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EDITORIAL

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The role of a drug regulatory authority is not only limited to drug authorization, but it is also responsible for maintaining the rigor of an approval process towards patients' safety. Achieving regulation is not an easy task as it is critical to monitor the stages of therapy availability, quality drug distribution channel, reports of fake/spurious drugs, and the safety of patients or consumer. Regulatory authorities with their comprehensive updated guidelines keep regulating these challenges globally; however, extra efforts are needed from the organizations and governments to combat the challenges in tandem.

We are pleased to present this Vol. III Issue III of S&A – Pharma Newsletter. Through this Newsletter, we aim to share recent information allied to regulatory reforms and updates from pharmaceutical sector in India as well as from foreign jurisdictions, based on information collated through research and appraisal of applicable statutory provisions.

In the present issue, we start with a discussion on the Central Government's notification asking Indian drug manufactures to write safety warning on the label of SGLT-2 inhibitors class of antidiabetic drugs. Going forward, this edition addresses DoP's draft Clinical Establishment (Central Government) Second Amendment Rules, 2019, which emphasizes that report or the lab test should be performed under the proper guidance of the medical practitioner. This issue then, discusses the new Drugs and Clinical Trials Rules, 2019, which aims to promote clinical research in the country via offering transparent and faster approvals clinical trial process. The issue then covers the new labelling specifications, which state that now generic names on new drug formulation too are to be labeled with larger font size than the brand name font size. The next article covers the National Pharmaceutical Pricing Authority slashing MRP of almost 462 branded anti-cancer drugs under Trade Margin rationalization method. Further, this edition addresses the Progress in Tuberculosis eradication program in India, where health ministry has stressed on the importance of health care professionals and community partners, while dealing with TB patients.

From the international arena, we talk about recent regulatory reforms concerning various health issues and the health reports focusing on improving health in countries. First is European Commission's approval to Roche's MabThera® (rituximab) , first biological treatment for moderate to severe pemphigus vulgaris (PV). Next, we discuss EMA's safety warning for Pfizer's Xeljanz. Going ahead,

there are notes on USFDA approval to 1) Cimzia (certolizumab pegol) injection for treatment of adults with a certain type of inflammatory arthritis, and 2) Zulresso (brexanolone) intravenous (IV) formulation for the treatment of postpartum depression (PPD) in adult women. We wrap this issue with a new guidance on Global Influenza Strategy for years 2019-2030 launched by World Health Organization.

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Trust you enjoy reading this issue as well. Please feel free to send your valuable inputs / comments at newsletter@singhassociates.in

Thank you.

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Contents

DCGI asked manufacturers to write safety warning for SGLT2 inhibitors

On 25 March 2019, in response to an alert raised by US FDA and Health Canada in regard to the safety of Sodium-Glucose Cotransporter -2 (SGLT-2) inhibitors of Johnson & Johnson and Boehringer Ingelheim India, the Drug Controller General of India (DCGI) has asked Indian Pharmacopoeia Commission (IPC) to provide information on Adverse Drug Reactions (ADRs) or any signal on SGLT-2 inhibitors emphasizing the acute pancreatitis and Fournier's gangrene in Indian patients received under Pharmacovigilance Programme of India (PvPI). Further to this response, 'Central Drugs Standard Control Organization has published a safety warning for all the manufactures dealing with manufacturing of Sodium-Glucose Cotransporter -2 (SGLT-2) inhibitors class of drug including canagliflozin, dapagliflozin and empagliflozin.

The basis of Safety Warnings:

Health Canada: It has published Summary safety Review of SGLT2 inhibitors by assessing the potential risk of inflammation of the pancreas on 20.07.2018. The review further concluded that there may be a link between the use of SGLT2 inhibitor and acute pancreatic.

USFDA: The safety announcement was given on 29.08.2018and warnings were given that cases of rare but serious infection of genitals and areas around the genitals have been reported with this class of type 2 diabetes. I.e. Sodium-Glucose Cotransporter -2 (SGLT-2) inhibitors.

