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S&A PHARMA NEWSLETTER

EDITORIAL

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Founding Partner

The pharmaceuticals & health care sector is an ever evolving sector constantly growing and creating new milestones. In terms of availability of new treatment, prevention and quality drug distribution channel, the various regulatory authorities with their comprehensive updated guidelines keep regulating the healthcare and pharmaceutical industries globally. This edition of our Pharma newsletter addresses regulatory developments in the area of Health Research, new therapy/drug molecule/medical device approvals for sales and marketing and public health survey reports.

The present edition covers the regulatory move of Department of Pharmaceuticals (DoP), Government of India regarding Constitution of an Experts Committee which functions with National Pharmaceutical Pricing Authority (NPPA) under Drug Price Control Order (DPCO), 2013. Then we cover the monthly updates of NPPA, where details of price ceiling of drugs including regulatory notifications related thereto have been highlighted. We have also covered the India's Health Ministry's annual updates regarding various National Health Missions/Programs launched till December 2017. Further, we discuss the Central Drugs Standard Control Organization (CDSCO)'s permission to Novartis to conduct clinical trial for its asthma drug (QAW039-Fevipiprant) which is currently under development phase globally.

In global updates we have covered USFDA's approval of Ogivri, which is the first Biosimilar approval for cancer drug Herceptin, then we discuss USFDA's first drug approval for the treatment of Eosinophilic Granulomatosis with Polyangiitis (formerly known as Churg-Strauss Syndrome). Further, we address the USFDA Novel Drug Approvals for the year 2017 and other USFDA approvals including 46 New Molecular Entities (NMEs). Then we highlighted the release of final rule released by US FDA on safety and effectiveness for certain active ingredients in over-the-counter health care antiseptic hand washes and rubs in the medical settings.

We have also highlighted the European Medicines Agency (EMA)'s Approval of seven medicines in its December Meeting, and also covers the EMA's recommendation to suspend Modified-release paracetamol-containing products from European Union (EU) market.

We wrap-up this newsletter with tsqw he article on a momentous achievement, As Union Health Minister of India declare 'India now free of infective trachoma'.

We sincerely hope that you find the articles of this newsletter interesting & enriching.

Please feel free to send your valuable inputs / comments at newsletter@singhassociates.in

Thank you.

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Supreme Court asks Drug Technical Advisory Board to decide fate of 349 banned Fixed Drug Combination (FDCs) medicines

The Supreme Court, in its judgment on December 15, 2017, on the matter of fixed drug combinations, has asked the Centre to make arrangement for experts to examine 349 fixed dose combination (FDC) medicines to first determine if there is any "therapeutic justification" to make these FDCs.

The Supreme Court bench of Justice Rohinton Fali Nariman and Justice Sanjay Kishan Kaul, was considering a special leave petition filed by the Union of India and the All India Drug Action Network, and a batch of transfer petitions, challenging an order of the Delhi High Court that quashed the ban of 344 FDCs in December 2016 on the ground of lack of mandatory consultations with the Drug Testing Advisory Board (DTAB) and the Drug Consultative Committee (DCC), statutory requirements under Section 26A.

The present appeals and transfer petitions relate to the interpretation of Section 26A of the Drugs and Cosmetics Act, 1940. By the impugned judgment of the learned single Judge of the Delhi High Court dated 1.12.2016, the learned Judge has held that the mandatory condition precedent for the exercise of the power by the Central Government under Section 26A of the Drugs Act is the prior consultation of the DTAB set up under Section 5 of the said Act.

Whereas, the FDCs, which contain two or more therapeutic ingredients, packed into a single dose, were banned on the recommendation of the government-appointed Kokate committee, which was set up to look into safety and efficacy of FDCs that lacked regulatory approval from the Central Government. The Kokate committee had deemed these FDCs irrational; and accordingly, the Government notified a ban on them.

About Kokate committee:

The Kokate committee was an expert committee set up by the Ministry of Health and Family Welfare (MoHFW) for examining and listing in categories, the safety and efficacy of FDCs as per the following terms of reference:

I. FDCs which are considered grossly irrational/unsafe based on pharmacokinetic and pharmacodynamic interaction, dosage compatibilities of FDCs vis-a-vis that of single ingredients present in the FDC and available literature/evidence.

II. FDCs which the Committee may consider necessary for further deliberation by any of the 10 Expert Committees already constituted.

III. FDCs which are considered as safe and effective based on pharmacokinetic and pharmacodynamics interaction, dosage compatibilities of FDCS vis-a-vis that of single ingredients present in the FDC, available literature/evidence, clinical experience and other data available.

IV. FDCs which may be considered as rational, based on present data and knowledge available. However, data in post market scenario is required to be generated within a period of 1 to 2 years to confirm the same.

The Kokate committee had reviewed over 6300 fixed dose combination products and classified them in the four categories as described above: a) irrational, b) require further deliberations, c) rationale and d) require additional data generation.

The Supreme Court Verdict -

The Supreme Court, in its verdict, stated that for the exercise of powers under Section 26 (A) of the Drugs and Cosmetics Act, the DTAB need not be mandatorily consulted by the Government in order to be convinced of reasons for banning a medicine. The Court remarked that the Government could be justified in declaring a ban even if it finds that the drug has been banned in other countries.

Insofar as the 15 drugs that have been banned by Central Government notifications and which were manufactured before September 21, 1988 are set aside, as these cases were never meant to be referred to Kokate Committee. However, it will be open for the Central Government, if it so chooses, de novo, to carry out an inquiry as to whether such drugs should be the subject matter of a notification under Section 26A of the Drugs Act.

Insofar the cases of 349 FDCs that have been banned Including 5 FDCs that banned recently pursuant to the Kokate Committee report, by notifications of the Central Government under Section 26A of the Drugs Act, should be sent to the DTAB, constituted under Section 5 of the Drugs Act, so that it can examine each of these cases and ultimately send a report to the Central Government.

Supreme Court (SC) directions to DTAB:

In order that an analysis be made in greater depth, the DTAB and/or a Sub-Committee formed by the DTAB for the purpose of taking a re-look into these cases, will not only hear the petitioners/appellants before SC, but they will also hear submissions from the All India Drugs Action Network.

The DTAB/Sub-Committee set up for this purpose will deliberate on the parameters set out in Section 26A of the Drugs Act, as follows.

1. First and foremost, in each case, the DTAB or the Sub-Committee appointed by it, must satisfy itself that the use of the Fixed Dose Combinations (FDC) in question is likely to involve any one of the aforesaid three things:
    a. That they are likely to involve any risk to human beings or animals; or
    b. That the said FDCs do not have the therapeutic value claimed or purported to be claimed for them; or
    c. That such FDCs contain ingredients and in such quantity for which there is no therapeutic justification.
2. The DTAB/Sub-Committee must also apply its mind as to whether it is then necessary or expedient, in the larger public interest, to regulate, restrict or prohibit the manufacture, sale or distribution of such FDCs. In short, the DTAB/Sub-Committee must clearly indicate in its report:
    a. As to why, according to it, any one of the three factors indicated above is attracted;
    b. Post such satisfaction, that in the larger public interest, it is necessary or expedient to (i) regulate, (ii) restrict, or (iii) prohibit the manufacture, sale or distribution of such FDCs.
3. The DTAB/Sub-Committee must also indicate in its report as to why, in case it prohibits a particular FDC, restriction or regulation is not sufficient to control the manufacture and use of the FDC[1].

Note - The SC suggested to DTAB/Sub-Committee to be set up for this purpose to afford the necessary hearing to all concerned, and thereafter decide whether the manufacture and sale of these drugs should be regulated, restricted or outright banned, and submit a report with its recommendations to the government within six months from the date on which this judgment is received by the DTAB.

1 http://sci.gov.in/supremecourt/2017/3271/3271_2017_Judgement_15-Dec-2017.pdf

The SC also suggested that the Central Government, thereafter, must give due regard to the report of the DTAB and to any other relevant information, and ultimately apply its mind to the parameters contained in Section 26A of the Drugs Act and, accordingly, either maintain the notifications already issued, or modify/substitute them or withdraw them.

Conclusion:

The Supreme Court judgment on the issue of Fixed Dose Combinations is a landmark judgment, as this now gives a clear direction to the government and regulator to look into this long- standing issue of fixed dose combination products in the country. The apex court has referred the issue of prohibition of 349 FDCs to the union health ministry's expert body on technical matters, the Drugs Technical Advisory Board (DTAB). The court has further asked the DTAB to submit a report with its recommendations to the government within 6-month.

