilar registered according to EMA regulations (Epoetin alfa)

5/2015 guideline for Biosimilars registration in Jordan Was issued.
History for biosimilar guidelines

All biosimilar products being registered before 5/2015

Should fulfil all the JFDA biosimilar guidelines at the time of the renewal of the file.
JFDA: adopted the EMA Model
Comparability studies

Guideline on Similar Biological Medicinal Products
Overarching

Guideline on Similar Biological Medicinal Products
Containing Biotechnology-Derived Proteins as Active Substance: Quality Issues

Guideline on Similar Biological Medicinal Products
Containing Biotechnology-Derived Proteins as Active Substance: Nonclinical & Clinical Issues

General Applicable to all Biosimilars

Specific: Product data requirements

Epoetin
G-CSF
Insulin
HGH
Heparin LMWH

MAB
Somatropin
FSH
Interferon Beta
Interferon Alpha
Divisions in the Drug Directorate – JFDA involved in evaluating the Biosimilar files

- Registration
- Inspection
- P.V
- Pricing
How the biosimilar application is reviewed

Submission of the application (process)

Reviewed by the committees (process)

Registered and priced
NCE & BLG product after being registered may get the following if the application met the requirement:

- Data protection (at registration)
- Indications protection (PAC)
<table>
<thead>
<tr>
<th>INN Name of biosimilar</th>
<th>Applications Status</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin sodium (LMWHs)</td>
<td>Rejected 2009</td>
<td>No data to prove comparability with reference</td>
</tr>
<tr>
<td>Erythropoietin (rHu EPO)</td>
<td>Rejected 2011</td>
<td>No data to prove comparability with reference</td>
</tr>
<tr>
<td>Filgrastim</td>
<td>Rejected 2012</td>
<td>No data to prove comparability with reference.</td>
</tr>
<tr>
<td>r-Streptokinase</td>
<td>Rejected 2012</td>
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<tr>
<td>Enoxaparin sodium (LMWHs)</td>
<td>Rejected 2019</td>
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**Biosimilars Rejected in Jordan**

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<td>Eptacog Alfa</td>
<td>Rejected 2019</td>
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<tr>
<td>Rituximab</td>
<td>Rejected 2019</td>
<td>No data to prove comparability with reference.</td>
</tr>
<tr>
<td>Follitropin Alfa</td>
<td>Rejected 2019</td>
<td>No data to prove comparability with reference.</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Rejected 2019</td>
<td>No data to prove comparability with reference.</td>
</tr>
<tr>
<td>Trade name</td>
<td>INN Name of biosimilar</td>
<td>Indication Refer to approved leaflet published on JFDA website</td>
</tr>
<tr>
<td>-----------------------</td>
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<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Binocrit PFS /Sandoz</td>
<td>Epoetin alfa</td>
<td>Anaemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic kidney failure</td>
</tr>
<tr>
<td>Omnitrope Cart. /Sandoz</td>
<td>Somatropin</td>
<td>Growth hormone deficiency in adults and children</td>
</tr>
<tr>
<td>Nivestim PFS /Hospira</td>
<td>Filgrastim</td>
<td>Cancer</td>
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<tr>
<td></td>
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<td>Haematopoietic stem cell transplantation</td>
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<tr>
<td>Insugen-R vial (Biocon/ JPM)</td>
<td>Soluble Insulin</td>
<td>DM</td>
</tr>
<tr>
<td>Ritox vial Mabsience/ MS Pharma- Jordan 500/ 50 ml Conc. For solution for infusion</td>
<td>Rituximab</td>
<td>Approved only for some indications of reference product</td>
</tr>
</tbody>
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# Biosimilars Registered in Jordan

<table>
<thead>
<tr>
<th>Trade Name</th>
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<th>Indication Refer to approved leaflet published on JFDA website</th>
<th>Reference Biological Product (company)</th>
<th>Date approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Truxima 100mg and 500 mg vial (Celltrion Inc Hikam –Jordan)</td>
<td>Rituximab</td>
<td>Approved for all indications of reference product</td>
<td>Mabthera (Roche)</td>
<td>2019</td>
</tr>
<tr>
<td>Hertraz 440 mg vial (Maylan –India)</td>
<td>Trastuzumab</td>
<td>Approved only for some indications of reference product</td>
<td>Herceptin (Roche)</td>
<td>10/2019</td>
</tr>
</tbody>
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## Biosimilars Registered in Jordan

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<th>Reference Biological Product (company)</th>
<th>Date approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amgevita Amgen -USA</td>
<td>Adalimumab</td>
<td>Approved only for some indications of reference product since the reference got data protection for them.</td>
<td>Humira</td>
<td>3/10/2019</td>
</tr>
<tr>
<td>Herzuma 440 mg &amp; 150 mg powder for concentrate for solution for infusion Celltrion Inc. / Korea &amp; Hikma / Jordan</td>
<td>Trastuzumab</td>
<td>Approved for all indications of reference product</td>
<td>Herceptin</td>
<td>24/9/2019</td>
</tr>
</tbody>
</table>
Challenges Related to Biosimilars

PAC
- Harmonization.
- Some not covered.
- Depend on case by case basis.

International differences in guidelines (FDA/EMA)
- No. of subjects
- No. of Batches
- Age of batches in the comparability exercise.

Limited resources
- Human (experts in field of biologicals)
- Financial

Reference product
- May not be registered.
- Limited data on reference product (No. of subjects of different studies, No. of batches used in comparability exercise.
- If registered may not be of same manufacturing site for e.g.

Extrapolation.

Use of Brand Names.
- Traceability
- PV

Interchangeability/Substitution
- Automatic substitution not allowed.
- Switching only by physician.
- Might not have same indications

Bridging.
- Complex heterogeneous compounds to be fully characterized.
- Depend on case by case basis.

Lab test.
Thank you!

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