Further Subject expert committee has recommended certain points based on these findings:

- Data should be obtained from PvPI regarding any new signal based on SGLT-2 inhibitors based on above two conditions in Indian patients.
- CDSCO should monitor any further new findings with SGLT-2 inhibitors.[1]

In response to above discussion, PvPI was requested to provide the information about the details ADRs and any signal on SGLT-2 inhibitors emphasizing the acute pancreatic and Fournier's gangrene in Indian Patients.

Warning:- *Cases of rare but serious infection of the genitals and area around the genitals have been reported with this class of type 2 diabetes medicines I.e. Sodium-Glucose Cotransporter -2 (SGLT-2) inhibitors.*

Conclusion:

The latest finding published by Health Canada and US FDA in concern of new adverse events associated with Sodium-Glucose Cotransporter -2 (SGLT-2) inhibitors (pancreatic and genitals infection) had made DCGI to further the information on Adverse Drug Reactions (ADRs) or any signal on SGLT-2 inhibitors from PVPI. Further, CDSCO has published a safety warning for all the manufacturers to be printed at the label of these class of drugs.

1 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NDI2Mg==the

Government proposes second draft amendment of Clinical Establishment Rules, 2019

Recently, Union Health and Family Welfare Ministry issued draft *Clinical Establishment (Central Government) Second Amendment Rules, 2019 (the 'Amendment Rules') on 18 march 2019* enforcing changes in the human resource at small diagnostic laboratories in the existing pathology laboratory rules.[2]

Key Points of the amendment:-

The existing Clinical Establishments (Central Government) Amendment Rules, 2018 (the 'Rules') do not mention the qualification of authorized signatory at basic composite laboratories; hence, the amendment made in the Rules has covered the following points:

- After entries relating to *serial No 1 of schedule of Clinical Establishment Rule 2018,* which states that test can be performed in mobile laboratory at field locations also. *Now the following note should be inserted "Medical test should normally be undertaken on the advice of a doctor".*

- *At serial No 3 of schedule of Clinical Establishment Rule 2018 which states about the* Minimum qualification of Technical Head of Laboratory or Specialist or Authorized Signatories *the following note should be inserted*

    - *In column two for "the word the authorized signatory will be liable for authenticity of laboratory test report" the word "the authorized signatory will be liable for authenticity of laboratory test report only" shall be substituted.*

    - In column three for the word *"Wherever interpretation of lab results or opinion there on are required, registered Bachelor of Medicine and Bachelor of Surgery (MBBS) medical practitioner is essential",* the words *"Interpretation of lab results or opinion there on when required, registered Bachelor of Medicine and Bachelor of Surgery (MBBS) medical practitioner is essential" shall be substituted.*

The amendment added the special instruction regarding the medical laboratories and their authorization status along with the need of the medical practitioner for checking the authenticity of the Report

Reported draft notification on revised Rules is based on recommendations of a panel set up by the ministry on August 04, 2018. The panel comprised of principal scientific advisor to government of India as chairman, secretary (health), secretary (health research) and secretary (biotechnology) as members.

Conclusion:

The current amendment provides the proper guideline for the laboratories performing the test and have all the rules and regulation which helps to check the authenticity of the report. Along with this the new amendment emphasizes that report or the lab test should be done under the proper guidance of the medical practitioner.

2 https://mohfw.gov.in/eventsandannouncements/draft-notification-regarding-clinical-establishment-central-government-second

The New Drugs and Clinical Trial Rules, 2019

On March 19, 2019, the Union Ministry for Health and Family Welfare notified the *new Drugs and Clinical Trials Rules, 2019*[3] (the 'Rules') aiming to promote clinical research in the country via transparent and faster approvals process. The new rule will be applicable to all new drugs, ethics Committee and investigational new drugs intended for human use, clinical trial, and bioequivalence study. The new rules brings more clarity in terms of:

Clinical Trial of New drugs:

Clinical trial of indigenously developed drug: The Rules provide that any drug discovered in India, or research and development of the drug are being done in India, and which is proposed to be manufactured and marketed in the country, will be deemed approval for clinical trials within 30 working days by Central Licensing Authority (CLA). If no communication has been received from the CLA to applicant, the permission to conduct clinical trial shall be deemed to have been granted.