Case Citation: Union of India Anr. (Appellants) vs Pfizer Limited and Ors. (Respondents), Supreme Court of India, Civil Appeal No. 22972 of 2017 (arising out of SLP (C) No. 7061 of 2017), D/d 15.12.2017.

Department of Pharmaceuticals (DoP) issues order regarding Constitution of a Committee of Experts to discharge the functions under DPCO, 2013

The Department of Pharmaceuticals (DoP), Ministry of Chemicals & Fertilizers, Government of India has issued an office order regarding constitution of a committee of experts for consultation on technical issues related to pharmaceuticals pricing, launch of new drugs along with other ancillary provisions where more clarity may be required[2].

In its order the DoP indicated that in view of the experience gained from implementation of Drugs (Prices Control) Order, 2013 (DPCO, 2013), it has been decided to constitute a single multi-disciplinary "Committee of Experts" by the Government as envisaged by two different nomenclatures i.e. Standing Committee of Experts under para 5(2)(i) & para 15(1) and the Committee of Experts under para 11(4) to discharge the functions under DPCO, 2103, and opine on matters referred to it by the National Pharmaceutical Pricing Authority (NPPA) in discharge of its functions.

The order also states that the Committee of Experts shall comprise of the following members:

- **Member Secretary**, National Pharmaceutical Pricing Authority (NPPA) - Convener;
- **Representative** (Scientist/Expert) from Central Drugs Standard Control Organization (CDSCO) (Subject matter expert) not below the rank of Deputy DCGI - Member;
- **Representative** (Scientist/Expert) from the Department of Health Research (DHR)/Indian Council of Medical Research (ICMR) (Subject matter expert) not below the rank of Deputy Secretary or equivalent - Member;
- **Representative** (Pharmacoeconomics expert) from NIPER (to be nominated by DoP) - Member;

The above said Committee would be empowered to invite or co-opt any other specialist (example a Medical Devices expert) depending on exigencies of the circumstances requiring resolution of any specific matter arising out of implementation of various provisions of DPCO, 2013, as and when it may be required.

The purpose of the Committee shall be as under:

- To deliberate and recommend its opinion on the claims of Pharma companies about additional therapeutic features associated with any formulation including in terms of Paragraph 11 (3) of DPCO, 2013 and recommending separate ceiling price of scheduled formulations or retail price of a new drug with specified therapeutic rationale, considering the type of packaging or pack size or dosage compliance or content in the pack namely liquid, gaseous or any other form, in the unit dosage as the case may be, conforming to Indian Pharmacopeia or other standards as specified in the Drugs and Cosmetics Act, 1940 (23 of 1940) and the rules made thereunder for the same formulation.
- To deliberate, interpret and recommend its opinion on the claims of Pharma companies about additional Pharmacoeconomics features associated with any formulation/API including in terms of Paragraph 15 (1) of DPCO, 2013.
- To deliberate, interpret and recommend its opinion on the technical issues whether the drug is scheduled or non-scheduled on the basis of ingredients used in the formulation.

2 http://pharmaceuticals.gov.in/sites/default/files/Final%20Expert%20Committee%20by%20DoP.pdf

- To deliberate, interpret and recommend its opinion on the claims of Pharma companies about novelty associated with indigenous R&D content passed through the development process of relevant API/ formulation; and recommend exemption from the application of provisions of Paragraph 32 of DPCO, 2013 for a period of five years.
- To discuss any other issue referred to the Committee of Experts concerning technical matters involved in disposing of any issue raised by any stakeholder.

In this regard, NPPA shall decide and refer the relevant issues within 4 weeks of receiving the applications, to the Committee for its opinion. Thereafter, the Committee shall submit its report with its findings and opinion in each case within a period of 4 weeks.

Further, the recommendations of this committee shall be considered by the NPPA which shall pass a reasoned order within 4 weeks from receiving the recommendations of the Committee, deciding the issue(s) in hand finally.

Note - The order was issued by Department of Pharmaceuticals with the approval of Hon'ble Minister, Ministry of Chemicals and Fertilizers, Government of India.

Conclusion:

The Department of Pharmaceuticals of Government of India has established this high-level, multidisciplinary committee of experts to provide recommendations concerning approval and pricing of new drugs or formulations. The decision to establish this committee came from the significant experience gained since implementation of Drugs Prices Control Order, 2013.

A momentous achievement - India now free of 'infective trachoma' declares Union Health Minister of India

On December 08, 2017, Shri J P Nadda, Union Minister of Health and Family Welfare released the National Trachoma Survey Report (2014-17)[3]. He declared that India is now free from 'infective trachoma', and termed this as a momentous achievement. Shri J P Nadda stated that the survey findings indicate that the active trachoma infection has been eliminated among children in all the survey districts with overall prevalence of only 0.7%. This is much below the elimination criteria of infective trachoma as defined by the WHO; active trachoma is considered eliminated if the prevalence of active infection among children below 10 years is less than 5%, he added.
The Union Health Minister stated that the survey results indicate that active trachoma is no longer a public health problem in India. "We have met the goal of trachoma elimination as specified by the WHO under its GET2020 program", he said. "This has been possible due to decades of inter-sectoral interventions and efforts that included provision of antibiotic eye drops, personal hygiene, availability of safe water, improved environmental sanitation, availability of surgical facilities for chronic trachoma, and a general improvement in the socio-economic status in the country", he added. Shri Nadda emphasized the need for constant surveillance by the states to report any fresh cases of trachoma and trachoma sequelae (TT cases) and to treat them promptly to finally be completely free of trachoma.

At the release of the Survey Report, the minister emphasized, "it is our aim to eliminate trachomatoustrichiasis from the country. States which still report cases of active trachoma need to develop a strategy for community-based case finding of patients of trachomatoustrichiasis (TT)". "These cases must be provided free entropion surgery/ treatment in local hospitals", he stated. Shri Nadda further said that a careful record of each identified case and its management status must be maintained as per the WHO Guidelines. Also, adequate surveillance of the disease must be done all over the country in order to certify India as trachoma free (eliminated). Monthly data on indicators of trachoma surveillance as per WHO guidelines must be regularly sent to the NPCB, he urged the states.

The National Trachoma Prevalence Surveys and the Trachoma Rapid Assessment Surveys were conducted by Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, in collaboration with National Program for Control of Blindness & Visual Impairment, Union Ministry of Health and Family Welfare from 2014 to 2017. This was conducted in 27 high-risk districts across 23 states and union territories. Trachoma Prevalence Surveys were carried out in 10 districts selected from the previously hyper-endemic states. Under the survey, 19662 children in 1-9 years age group were examined by trained ophthalmologists. As many as 44135 persons were examined among the 15yr+ age group. The Trachoma Rapid Assessment Surveys (TRA) was done in 17 other districts from other parts of the country in places where trachoma cases have been reported, which were not previously hyper-endemic.

Trachoma is a chronic infective disease of the eye and is the leading cause of infective blindness globally. Trachoma results from poor environmental and personal hygiene and inadequate access to water and sanitation. It affects the conjunctiva under the eyelids. Repeated infections cause scarring leading to in-turning of the eyelashes and eyelids. This further causes damage to the cornea and blindness. It is found affecting the population in certain pockets of the States of North India like Gujarat, Rajasthan, Punjab, Haryana, Uttar Pradesh and Nicobar Islands. Trachoma infection of the eyes was the most important cause of blindness in India in 1950s and over 50% population was affected in Gujarat, Rajasthan, Punjab, and Uttar Pradesh. It was the most important cause of corneal blindness in India, affecting young children.

3 http://pib.nic.in/newsite/erelease.aspx?relid=174210

According to the World Health Organization (WHO), Trachoma is hyperendemic in many of the poorest and most backward rural areas in 41 countries of Africa, Central and South America, Asia, Australia and the Middle East. It is responsible for blindness or visual impairment of about 1.9 million people. It causes about 1.4% of all blindness worldwide[4]. Overall, Africa remains the most affected continent.

For Prevention and Control, WHO recommends elimination programmes in endemic countries using **SAFE** strategy which consists of:

- **S**urgery to treat the blinding stage of the disease (trachomatous trichiasis);
- **A**ntibiotics to clear infection, particularly mass drug administration of the antibiotic azithromycin, which is donated by the manufacturer to elimination programmes, through the International Trachoma Initiative;
- **F**acial cleanliness; and
- **E**nvironmental improvement, particularly improving access to water and sanitation.

The World Health Organization leads an international alliance of interested parties to work for the global elimination of trachoma, named as the Alliance for Global Elimination of Trachoma by the year 2020 (GET 2020).

4 http://www.who.int/mediacentre/factsheets/fs382/en/

CDSCO approves Macitentan for the treatment of Pulmonary Arterial Hypertension (PAH)

The Central Drugs Standard Control Organization (CDSCO) is the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act, 1940 and Rules, 1945.

On December 07, 2017, CDSCO approved Macitentan Bulk/Tablets 10 mg, which is indicated for the treatment of Pulmonary Arterial Hypertension (PAH, World Health Organization (WHO) group I) to delay disease progression[5]. The manufacture and marketing approval for Macitentan Tablet was granted to MSN laboratories Private Limited. The Subject Expert Committee (SEC) of Cardiovascular & Renal, CDSCO, after detailed deliberation has recommended grant of manufacturing and marketing permission with local clinical trial (Phase IV) waiver and submission of Bioequivalence (BE) study data.

The committee also observed that -

I. PAH is a rare disease and not many therapeutic options are available at present.

II. The drug has shown a significant 45% reduction in composite of first morbidity and mortality.

III. The drug is approved as orphan drug by United States Food & Drug Administration (USFDA) and Europe, the Middle East and Africa (EMEA)[6].

About Macitentan

Macitentan is a nonselective inhibitor of endothelin-1 receptors (both type A and B). Inhibition of endothelin receptors disrupts the intracellular pathways that leads to vasoconstriction, thus causing vasodilation. Because macitentan has high affinity for pulmonary endothelin receptors, it preferentially causes vasodilation in the pulmonary vasculature, thereby decreasing pulmonary vascular pressure. The current indications are for symptomatic pulmonary arterial hypertension, classified as WHO group 1 (idiopathic). Macitentan has been associated with a low rate of serum enzyme elevations during therapy, but has yet to be implicated in cases of clinically apparent acute liver injury.[7] Macitentan was first approved by the United States Food and Drug Administration (FDA) on December 18, 2013 for the treatment of pulmonary arterial hypertension (PAH) to delay disease progression[8].

About Pulmonary Arterial Hypertension (PAH)

Pulmonary hypertension (PH) is a severe, rare lung disease characterized by high blood pressure in the pulmonary arteries. Due to the condition, the pulmonary arteries, which are responsible for transporting the blood from the right heart ventricle to the lungs, become narrowed and thickened. In order to properly pump the blood, the heart needs to work harder, which can lead to enlargement and weakening of the organ, as well as potential right heart failure.

Pulmonary Arterial Hypertension (PAH, WHO Group I) is a subtype of Pulmonary Hypertension (PH) associated with abnormalities in the arterioles, when the causes of the disease are not known. The PH including inherited pulmonary hypertension, as well as pulmonary hypertension caused by connective tissue diseases that affect the

5 http://www.cdsco.nic.in/forms/list.aspx?lid=2034&ld=11

6 http://www.cdsco.nic.in/writereaddata/36th%20%20MOM%20SEC%20Cardiovascular%20&%20Renal%20%2009_02_2017%20(1).pdf

7 https://livertox.nlm.nih.gov/Macitentan.htm

8 https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/204410Orig1s000ltr.pdf

body's structure or composition of the tissue like congenital heart problems, high blood pressure in liver (portal hypertension), HIV, thyroid gland disorder, sickle cell disease, glycogen storage disorders, and rare blood conditions like pulmonary veno-occlusive disease or pulmonary capillary hemangiomatosis[9].

9 https://pulmonaryhypertensionnews.com/pulmonary-hypertension-who-classification/

Mylan Launches HepBest for management of chronic Hepatitis B

Mylan Launches HepBest™, First Drug Approved in Eight Years for Management of Chronic Hepatitis B Infection in India

On December 07, 2017, Mylan Pharmaceuticals Private Limited announced that it has launched HepBest™ 25 mg (tenofovir alafenamide, TAF), a once-daily tablet for the treatment of chronic hepatitis B in adults. According to World Health Organization (WHO) estimates, more than 2 billion people worldwide are infected with the hepatitis B virus (HBV), of which more than 240 million have chronic liver infection. These patients are at risk of developing serious illness and death, largely resulting from liver cirrhosis and liver cancer. HepBest™ (TAF) is the first drug in eight years to be approved for the management of chronic hepatitis B in India[10].

Compared to the earlier formulation of tenofovir (tenofovir disoproxil fumarate), TAF demonstrates not only comparable efficacy but also an enhanced renal and bone safety profile. TAF also has greater plasma stability, which ensures efficient drug delivery to the site of action.

In 2014, Mylan signed an agreement with Gilead to increase access to TAF-based HIV treatments in developing countries. As part of the licensing agreement, on U.S. Food and Drug Administration (FDA) approval, Mylan received a technology transfer from Gilead, enabling it to manufacture low-cost versions of TAF.

Earlier in November 2017, Indian Drug Regulator, CDSCO approved Tenofovir Alafenamide Fumarate bulk & 25 mg capsules[11]. Tenofovir Alafenamide Fumarate bulk & 25 mg capsules are indicated for the treatment of chronic Hepatitis B virus infection in adults with compensated liver disease.

Mylan Labs presented the data on the drug including data from global clinical trials conducted, in which India was a participating country. The data presented shows that Tenofovir Alafenamide and TDF are equivalent in terms of efficacy but Tenofovir Alafenamide has reduced toxicity. The data was presented on June 14, 2017, before the CDSCO's advisory committee of Antimicrobial & Antiviral.

After review of the data, the committee considered the request for waiver of local clinical trial and recommended for conduct of the BE study as per the protocol submitted[12].

Tenofovir Alafenamide is a nucleotide reverse transcriptase inhibitor and a prodrug of tenofovir. It was developed by Gilead Sciences for use in the treatment of HIV infection and chronic hepatitis B, and is applied in the form of tenofovir alafenamide fumarate (TAF).

10 http://www.mylan.in/en/news/press-releases/2016/mylan-launches-hepbest-in-india

11 http://www.cdsco.nic.in/forms/list.aspx?lid=2034&ld=11

12 http://www.cdsco.nic.in/writereaddata/MOM%20of%20SEC%20Antimicrobial%20and%20Antiviral%20 14_06_2017%20(Website)%20(1).pdf

Novartis India granted permission for conduct of clinical trial in India for its Asthma Drug

The Central Drugs Standard Control Organization (CDSCO)'s, Pulmonary Subject Expert Committee (SEC) during its meeting held on December 05, 2017, at CDSCO Headquarters New Delhi, granted permission to Novartis to conduct clinical trial for its asthma drug (QAW039-Fevipiprant) which is currently in development phase globally. The SEC opined that there is an unmet need in the country, and the test drug may be an alternative treatment option in patients with uncontrolled severe asthma[13].

After detailed deliberation, the committee concluded that the risk versus benefit to the patients justified the approval for a clinical trial. The safety profile of the test drug from various pre-clinical toxicities including single dose, repeat dose, genotoxicity and clinical phase I, II studies also justified the conduct of the study since this provides innovation vis-a-vis existing therapeutic option.

The purpose of the study will be to demonstrate the efficacy of QAW039 150 mg once daily as measured by change from baseline in pre-dose FEV1 [in liters], compared with placebo, at the end of the 12-week active treatment period.

QAW039 (fevipiprant) is CRTH2 antagonist, which is currently in phase III of drug development; Novartis is intending to file the drug in 2019[14]. Phase III of drug development consists of large-scale clinical studies, covering several hundred to several thousand patients, which are conducted to establish the safety and efficacy of the drug in specific indications for regulatory approval. Phase III trials also may be used to compare a new drug against a current standard of care to evaluate the overall benefit-risk relationship of the new medicine.

What is asthma?

Asthma attacks all age groups but often starts in childhood. It is a disease characterized by recurrent attacks of breathlessness and wheezing, varying in severity and frequency from person to person. This condition is due to inflammation of the air passages in the lungs and affects the sensitivity of the nerve endings in the airways, so they become easily irritated. During an attack, the lining of the passages swells, causing constriction of the airways thereby reducing the inflow and outflow of air from the lungs.