Clinical trial of Drug developed outside of India: For the clinical trial of drugs developed outside of India, which is already approved and marketed in a country, 90 working days is set as the limit for the CLA to respond.

The validity of clinical trial approvals has been determined as two years for pharmaceutical companies to initiate a study, which is extendable by one year.

Post-trial access of new drug:

The Rules introduced the conditions for providing post-trial access of drugs to patients who require it for the first time. According to this the sponsor shall provide the investigational drug to the trial subject free of cost-

- if the clinical trial is being conducted for an indication for which no alternative therapy is available and the investigational new drug or new drug has been found to be beneficial to the trial subject by the investigator; and
- if the trial subject or legal heir of such subject, as the case may be, has consented

Drug import for sale or distribution:

The Rules exempts local clinical trials for new drugs permitted to be imported for sale or distribution in India, to provide early access to patients to drugs already approved in the countries specified by the DCGI provided that -

- if no major unexpected serious adverse events have been reported for the drug, and
- where the applicant is agree to conduct Phase IV clinical trial to establish safety and effectiveness of such new drug, and
- If the drug is indicated in life threatening or serious diseases or diseases of special relevance to Indian health scenario or for a condition which is unmet need in India such as XDR tuberculosis, hepatitis C, H1N1, dengue, malaria, HIV, or for the rare diseases for which drugs are not available or available at a high cost or if it is an orphan drug.

Compensation and monitoring:

The Rules aim to ensure patient safety in clinical trials via defining the process of informed consent, ethics committee, monitoring and compensation in cases of adverse events.

3 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NDI2MQ==

The Rules mandate that in case of injury to the clinical trial subject, medical management will be provided as long as required as per the opinion of the investigator or till such time it is established that the injury is not related to the clinical trial.

Compensation in cases of death and permanent disability or other injuries to a trial subject will be decided by the Drug Controller General of India.

Orphan drugs:

For the first time, orphan drugs have been defined as a drug intended to treat conditions which affects not more than five lakh persons in India. In addition No fee shall be chargeable in respect of application for conduct of clinical trial for orphan drugs for rare diseases in India. Moreover, the Rules exempt local clinical trials for orphan drugs permitted to be imported for sale or distribution.

Conclusion:

the Rules are comprehensive, well balanced policy and will improve the ethical and quality standards of clinical trials in the country, which will further benefit patients. The conditions of waiving local clinical trial under these Rules will help early access to drugs for patients in India. Where the deemed approval for clinical trials in 30 working days for indigenous drug will speed up the trial process and also encourage local drug development.

Now New drug formulation too be labeled with bigger generic names than brand name

On March 06, 2019, the Central Government proposed labeling specifications for import and manufacturing permission of New Drug Formulation under form 45/46 of Schedule A of Drugs and Cosmetics Act, 1940 (the 'Act') shall come into force from April 1st 2019[4].

Earlier the Central Government via Drugs and Cosmetics (First Amendment) Rules, 2018 has amended the manner of labeling of drugs under Rule 96 of Drugs and Cosmetics Rules, 1945[5] (the 'Rules'). Which instructed drug manufacturers to label generic name of drug or fixed dose combination drug at least two font size larger than the brand name or the trade name, if any. Further, the implementation of these labeling norms was announced on voluntary basis for a period from September 13th 2018 to March 31st 2019 and mandatory from April 1st 2019[6]. The said labeling norms was applicable on:

- Schedule F or Schedule F (1) drugs as provided under the Act;
- drugs included in the Indian Pharmacopoeia (IP) or the official pharmacopoeias and official compendia of drug standards prescribed in Rule 124 of the Rules,
- drugs included in the National Formulary of India (NFI),
- other drugs, the international non-proprietary name, if any, published by the World Health Organisation or where an international non-proprietary name is not published, the name descriptive of the true nature or origin of the substance;

However, these norms would not cover the fixed dose combinations of vitamin and other fixed dose combinations containing three or more than three drugs.