According to the World Health Organization (WHO), India has an estimated 15-20 million asthmatics, with further estimates indicating the prevalence of asthma to be between 10% and 15% in 5-11 years old children[15].

Conclusion:

QAW039 (Fevipiprant) is a promising drug for relief in patients with uncontrolled severe asthma. Researchers have hailed this drug as a game-changer in asthma treatment after a Lancet-published trial showed its potential to significantly reduce the severity of the condition[16]. Also the possibility of taking a pill instead of using an inhaler will be a very welcome one among patients with asthma, some of whom may struggle with the complexities required to use/operate an inhaler device.

13 http://cdsco.nic.in/writereaddata/Pulmonary%20recommendation_05_12_2017.pdf

14 https://www.novartis.com/sites/www.novartis.com/files/novartis-pipeline-2016-annual-report.pdf

15 http://www.who.int/mediacentre/factsheets/fs206/en/

16 http://www.thelancet.com/journals/lanres/article/PIIS2213-2600(16)30179-5/fulltext

Health Ministry Annual Updates on National Health Missions/ Programs for year 2017

Year 2017 was the year of health survey and regulatory reforms, as many survey reports were published in various areas of health such as – reports on Universal Health Coverage (UHC); Global Hunger Index (GHI); National Nutrition Strategy; Health of the Nation's state; and Global Status Report on Non-Communicable Diseases (NCDs). In the area of regulatory reforms, many new/updated guidelines were released for example – Institute of Chemical and Medicinal Research released "Handbook on Intellectual Property Rights & Technology Transfer", release of National Ethical Guidelines for Bio-Medical Research Involving Children, for Stem Cell Research, and for Biomedical and Health Research Involving Human Participants etc.

On December 18, 2017, the Minister of state, Ministry of Health and Family Welfare, has submitted the written annual updates of ongoing and planned health programs/missions in the Lok Sabha; some of the key programs are mentioned below -

1. **Global Hunger Index**
2. **Licensed blood banks in the country**
3. **Fee Structure of Medical Colleges**
4. **Malnutrition Deaths**
5. **Charges on Health Services**
6. **National Nutrition Strategy**
7. **Cardiovascular Diseases in India**
8. **Patented Drugs**
9. **Additional Medical Seats**
10. **Prescribing Generic Drugs**
11. **Committed to advancing the agenda of Universal Health Coverage through affordable and accessible healthcare for all**

1. Global Hunger Index: The International Food Policy Research Institute (IFPRI) publishes Global Hunger Index (GHI) every year. According to the GHI 2017 report, India ranks 100 out of 119 countries which indicates a serious hunger problem in the country.

To deal with the problem of hunger in the country and to improve the country's standing in GHI, the Government has implemented some interventions like - provision of food grains at highly subsidized prices to the targeted population through State Governments/ UT Administrations under the Targeted Public Distribution System (TPDS) in terms of Nation Food Security Act, 2013. Some other Welfare Schemes (OWS) are Mid-Day Meal Scheme, Integrated Child Development Services (ICDS) Scheme, and Rajiv Gandhi Scheme for Empowerment of Adolescent Girls, Annapurna Scheme, and National Nutrition Mission (NNM) etc.[17]

17 http://pib.nic.in/newsite/erelease.aspx?relid=174450

2. Licensed blood banks in the country: The Health Minister reported the total number of functioning licensed blood banks in various State/Union Territories (UT) till June 2017. There are 2903 total licensed blood banks in36 state/UT[18].

3. Fee Structure of Medical Colleges: Health Ministry also reported that the fee structure of private unaided medical colleges is decided by the Committee set up by the respective State Governments under the Chairmanship of a retired High Court Judge in pursuance of the directions of the Hon'ble Supreme Court of India. It is for the Committee to decide whether the fee proposed by an Institute is justified and the fee fixed by the Committee is binding on the Institute. Whereas, in case of Government medical colleges the respective State Governments are responsible for fixing the fee[19].

4. Malnutrition Deaths: Malnutrition means the affected person is either undernourished or overnourished. Malnutrition is not a direct cause of death but can increase morbidity and mortality by reducing resistance to infections. Addressing malnutrition is a preventive strategy, as it has the potential to minimize the healthcare costs by reducing the requirement for curative healthcare.

The National Health Mission (NHM), under the Health Ministry, has implemented following schemes /programs which address malnutrition:

- Promotion of appropriate Infant and Young Child Feeding (IYCF)
- Mothers' Absolute Affection (MAA) programme
- Treatment of sick children with Severe Acute Malnutrition (SAM) at Nutrition Rehabilitation Centres (NRCs)
- Vitamin A supplementation (VAS) for children till the age of 5 years.
- National Iron Plus Initiative
- National Deworming Day
- Intensified Diarrhoea Control Fortnight (IDCF)
- Rashtriya Bal Swasthya Karyakram (RBSK)
- Village Health and Nutrition Days (VHNDs)

The Supplementary Nutrition Programme is being implemented through the Anganwadi Centres (AWCs) for addressing undernourishment in pregnant and lactating women, children under the age of 6 years and out-of-school adolescent girls[20].

5. Charges of Health Services: The Government of India has enacted Clinical Establishments (Registration and Regulation) Act, 2010 to regulate hospitals including private hospitals. Further, Clinical Establishments (Central Government) Rules, 2012 has been notified for registration and regulation of the Clinical Establishments which has approved a standard list of medical procedures and a standard template for costing of medical procedures. Currently, the Act is applicable in 10 states, Sikkim, Mizoram, Arunachal Pradesh, Himachal Pradesh, Uttar Pradesh, Bihar, Jharkhand, Rajasthan Uttarakhand and Assam and all Union Territories except Delhi. Other States may adopt the Act under clause (1) of Article 252 of the Constitution[21].

18 http://pib.nic.in/newsite/erelease.aspx?relid=174448

19 http://pib.nic.in/newsite/erelease.aspx?relid=174447

20 http://pib.nic.in/newsite/erelease.aspx?relid=174445

21 http://pib.nic.in/newsite/erelease.aspx?relid=174444

6. National Nutrition Strategy (NNS): The NNS was published by NITI Aayog in 2017 to reduce 3 point percentage underweight prevalence/year in children (0-3 years) by 2022 and a 1/3rd reduction in anemia in children, adolescent & Women of Reproductive Age (WRA) by nutrition specific interventions like:

- Infant and Young Child care and Nutrition,
- Infant and Young Child Health,
- Maternal Care, Nutrition and Health,
- Adolescent care, nutrition and Health,
- Addressing micronutrient deficiencies- including anaemia, and
- Community nutrition (Interventions addressing community)[22].

7. Cardiovascular Diseases in India: According to a report released by ICMR "India: Health of the Nation's States – The India State Level Disease Burden Initiative", the disease burden trends in the States of India shows an increase in the contribution of Non-Communicable Diseases (NCDs) from 30% of total disease burden in 1990 to 55% in 2016.

Ischemic Heart Disease was the top cause of disease burden in the country in 2016. Unhealthy diet, lack of physical activity, harmful use of alcohol, overweight, obesity, tobacco use inter-alia, are the risk factors of Cardiovascular Diseases (CVDs).

To combat this risk factor, the Government of India has launched National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) which is implemented for interventions up to the District level under the National Health Mission. NPCDCS focuses on awareness generation for behaviour and life-style changes, screening and early diagnosis of people with high levels of risk factors and their treatment and referral (if required) to higher facilities for appropriate management for Non-Communicable Diseases (NCD) including cardiovascular diseases[23].

8. Patented Drugs: As per data submitted by Indian Patent Office (IPO) to Health Ministry, a total of 7083 patents have been granted by IPO in the pharmaceutical field from 2005-06 till October 2017.

Table 1: Number of patents granted annually from year 2005-06

Year	Patents Granted
2005-06	457
2006-07	798
2007-08	905
2008-09	1207
2009-10	530
2010-11	596
2011-12	282
2012-13	344
2013-14	256
2014-15	389

22 http://pib.nic.in/newsite/erelease.aspx?relid=174442

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2015-16	370
2016-17	551
2017-18 (Up to 31/10/2017)	398
Total	**7083**

9. Additional Medical Seats: The Health Ministry permitted 2990 additional Postgraduate seats in Clinical subjects/Courses in Government Medical Colleges for the year 2017-18 including 153 seats in Andhra Pradesh as a one-time measure to revise Teacher Student ratio in respect of Clinical subjects at Public Funded Government Medical Colleges, consequent to amendment to MCI Postgraduate Medical Education Regulations, 2000.