Labelling of medicines with a caution or warning

Earlier, the Drugs and Cosmetics (Fifth Amendment) Rules, 2018 notified the voluntarily labeling of high-risk medicines with caution and warning effective from November 1st 2018. The high-risk medicines includes the 'Narcotic analgesics, hypnotics, sedatives, tranquillisers, corticosteroids, hormones, hypoglycemic, antimicrobials, antiepileptics, antidepressants, anticoagulants, anti-cancer drugs and all other drugs falling under Schedules G, H, H1 and Schedule X whether covered or not in the said schedules[7]. However, the Drugs and Cosmetics (Ninth Amendment) Rules, 2019 has announced this labeling requirements shall be mandatory from April 1st, 2019[8].

Now, the import and manufacturing permission of drug formulation granted under Form 45/46 also requires Labelling of these formulation with a caution or warning, as applicable, depending on whether the drug is covered under Schedule G or Schedule H or Schedule H1 or Schedule X, as specified in rule 97, in legible black colored font size in a completely red rectangular box.

Conclusion:

The labelling changes will not affect the quality, safety and efficacy of drug product. But it is expected to promote the usability of generic drugs to the patients. Whereas, the implementation date of labelling changes will create difficulty for drug manufacturers, as they generally keep one year stock of packing materials in advance, and the

4 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NDE0Ng

5 http://egazette.nic.in/WriteReadData/2018/183769.pdf

6 https://lexcomply.com/rsjadmin/news/201812195052Notification%20GSR%201161(E)-%20%20Drugs%20and%20Cosmetics%208th%20Amendment%20Rules%202018.pdf

7 http://www.cdsco.nic.in/writereaddata/gsr408.pdf

8 http://www.egazette.nic.in/WriteReadData/2019/200553.pdf

products get consumed during peak season ranging from April to September. Hence manufacturers expects some more time to implement this packaging changes to avoid losses.

NPPA slashed Prices for 462 branded anti-cancer drugs

Earlier On 27th February, 2019, National Pharmaceuticals Pricing Authority (the 'NPPA') listed 42 anti-cancer drugs under 30% Trade Margin rationalization. In this view, drug manufacturers and Hospitals were asked to convey revised MRP of these drugs on the basis of revise Trade Margin (TM) formula.

Now therefore, the NPPA listed out the MRP price of 390[9] non-scheduled anti-cancer medicines based on the data received till March 07, 2019. The revised prices made effective from March 08, 2019[10]. In addition to this NPPA on March 19, 2019 listed out 54[11] more branded anti-cancer drugs under this price revision, making it effective from March 08, 2019. Prices of more brands are expected to show downward reduction in near future, as data is received from other manufacturers.

The MRP reduction of 390 anti-cancer non-scheduled medicines were recorded up to 87%. 390 brands i.e. 91% of the 426 brands reported by manufacturers, showed downward price movement as described below:

Range	No. of Brands
75% & above	38
50% to <75%	124
25% to <50%	121
Below 25%	107
Total	**390**

The price so fixed shall be valid for one year from the date of notification. The price computed for non-scheduled formulations (all strengths and doses form) (whether individual or in combination, irrespective of dosage strength, dosage form and /or route of administration) under this Order containing any of the drugs listed in 42 drugs shall be applicable even if the formulation is being used for other therapeutic uses.

The manufacturers of the formulations are required to maintain the present production levels. Any manufacturer intending to lower the average monthly production levels will seek prior permission from NPPA. Further, any manufacturer intending to discontinue production of above said formulations shall furnish information to the NPPA, in respect of discontinuation of production and / or import of said formulation in Form-IV of Schedule-II of the Drugs Price Control Order, 2013 at least six months prior to the intended date of discontinuation.

State Drug Controllers shall monitor the compliance of this Order by the manufacturers / dealers / Hospitals / Medical Institutions and the manufacturers / dealers / Hospitals / Medical Institutions shall assist the State Drug Controllers in verifying the compliance to this order. Any violation of this Order is required to be brought to the notice of NPPA.

Conclusion:

The average out of pocket expenditure for cancer patients is 2.5 times that for other diseases. This move is expected to benefit 22 lakh cancer patients in the country and would result in annual savings of approx. INR 800 crores to the consumers. The Trade Margin rationalizations for these 42 anti-cancer drugs was rolled out as Proof of Concept, stressing on the new paradigm of self-regulation by the Industry.

9 http://www.nppaindia.nic.in/wp-content/uploads/2019/03/Brands-List-for-OM.pdf

10 http://pib.nic.in/PressReleaseIframePage.aspx?PRID=1568297

11 http://www.nppaindia.nic.in/wp-content/uploads/2019/03/Annexure-Z.pdf

Progress in Tuberculosis eradication in India

On Mar 20, 2019, World Health Organization (WHO) issued guidelines "WHO Consolidated Guidelines on Drug-Resistant Tuberculosis Treatment" (the 'Guidelines') to accelerate the treatment of tuberculosis for proper eradication of the multidrug resistant TB (MDR-TB) as the Guidelines recommend the complete use of oral regimens to treat the patients with multidrug resistant TB (MDR-TB). According to the reports, the strains of drug resistance (DR-TB) Tuberculosis are more difficult to treat than drug-susceptible ones, hence there was a critical need for the policy for the treatment and care of patients with DR-TB.

The main feature of the WHO guidance for the proper eradication multidrug resistant TB (MDR-TB) are:

- The consolidated guidelines include policy recommendations on treatment regimens for isoniazid-resistant TB (Hr-TB) and MDR/RR-TB, including longer and shorter regimens, culture monitoring of patients on treatment, the timing of antiretroviral therapy (ART) in MDR/RR-TB patients infected with the human immunodeficiency virus (HIV), and use of surgery for patients receiving MDR-TB treatment, and optimal models of patient support and care.
- A dashboard to help countries know more about their own epidemics through real-time monitoring – by moving to electronic TB surveillance systems.
- A guide for effective prioritization of planning and implementation of impactful TB interventions based on analyses of patient pathways in accessing care.
- New WHO guidelines on infection control and preventive treatment for latent TB infection
- A civil society task force to ensure effective and meaningful civil society engagement

In India, the government is committed to elimination of TB in the country by 2025. On the occasion of '*World TB Day 2019*[12]' the health ministry has stressed on the importance of more sensitive and responsive doctors, paramedics, frontline health workers and community partners, while dealing with TB patients. The ministry also announced the significant progress in TB eradication programme, as India is now closest ever to covering all TB cases with 21.5 lakh new TB patients notified in 2018.

The health ministry also announced that a total of 15 lakh patients have been initiated in the Fixed Dose Combination (FDC) regime till date. TB forums at various levels in the states have been formed to remove stigma and to create awareness about the symptoms of the disease and the free treatment available at the government health facilities. 1180 CBNAAT labs have been made operational throughout the country, along with 4 lakh treatment support centres at the village level. These efforts have resulted in increased from 25% to 83% in the treatment success rates (2017-2018), and the TB prevalence rates have come down from 29% to 4%.

Conclusion:

The treatment of DR-TB and MDR-TB stains has raised a biggest concern worldwide. Hence, These guidance will help the countries all around the world to accelerate progress and act on the high-level commitments made in the first-ever UN High Level Meeting on TB last September, especially communities facing socio-economic challenges, those working and living in high-risk settings, the poorest and marginalized.

12 http://pib.nic.in/newsite/PrintRelease.aspx?relid=189521

European Commission approval to rituximab is first biologic treatment for a rare autoimmune disease

On March 15, 2019 European Commission has approved Roche's MabThera® (rituximab) for the treatment of adults with moderate to severe pemphigus vulgaris (PV), a rare condition characterized by progressive painful blistering of the skin and/or mucous membranes. Extensive blistering can lead to serious, life-threatening fluid loss, infection and/or death[13].

MabThera is the first biologic therapy approved by the European Commission for PV and the first major advancement in the treatment of the disease in more than 60 years.