However, 54 Medical Colleges have not been granted renewal permission for the year 2017-18. Further, in three cases where the State Government has withdrawn Essentiality Certificate earlier granted to the College, such Colleges are ordered to be closed and the students in the College are allowed to be shifted to other Colleges of the State as proposed by the concerned State Government[24].

10. Prescribing Generic Drugs: The government has published a draft notification vide GSR 302 (E) dated March 30, 2017, for amendment of Rule 96 of the Drugs & Cosmetics Rules, 1945, which is to provide that the proper name of the drugs shall be printed in a conspicuous manner, and which shall be in the same font but at least two font sizes larger than the brand name or the trade name, if any.

Moreover, an amendment in Clause 1.5 of Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002 was also notified; which stipulates that "every physician should prescribe drugs with generic names legibly and preferably in capital letters and he/she shall ensure that there is a rational prescription and use of drugs"[25].

11. Committed to advancing the agenda of Universal Health Coverage through affordable and accessible healthcare for all: The government has updated to the ongoing Health programs/missions -

National Health Policy 2017: Release of a new National Health Policy (NHP) for the country after a gap of 15 years. NHP 2017 addresses current and emerging challenges necessitated by the changing socio-economic, technological and epidemiological landscapes. The major commitment of the NHP 2017 is raising public health expenditure progressively to 2.5% of the Gross Domestic Product (GDP) by 2025. NHP 2017 has been duly supported by the Government through provision of Rs. 47352.51 crores to the Ministry of Health and Family Welfare (MoHFW) under the Union Budget 2017-18. The amount is 27.7% higher in allocation as compared to the previous year.

National Medical Commission (NMC) Bill, 2017: The Cabinet approved the National Medical Commission Bill 2017 on December 15, 2017, and envisages to:

- Replace the Medical Council 1956 Act.
- Enable a forward movement in the area of medical education reform.
- Move towards outcome based regulation of medical education rather than process oriented regulation.
- Ensure proper separation of functions within the regulator by having autonomous boards.
- Create accountable and transparent procedures for maintaining standards in Medical Education.
- Create a forward-looking approach towards ensuring sufficient healthcare workforce in India.

24 http://pib.nic.in/newsite/erelease.aspx?relid=174439

25 http://pib.nic.in/newsite/erelease.aspx?relid=174438

National Nutrition Mission (NNM): A joint effort of MoHFW and the Ministry of Women and Child Development (WCD), this mission aims to benefit more than 10 crore people by a life-cycle approach by interrupting the intergenerational cycle of undernourishment.

Mental Healthcare Act, 2017: The Act adopts a rights-based statutory framework for mental health in India, and strengthens equality and equity in provision of mental healthcare services in order to protect the rights of people with mental health problems to ensure that they are able to receive optimum care and are able to live a life with dignity and respect.

HIV & AIDS (Prevention & Control) Act, 2017: The Act aims to end the epidemic by 2030 in accordance with the Sustainable Development Goals set by the United Nations. A person living with AIDS cannot be treated unfairly at employment, educational establishments, renting a property, standing for public or private office or for healthcare and insurance services. The Act also aims to enhance access to healthcare services by ensuring informed consent and confidentiality for HIV-related testing, treatment and clinical research.

Universal Immunization Programme (UIP): One of the largest public health programmes in the world, UIP annually targets 3 crore pregnant women and 2.7 crore newborns. More than 90 lakh immunization sessions are conducted annually. Mission Indradhanush and Intensified Mission Indradhanush are new initiatives under UIP. Apart from this, some new vaccines have been introduced in UIP such as – Inactive Polio Vaccine (IPV), Adult Japanese Encephalitis (JE) Vaccine, Rotavirus Vaccine, Measles-Rubella (MR) Vaccine, and Pneumococcal Vaccine (PCV).

Labour room Quality Improvement Initiative - LaQshya: MoHFW has launched LaQshya to improve the quality of care that is being provided to pregnant mothers in the Labour Room and Maternity Operation Theatres; thereby, preventing the undesirable adverse outcomes associated with childbirth. The initiative will be implemented in Government Medical Colleges (MCs) besides District Hospitals (DHs), and high delivery load Sub-District Hospitals (SDHs) and Community Health Centres (CHCs).

Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA): The program aims to provide assured, comprehensive and quality antenatal care - free of cost, universally to all pregnant women on the 9th of every month. More than 90 lakh antenatal checkups have been conducted at PMSMA sites for comprehensive services under the programme, and more than 5 lakh high risk pregnancies have been identified under PMSMA.

Intensified Diarrhea Control Fortnight (IDCF): Every fortnight, health workers visit the households of under five children, conduct community level awareness generation activities and distribute ORS. In 2017 (July-August), more than 7.0 Crore children under 5 years of age were visited by ASHAs for Prophylactic ORS.

Rashtriya Kishor Swasthya Karyakram (RKSK): Is a comprehensive programme focusing on Sexual Reproductive Health, Nutrition, Injuries and Violence (including gender based violence), Non-Communicable Diseases, Mental Health and Substance Misuse with a promotive and preventive approach.

Health and Wellness Centers (HWCs): In 2017-18, the Ministry announced transformation of Sub-health Centres to Health and Wellness Centres (HWCs) to expand the basket of services of primary care to make it comprehensive. The HWCs are expected to provide preventive, promotive, rehabilitative and curative care for a package of services related to RMNCH+A, communicable diseases, non- communicable diseases, Ophthalmology, ENT, Dental, Mental, Geriatric care, treatment for acute simple medical conditions and emergency & trauma services.

Affordable Medicine and Reliable Implants for Treatment (AMRIT): 105 pharmacies have been set up across 19 states for providing medicines for Diabetes, CVDs, Cancer and other diseases at discounted prices to the patients. A total of more than 5000 drugs and other consumables are being sold at up to 50% discounts.

Revised National Tuberculosis Programme (RNTCP): As per the Global TB Report 2017, the updated estimate of incidence of disease is 27 lakh cases in 2016 as compared to 28 lakhs in 2015 (Rate: 211 per 100,000 population in 2016 as compared to 217 per 100,000 population in 2015)[26]

Conclusion:

Merely launching a large number of healthcare programs will not help to achieve the Universal Health Coverage, unless they are also implemented at the ground level and serve the larger area and/or population. Progress in health services also demands continuous regulatory reforms and timely field research to reach the desired milestone.

26 http://pib.nic.in/newsite/erelease.aspx?relid=174423

National Pharmaceutical Pricing Authority (NPPA) updates for month of December 2017

National Pharmaceutical Pricing Authority (NPPA) is an organization of the Government of India which is an executive body under the Drugs (Prices Control) Order (DPCO), 2013 established to fix/ revise the prices of controlled bulk drugs and formulations and to enforce prices and availability of the medicines in the country. There are some key announcements/notice released by NPPA for the month of December 2017 as described below -

1. **National List of Essential Medicines (NLEM), 2015 formulations under provisions of DPCO, 2013 (Consolidated list as on 30.11.2017)**
2. **NPPA fixed/revised ceiling prices/Retail Prices of 65 scheduled formulations under DPCO, 2013**
3. **Form -I application for price fixation of new drug under Para 2(u) of DPCO, 2013**
4. **NPPA fixed/revised ceiling prices/Retail Prices of 27 scheduled formulations under DPCO, 2013**
5. **NPPA's consideration of Medtronic's request for discontinuation of Endeavour Sprint RX Zotarolimus Eluting Coronary Stent System**

National List of Essential Medicines (NLEM), 2015 formulations pending for price fixation

On December 06, 2017, NPPA released the list of formulations pending for ceiling price fixations as on November 2017 under NLEM 2015, as the All Indian Origin Chemists & Distributors (AIOCD) association's Pharmatrac is not capturing the Price to Retailer (PTR) and Moving Annual Turnover (MAT) of said formulations. Therefore, NPPA requested all the concerned manufacturers / marketing companies to furnish the PTR & MAT in terms of value, duly self-attested with proper authorized signature & seal of the authorized officer of the company, for the formulations listed in NLEM, 2015 (revised Schedule - I of DPCO, 2013) i.e. Annexure -I for the month of August 2015 by December 22, 2017 for enabling NPPA to take appropriate action for ceiling price fixation under provisions of DPCO, 2013[27].

NPPA has fixed/revised ceiling prices/Retail Prices of 65 scheduled formulations under DPCO, 2013

On December 18, 2017, the NPPA has fixed/revised the ceiling /retail prices of 65 scheduled formulations under DPCO. The 65 scheduled formulations under price cap are mostly from anti-cancer, anti-HIV, anti-diabetics, lipid lowering drugs and other antibiotics categories as described below under various provisions -

Table1-Notified Retail price of 63 formulations under Drugs (Prices Control) Order, 2013

S l . No.	Name of the Scheduled Formulation / Brand Name	Strength	Unit
1.	Ferrous Ascorbate + Folic Acid + Cyanocobalamin +Zinc Sulphate Monohydrate tablet (Autrin - XT)	Ferrous Ascorbate eq. to Elemental Iron 100mg, Folic Acid IP 1.5mg, Cyanocobalamin IP 15 mcg, Zinc Sulphate Monohydrate IP eq. to Elemental Zinc 22.5mg	1 Tablet

27 http://www.nppaindia.nic.in/order/om_07-12-2017.pdf

2.	Rosuvastatin + Clopidogrel Capsule (Roseday CV 10)	Rosuvastatin Calcium IP eq. to Rosuvastatin (As granules) 10mg, Clopidogrel Bisulphate IP eq. to Clopidogrel (As a film coated tablet) 75mg	1 Capsule
3.	Rosuvastatin + Clopidogrel Capsule (Roseday CV 10)	Rosuvastatin Calcium IP eq. to Rosuvastatin (As granules) 10mg, Clopidogrel Bisulphate IP eq. to Clopidogrel (As a film coated tablet) 75mg	1 Capsule
4.	Teneligliptin + Metformin tablet (Ten20 M 1000)	Teneligliptin Hydrobromide hydrate eq. to Teneligliptin 20mg, Metformin HCL 1000mg (as extended release)	1 Tablet
5.	Clobetasol + Clotrimazole + Neomycin Sulphate Cream	Clobetasol Propionate IP 0.05%w/w, Clotrimazole IP 1.00% w/w, Neomycin Sulphate IP 0.50%w/w	1 GM
6.	Moxifloxacin + Cefixime Tablets (Moximac Plus)	Moxifloxacin Hydrochloride BP eq. to Moxifloxacin 400mg, Cefixime IP (as trihydrate) eq. to Ahydrous Cefixime 400mg	1 Tablet
7.	Tramadol + Paracetamol Tablet	Tramadol Hydrochloride IP 37.5mg, Paracetamol IP 325mg	1 Tablet
8.	Rosuvastatin + Aspirin + lopidogrel Tablet	Rosuvastatin Calcium IP eq. to Rosuvastatin 10mg, Aspirin IP 75mg, Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg	1 Tablet
9.	Teneligliptin + Metformin Tablet	Teneligliptin Hydrobromide hydrate eq. to Teneligliptin 20mg, Metformin HCL 500mg (as extended release)	1 Tablet
10.	Teneligliptin + Metformin Tablet	Teneligliptin Hydrobromide hydrate eq. to Teneligliptin 20mg, Metformin HCL 1000mg (as extended release)	1 Tablet
11.	Paracetamol + Caffeine + Phenylephrine + Diphenhydramine Tablet	Paracetamol IP 500mg, Caffeine (Anhydrous) IP 30mg, Phenylephrine Hydrochloride IP 5mg, Diphenhydramine Hydrochloride IP 25mg	1 Tablet
12.	Ramipril + Amlodipine Tablet	Ramipril IP 5mg, Amlodipine Besilate IP eq. to Amlodipine 5mg	1 Tablet
13.	Teneliglitptin + Metformin Tablet	Teneliglitptin Hydrobromide Hydrate 20mg eq. to Tenegliptin 20mg, Metformin Hydrochloride IP 1000mg (In Sustained Release form)	1 tablet
14.	Teneliglitptin + Metformin Tablet	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin Hydrochloride IP 500mg	1 Tablet
15.	Rosuvastatin + Clopidogrel Capsule (Roistar CV 10/75)	Rosuvastatin Calcium IP eq. to Rosuvastatin 10mg (As Pellets), Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg (as Pellets)	1 Capsule
16.	Rosuvastatin + Clopidogrel Capsule (Roistar CV 20/75)	Rosuvastatin Calcium IP eq. to Rosuvastatin 20mg (As Pellets), Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg (as Pellets)	1 Capsule

17.	Diclofenac Injection	Diclofenac Sodium IP 75mg Injection	1 ML
18	Teneligliptin + Metformin Tablet (EFIGLIN M)	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin HCl 500mg	1 Tablet
19.	Rosuvastatin + Clopidogrel Capsule	Rosuvastatin Calcium IP eq. to Rosuvastatin 20mg (As granules), Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg (as to film coated tablets)	1 Capsule
20.	Rosuvastatin + Clopidogrel Capsule (Roseday CV 20)	Rosuvastatin Calcium IP eq. to Rosuvastatin (As Pellets) 20mg, Clopidogrel Bisulphate IP eq. to Clopidogrel (As Pellets) 75mg	1 Capsule
21.	Teneligliptin + Metformin Tablet	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin HCL 500mg (as sustained release)	1 Tablet
22.	Teneligliptin + Metformin Tablet	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin HCL 1000mg (as sustained release)	1 Tablet
23.	Metformin + Glimepiride + Voglibose Tablet	Metformin HCL 500mg (as sustained release form), Glimepiride 2mg, Voglibose 0.3mg	1 Tablet
24.	Paracetamol Tablet	Paracetamol IP (as Immediate Release) 300mg, Paracetamol IP (as Sustained Release) 700mg	1 Tablet
25.	Aceclofenac + Paracetamol Tablet	Aceclofenac IP 100mg, Paracetamol IP 325mg	1 Tablet
26.	Rosuvastatin + Clopidogrel Capsule	Rosuvastatin 10mg, Clopidogrel 75mg	1 Capsule
27.	Teneligliptin + Metformin Tablet (EFIGLIN M 1000)	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin Hydrochloride IP 1000mg (as Sustained Release form)	1 Tablet
28.	Olmesartan + Amlodipine Tablet	Olmesartan Medoxomil IP 20mg, Amlodipine Besylate IP eq. to Amlodipine 5mg,	1 Tablet
29.	Telmisartan + Metoprolol Tablet (Xstan-Beta 25mg)	Telmisartan IP 40mg, Metoprolol Tartrate IP 25mg (ER)	1 Tablet
30.	Telmisartan + Metoprolol Tablet (Xstan-Beta 50mg)	Telmisartan IP 40mg, Metoprolol Tartrate IP 50mg (ER)	1 Tablet
31.	Voglibose + Glimepride + Metformin Tablet	Voglibose IP 0.2mg, Glimepride IP 1mg, Metformin HCL IP 500mg (SR)	10 Tablets
32.	Atorvastatin + Clopidogrel Capsules (Atchol CV 10mg)	Atorvastatin Calcium eq. to Atorvastatin (as pellets) 10mg, Clopidogrel (as pellets) 75mg.	10 Capsule
33.	Voglibose + Glimepride + Metformin Tablet	Voglibose IP 0.2mg, Glimepride IP 2mg, Metformin Hydrochloride IP 500mg (SR)	1 Tablet
34.	Teneligliptin + Metformin Tablet (Tenephron M)	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin Hydrochloride 500mg (SR)	1 Tablet