The approval of MabThera is based on data from the phase III Ritux 3 trial, a Roche-supported randomised controlled study, conducted in France, which evaluated MabThera plus a tapering regimen of oral corticosteroids (CS) compared to a standard dose of CS alone, as a first-line treatment in patients with newly diagnosed moderate to severe pemphigus. The primary endpoint of the study was complete remission at month 24 without the use of CS for two or more months. The study demonstrated that 89.5% of people with PV treated with MabThera, in combination with short-term oral CS treatment, achieved complete remission without the use of CS for two or more months, compared to 27.8% of people with PV receiving CS alone.

About MabThera?

MabThera (rituximab) is the first therapeutic monoclonal antibody to target cells that have the CD20 marker on their surface. These cells are central to many blood cancers, including common forms of lymphoma and leukaemia. MabThera attacks these cells both directly and together with the body's immune system.

MabThera is already approved to treat four autoimmune diseases:

- Rheumatoid arthritis: MabThera in combination with methotrexate is indicated for the treatment of adults with severe active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies.
- Granulomatosis with polyangiitis and microscopic polyangiitis: MabThera/Rituxan, in combination with glucocorticoids, is indicated for the treatment of adults with severe, active granulomatosis with polyangiitis (Wegener's, GPA) and microscopic polyangiitis (MPA). People with serious infections should not receive MabThera/Rituxan. It is not known if MabThera/Rituxan is safe or effective in children
- Chronic lymphocytic leukaemia (CLL): MabThera in combination with chemotherapy is indicated for the treatment of patients with previously untreated and relapsed/refractory CLL.
- Non-Hodgkin's lymphoma (NHL): MabThera is indicated for the treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy. MabThera is indicated for the treatment of patients with CD20 positive diffuse large B cell non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy.

About pemphigus vulgaris (PV)

Pemphigus vulgaris is an autoimmune, blistering disease, occurring within the epidermis, affecting the skin and mucous membranes. It is the most common type of a group of autoimmune disorders collectively called pemphigus. It is estimated that around three in every 100,000 people are diagnosed with this disease globally.

Note- MabThera is marketed as Rituxan in in the United States, Japan and Canada. Following approval by EC the MabThera is now approved to treat four autoimmune diseases in the US and Europe.

13 https://www.roche.com/media/releases/med-cor-2019-03-15.htm

EMA Publishes safety warning for Pfizer's Xeljanz

On Mar 20, 2019 the European Medical Agency (EMA) has issued advice to healthcare professionals and patients on the increased risk of blood clots in the lungs and death when exceeding dose of Xeljanz (tofacitinib) for treating rheumatoid arthritis then the recommended dose[14]. In the European Union (EU), 5 mg twice daily is the recommended dose for rheumatoid arthritis and psoriatic arthritis. The higher dose of 10 mg twice daily is approved for the initial treatment of patients with ulcerative colitis.

The advice follows early results from an ongoing, open-label clinical study (A3921133) evaluating the safety of tofacitinib 5 mg twice daily and tofacitinib 10 mg twice daily compared with a tumour necrosis factor (TNF) inhibitor in patients with rheumatoid arthritis. Patients in the study are 50 years of age or older with at least one additional cardiovascular risk factor. The preliminary results of the study showed the overall incidence of pulmonary embolism to be 5-fold higher in the tofacitinib 10 mg twice daily arm of the study compared with the TNF inhibitor arm, and approximately 3-fold higher than tofacitinib in other studies across the tofacitinib program. While full results are awaited, EMA has published advice:

For patients:

- If you are being treated with Xeljanz, you should not change the dose or stop taking the medicine without discussing it with your doctor.
- You should seek medical attention immediately if you experience the sign and symptoms which of a blood clot in your lungs such as: difficulty breathing, chest pain or pain in your upper back, coughing up blood, excessive sweating and bluish skin.
- If you have any concerns about your medicine, you should discuss them with a healthcare professional.