35.	Teneligliptin + Metformin Tablet (Tenephron M Forte)	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin HCl 1000mg (SR)	1 Tablet
36.	Teneligliptin + Metformin Tablet (TYTIN M)	Teneligliptin Hydrobromide hydrate eq. to Teneligliptin 20mg, Metformin Hydrochloride 500mg (as extended release)	1 Tablet
37.	Tacrolimus Capsule	Tacrolimus IP 0.25mg	1 Capsule
38.	Telmisartan + Amlodipine Tablet	Telmisartan IP 80mg, Amlodipine Besilate IP 5mg	10 Tablet
39.	Telmisartan + Amlodipine Tablet (Tigatel AM 40)	Telmisartan IP 40mg, Amlodipine Besylate IP eq. to Amlodipine 5mg	1 Tablet
40.	Cefixime + Ofloxacin Tablet (Ranixime Plus)	Cefixime Trihydrate eq. to Cefixime Anhydrous IP 200mg, Ofloxacin IP 200mg	1 Tablet
41.	Teneligliptin + Metformin Tablet (Glypte M)	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin Hydrochloride 500mg	1 Tablet
42.	Teneligliptin + Metformin Tablet (Glypte M Forte)	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin Hydrochloride 1000mg	1 Tablet
43.	Glemipiride + Metformin Tablet (Ziglim – M1 Forte)	Glemipiride IP 1mg, Metformin Hydrochlorde IP 1000mg (as SR form)	1 Tablet
44.	Glemipiride + Metformin Tablet (Ziglim – M2 Forte)	Glimepiride IP 2mg, Metformin Hydrochlorde IP 1000mg (as SR form)	1 tablet
45.	Diclofenac Injection	Diclofenac Sodium IP 75mg/ml	1 ml
46.	Doxorubicin (Pegylated Liposomal) Injection	Doxorubicin HCL 2mg (Pegylated Liposomal) water for Injection	1 ml
47.	Telmisartan + Indapamide Tablet	Telmisartan IP 40mg Indapamide IP 1.5mg	1 Tablet
48.	Paracetamol + Mefenamic Acid Injection (Zydol- P DS)	Paracetamol 250mg Mefenamic Acid 100mg	1 ml
49.	Paracetamol + Phenylephrine + Chlorpheniramine + Sodium Citrate + Menthol Injection	Each 5ml contains: Paracetamol 125mg Phenylephrine Hydrochloride IP 5mg, Chlorpheniramine Maleate IP 0.5mg, Sodium Citrate IP 60mg, Menthol IP 1mg	1 ml
50.	Atorvastatin + Clopidogrel Capsule (Atocor CV)	Atorvastatin Calcium IP eq. to Atorvastatin 10mg (As film coated tablet), Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg (As 2 film coated 37.5mg each tablet)	10 Capsule
51.	Tacrolimus Capsule	Tacrolimus premix (20%) eq. to Tacrolimus IP 0.25mg	1 capsule
52.	Atorvastatin + Clopidogrel Capsule (Avas 10 Gold)	Atorvastatin Calcium IP eq. to Atorvastatin 10mg (As film coated tablet) Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg (As 2 film coated 37.5mg each tablet)	10 Capsule

53.	Atorvastatin + Clopidogrel Capsule (Astin 10 Gold)	Atorvastatin Calcium IP eq. to Atorvastatin 10mg (As film coated tablet), Clopidogrel Bisulphate IP eq. to Clopidogrel 75mg (As 2 film coated 37.5mg each tablet)	10 Capsule
54.	Glimepiride + Metformin Tablet (DIAPRIDE M 0.5)	Glimepiride IP 0.5mg, Metformin Hydrochloride IP 500mg (SR)	1 Tablet
55.	Telmisartan + Hydrochlorothiazide Tablet (Tigatel H 40)	Telmisartan IP 40mg, Hydrochlorothiazide IP 12.5mg	1 Tablet
56.	Telmisartan + Hydrochlorothiazide Tablet (Tigatel H 80)	Telmisartan IP 80mg, Hydrochlorothiazide IP 12.5mg	1 Tablet
57.	Telmisartan + Amlodipine Tablet (Tigatel AMH 40)	Telmisartan IP 40mg, Amlodipine Besylate IP Eq. to Amlodipine 5mg, Hydrochlorothiazide IP 12.5mg	1 Tablet
58.	Telmisartan + Amlodipine Tablet (Tigatel AMH 80)	Telmisartan IP 80mg, Amlodipine Besylate IP Eq. to Amlodipine 5mg, Hydrochlorothiazide IP 12.5mg	10 Tablet
59.	Sofosbuvir + Velpatasvir Tablet	Sofosbuvir 400mg, Velpatasvir 100mg	28 tablets
60.	Methylprednisolone Injection	Methylprednisolone Sodium Succinate USP. Eq. to Methylprednisolone 125mg	1 Vial
61.	Methylprednisolone Injection	Methylprednisolone Sodium Succinate USP. Eq. to ethylprednisolone 500mg	1 Vial
62.	Methylprednisolone Injection	Methylprednisolone Sodium Succinate USP. Eq. to Methylprednisolone 1000mg	1 Vial
63.	Bortezomib Injection (BortiRel)	Bortezomib IP 3.5mg Injection	1 Vial[1]

Table 2 - Notified Retail price of 1 scheduled formulation of Schedule-I under Drugs (Prices Control) Order, 2013.

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
1.	Anti-D Immunoglobulin	Injection 150mcg	Each Vial[2]

Table 3 - Notified ceiling price of 1 scheduled formulation of Schedule-I under para 19 of Drugs (Prices Control) Order, 2013.

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
1.	Phenylephrine	Drops 5%	1 ML[3]

Form -I application for price fixation of new drug under Para 2(u) of DPCO, 2013

On December 19, 2017, the NPPA has decided to de-link the price approval of new drugs with its internal guidelines. Earlier, in September 2014, the drug pricing regulator had asked all pharmaceutical firms to register themselves under its Integrated Pharmaceutical Database Management System (IPDMS), making this a requirement for fixing and revising drug prices. Now, NPPA in an office memorandum, has said that "price approval of new drugs shall not be linked to IPDMS and any other conditionality"[28].

28 http://www.nppaindia.nic.in/order/om_19-12-2017.pdf

NPPA has fixed/revised ceiling prices/Retail Prices of 27 scheduled formulations under DPCO, 2013

On December 20, 2017, the NPPA has fixed/revised the retail prices of 27 scheduled formulations under DPCO, 2013; the formulations with price caps are mostly from anti-diabetics, anti-hypertensive including other antibiotics categories as described below under various provisions –

Table 4 - Notified Retail price of 12 formulations under Drugs (Prices Control) Order, 2013

Sl. No.	Name of the Scheduled Formulation / Brand Name	Strength	Unit
1.	Voglibose + Metformin	Voglibose 0.2mg Metformin 500mg	1 Tablet
2.	Voglibose + Metformin	Voglibose 0.3mg Metformin 500mg	1 Tablet
3.	Voglibose + Metformin + Glimepirid	Voglibose 0.2mg Metformin 500mg Glimepirid 1mg	1 Tablet
4.	Voglibose + Metformin + Glimepirid	Voglibose 0.2mg Metformin 500mg Glimepirid 1mg	1 Tablet
5.	Voglibose + Metformin + Glimepirid	Voglibose 0.2mg Metformin 500mg Glimepirid 1mg	1 Tablet
6.	Voglibose + Metformin + Glimepirid	Voglibose 0.2mg Metformin 500mg Glimepirid 2mg	1 Tablet
7.	Voglibose + Metformin + Glimepirid	Voglibose 0.2mg Metformin 500mg Glimepirid 2mg	1 Tablet
8.	Voglibose + Metformin + Glimepirid	Voglibose 0.2mg Metformin 500mg Glimepirid 2mg	1 Tablet
9.	Voglibose + Metformin + Glimepirid	Voglibose 0.3mg Metformin 500mg Glimepirid 1mg	1 Tablet
10.	Voglibose + Metformin + Glimepirid	Voglibose 0.3mg Metformin 500mg Glimepirid 1mg	1 Tablet
11.	Voglibose + Metformin + Glimepirid	Voglibose 0.3mg Metformin 500mg Glimepirid 2mg	1 Tablet
12.	Diclofenac + Tramadol	Diclofenac 75mg Tramadol 50mg	1 Tablet[4]

Table 5 - Notified Retail Price of 15 formulations under Drugs (Prices Control) Order, 2013