For healthcare professionals:

- While further assessment of the study results continues, prescribers should continue to adhere to the authorised dose of 5 mg twice daily for the treatment of rheumatoid arthritis.
- Patients receiving tofacitinib, irrespective of indication, should be monitored for the signs and symptoms of pulmonary embolism, and be advised to seek medical attention immediately if they experience them.

Moreover, a letter is also being sent to all healthcare professionals expected to prescribe the medicine to inform them of the preliminary results of the study and the current treatment recommendations.

About Xeljanz (tofacitinib)

Xeljanz is a prescription medicine called a Janus kinase (JAK) inhibitor indicated to treat adults with moderate to severe rheumatoid arthritis and psoriatic arthritis. In these indications, Xeljanz is used together with methotrexate after treatment with one or more medicines known as disease-modifying anti-rheumatic drugs (DMARDs) has not worked well enough or has led to troublesome side effects. In patients with rheumatoid arthritis, Xeljanz can also be used alone in patients who cannot take or are intolerant to methotrexate. Xeljanz is also authorised to treat adults with moderate to severe ulcerative colitis (a disease causing inflammation and ulcers in the lining of the gut), after treatment with other medicines has not worked well, has stopped working or has led to troublesome side effects.

14 https://www.ema.europa.eu/en/news/increased-risk-blood-clots-lungs-death-higher-dose-xeljanz-tofacitinib-rheumatoid-arthritis

USFDA approves first and only treatment for a type of inflammatory arthritis

On March 28, 2019, the U.S. Food and Drug Administration (USFDA) approved Cimzia (certolizumab pegol) injection for treatment of adults with a certain type of inflammatory arthritis called non-radiographic axial spondyloarthritis (nr-axSpA), with objective signs of inflammation[15]. This is the first and only treatment for nr-axSpA approved by USFDA.

The approval followed by the efficacy trial *C-AXSPAND Phase 3*, Cimzia was studied in 317 adult patients with nr-axSpA with objective signs of inflammation, indicated by elevated C-reactive protein (CRP) levels and/or sacroiliitis (inflammation of the sacroiliac joints) on MRI. The trial measured the improvement response on the Ankylosing Spondylitis Disease Activity Score, a composite scoring system that assesses disease activity including patient-reported outcomes and CRP levels. Responses were greater for patients treated with Cimzia compared to patients treated with placebo. The overall safety profile observed in the Cimzia treatment group was consistent with the known safety profile of Cimzia.

The FDA granted the approval of Cimzia to UCB.

About Nr-axSpA

Nr-axSpA is a type of inflammatory arthritis that causes inflammation in the spine and other symptoms. There is no visible damage seen on x-rays, so it is referred to as non-radiographic. Disease onset typically begins in early adulthood and causes chronic and debilitating back pain, stiffness and fatigue, often having a profound impact on patients' lives.

About Cimzia

CIMZIA® is the only Fc-free, PEGylated anti-TNF (Tumor Necrosis Factor). CIMZIA® has a high affinity for human TNF-alpha, selectively neutralizing the pathophysiological effects of TNF-alpha.

CIMZIA® is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA), adults with active psoriatic arthritis (PsA), and adults with active ankylosing spondylitis (AS). CIMZIA is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation[16].

Note- CIMZIA can lower the ability of patient's immune system to fight infections. Some people who received CIMZIA have developed serious infections, including tuberculosis (TB) and infections caused by viruses, fungi, or bacteria that have spread throughout the body. Some of these serious infections have caused hospitalization and death.

15 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm634671.htm

16 https://www.ucb.com/stories-media/Press-Releases/article/CIMZIA-certolizumab-pegol-is-Now-the-First-and-Only-U-S-FDA-Approved-Treatment-for-nbsp-Non-Radiographic-Axial-Spondyloarthritis-nbsp

USFDA approval to first treatment for post-partum depression

On March 19, 2019 the U.S. Food and Drug Administration approved Zulresso (brexanolone) intravenous (IV) formulation for the treatment of postpartum depression (PPD) in adult women. This is the first drug approved by the USFDA specifically for PPD[17].

The approval of Zulresso was based on two placebo controlled clinical efficacy studies on participants with severe to moderate PPD, where participants received a 60-hour continuous intravenous infusion of Zulresso or placebo and were then followed for four weeks. The studies primary measure in the study was the mean changes in depressive symptoms using depression rating scale. In both placebo controlled studies, Zulresso demonstrated superiority to placebo in improvement of depressive symptoms at the end of the first infusion. The improvement in depression was also observed at the end of the 30-day follow-up period

Zulresso will be available through a restricted distribution program only at certified health care facilities for Risk Evaluation and Mitigation Strategy (REMS), where the health care provider can carefully monitor the patient for drug safety and efficacy.

The approval of Zulresso was granted to Sage Therapeutics, Inc. The FDA granted this application Priority Review and Breakthrough Therapy designation.

About postpartum depression

PPD is a major depressive episode that occurs following childbirth, although symptoms can start during pregnancy. As with other forms of depression, it is characterized by sadness and/or loss of interest in activities that one used to enjoy and a decreased ability to feel pleasure (anhedonia) and may present with symptoms such as cognitive impairment, feelings of worthlessness or guilt, or suicidal ideation.

About ZULRESSO™

ZULRESSO, the first medicine specifically approved by the U.S. Food and Drug Administration for the treatment of postpartum depression, is an allosteric modulator of both synaptic and extra-synaptic GABAA receptors. Allosteric modulation of neurotransmitter receptor activity results in varying degrees of desired activity rather than complete activation or inhibition of the receptor[18].

About REMS

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks. REMS are designed to reinforce medication use behaviors and actions that support the safe use of that medication. While all medications have labeling that informs health care stakeholders about medication risks, only a few medications require a REMS.

Note - ZULRESSO is approved by the FDA for the treatment of PPD in adults, pending DEA scheduling. ZULRESSO has been granted PRIority MEdicines (PRIME) designation from the European Medicines Agency (EMA).

17 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm633919.htm

18 https://investor.sagerx.com/news-releases/news-release-details/sage-therapeutics-announces-fda-approval-zulressotm-brexanolone

WHO launches new global influenza strategy

In order to protect the people globally form the threat of influenza World Health Organization (WHO) had launched a Global Influenza Strategy for year 2019-2030[19]. The main objective of these strategy is to control the spread of influenza from animals to humans, and prepare for the next influenza pandemic. "The on-going risk of a new influenza virus transmitting from animals to humans and potentially causing a pandemic is real.

The WHO strategy for the influenza provides an outline a path to protect populations every year and helps prepare for a pandemic through strengthening routine programmes. It has two overarching goals:

- Build stronger country capacities for disease surveillance and response, prevention and control, and preparedness. To achieve this, it calls for every country to have a tailored influenza programme that contributes to national and global preparedness and health security.
- Develop better tools to prevent, detect, control and treat influenza, such as more effective vaccines, antivirals and treatments, with the goal of making these accessible for all countries.

For proper implementation of the strategy WHO will plan to increase the partnership in the field of research and will work closely with countries to improve their capacities to prevent and control influenza. For more than 65 years, the Global Influenza Surveillance and Response System (GISRS), comprised of WHO Collaborating Centres and national influenza centers, have worked together to monitor seasonal trends and potentially pandemic viruses.

Benefits of the strategy

- The strategy meets one of WHO's mandates to improve core capacities for public health, and increase global preparedness and was developed through a consultative process with input from Member States, academia, civil society, industry, and internal and external experts.
- Supporting countries to strengthen their influenza capacity will have collateral benefits in detecting infection in general, since countries will be able to better identify other infectious diseases like Ebola or Middle East respiratory syndrome-related coronavirus (MERS-CoV).

Conclusion:

The global influenza strategy will guide the countries across the globe to fight against various issues of influenza and will certainly prove to be influential in preventing the pandemic of influenza. This strategy if implemented will bring the countries across the globe into collaboration to lend their hand of support in treating the disease with effect.

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19 https://www.who.int/news-room/detail/11-03-2019-who-launches-new-global-influenza-strategy

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