Sl. No.	Name of the Scheduled Formulation / Brand Name	Strength	Unit
1.	Glimepiride + Metformin Tablets	Glimepiride 1mg & Metformin 500mg.	1 tablet
2.	Glimepiride + Metformin Tablets	Glimepiride 2mg & Metformin 500mg.	1 Tablet
3.	Metoprolol + Chlorthalidone Tablets	Metoprolol 25mg & Chlorthalidone 12.5mg.	1 Tablet
4.	Metoprolol + Chlorthalidone Tablets	Metoprolol 25mg & Chlorthalidone 12.5mg	1 Tablet
5.	Metoprolol + Chlorthalidone Tablets	Metoprolol 50mg & Chlorthalidone 12.5mg	1 Tablet
6.	Metoprolol + Chlorthalidone Tablets	Metoprolol 50mg & Chlorthalidone 12.5mg	1 Tablet
7.	Moxifloxacin + Cefixime Tablets	Moxifloxacin 400mg & Cefixime 400mg	1 Tablet
8.	Gliclazide + Pioglitazone + Metformin Tablets	Gliclazide 60mg, Pioglitazone 7.5mg & Metformin 500mg	1 Tablet
9.	Teneligliptin + Metformin Tablets	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg, Metformin HCl 1000mg	1 Tablet
10.	Teneligliptin + Metformin Tablets	Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20mg Metformin HCl 500mg	1 Tablet
11.	Glimepiride + Metformin Tablets	Glimepiride 1mg & Metformin 1000mg	1 Tablet
12.	Glimepiride + Metformin Tablets	Glimepiride 2mg & Metformin 1000mg.	1 Tablet
13.	Glimepiride + Metformin Tablets	Glimepiride 3mg & Metformin 1000mg	1 Tablet
14.	Metformin + Glimepiride + Pioglitazone Tablets	Metformin 500mg, Glimepiride 1mg & Pioglitazone 15mg	1 Tablet
15.	Metformin + Glimepiride + Pioglitazone Tablets	Metformin 500mg, Glimepiride 2mg & Pioglitazone 15mg	1 Tablet[5]

NPPA's consideration of Medtronic's request for discontinuation of Endeavour Sprint RX Zotarolimus Eluting Coronary Stent System

On December 27, 2017, the NPPA has considered the request of M/s India Medtronic Pvt. Ltd for discontinuation of Endeavor Sprint RX Zotarolimus Eluting Coronary Stent based on unavailability because of stoppage of its production globally; and noted in the Authority meeting No 51 held on 15/12/2017. The consideration was under para 21(2) of Drugs Prices Control Order (DPCO), 2013 on the ground of stoppage of manufacturing of these stent brands globally.

Para 21 (2) of the DPCO, 2013 reads as follows:

21. Monitoring the availability of scheduled formulations:

(1)…

(2) *Any manufacturer of scheduled formulation, intending to discontinue any scheduled formulation from the market shall issue a public notice and also intimate the government in Form- IV of Schedule-II of this order in this regard at least six months prior to the indented date of discontinuation and the Government may, in public interest, direct the manufacturer of the scheduled formulation to continue with required level of production or import for the period not exceeding one year, from the intended date of such discontinuation within a period of sixty days of receipt of such intimation*

NPPA has further advised that, in order to formally 'complete' the process of 'withdrawal' the company will issue a public notice in the prescribed format, in at least two national newspapers (one English and one in Hindi) and also publish the same on their website and send a copy of the same to NPPA[29].

29 http://www.nppaindia.nic.in/order/om_27-12-2017.pdf

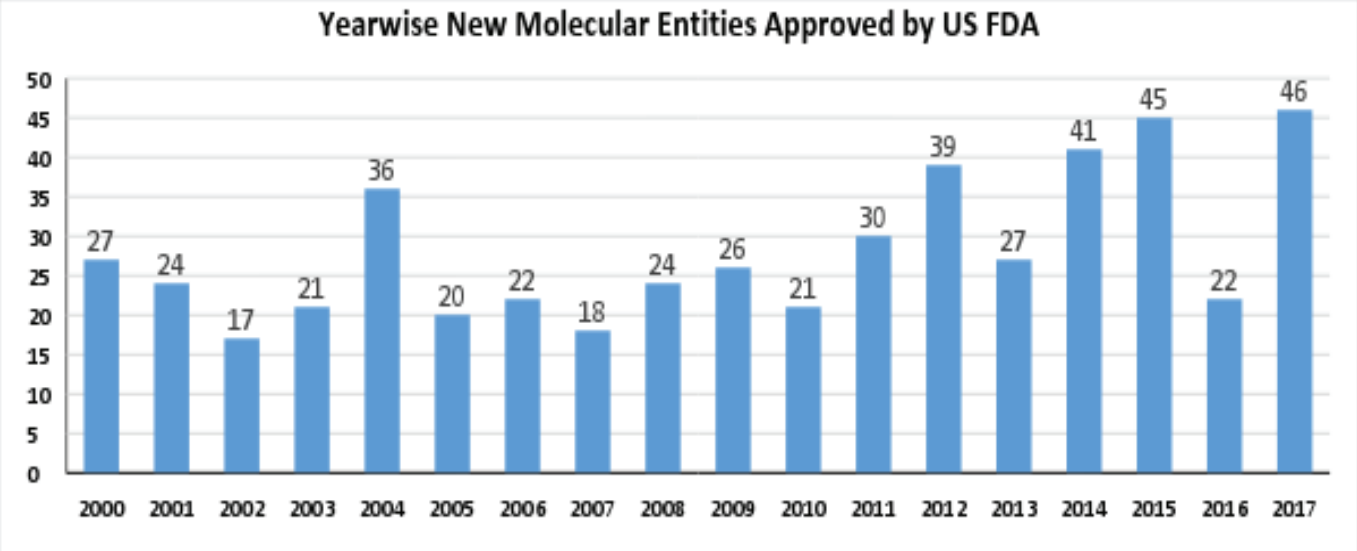
United States Food and Drug Administration (US-FDA): Novel Drug Approvals for 2017

The availability of new drugs and biological products often means new treatment options for patients and advances in health care. Each year, FDA's Center for Drug Evaluation and Research (CDER) approves a wide range of new drugs and biological products. Some of these products are innovative new products that have never been used in clinical practice. Other approved products are either similar to or related to, previously approved products, and they will compete with the existing ones in the market.

Certain drugs are classified as new molecular entities ("NMEs") for purpose of FDA review. Many of these products contain active moieties that have not been approved by FDA earlier, either as a single ingredient drug or as part of a combination product; but they frequently provide important new therapies for patients. Some drugs are characterized as NMEs for administrative purposes, but nonetheless contain active moieties that are closely related to active moieties in products that have previously been approved by FDA. For example, CDER classifies biological products submitted in an application under section 351(a) of the Public Health Service Act as NMEs for FDA review, regardless of whether the Agency previously has approved a related active moiety in a different product. FDA's classification of a drug as a "NME" for review purposes is distinct from its determination whether a drug product is a "new chemical entity" (NCE) within the meaning of the Federal Food, Drug, and Cosmetic Act.

The number of new molecular entities (NMEs) approved by the US Food and Drug Administration (FDA) in 2017 is 46,[30] the second highest number of NMEs approved in any year, only surpassed in the year 1996, when it approved 53 new molecular entities[31].

A year wise approval of NMEs by USFDA from 2000 to 2017 is represented in the graph below.



30 https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm537040.htm

31 https://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothepresent/default.htm

The 46 New Molecular Entities Approved by US FDA in 2017 are tabulated below:

Sr. No.	Drug Name	Active Ingredient	Approval Date	FDA-approved use on approval date
1.	Trulance	plecanatide	1/19/2017	To treat Chronic Idiopathic Constipation (CIC) in adult patients.
2.	Parsabiv	etelcalcetide	2/07/2017	To treat secondary hyperparathyroidism in adult patients with chronic kidney disease undergoing dialysis
3.	Emflaza	deflazacort	2/09/2017	To treat patients age 5 years and older with Duchenne muscular dystrophy (DMD)
4.	Siliq	brodalumab	2/15/2017	To treat adults with moderate-to-severe plaque psoriasis
5.	Xermelo	telotristat ethyl	2/28/2017	To treat carcinoid syndrome diarrhea
6.	Kisqali	ribociclib	3/13/2017	To treat postmenopausal women with a type of advanced breast cancer
7.	Xadago	safinamide	3/21/2017	To treat Parkinson's disease
8.	Bavencio	avelumab	3/23/2017	To treat metastatic Merkel cell carcinoma
9.	Symproic	naldemedine	3/23/2017	For the treatment of opioid-induced constipation
10.	Zejula	niraparib	3/27/2017	For the maintenance treatment for recurrent epithelial ovarian, fallopian tube or primary peritoneal cancers
11.	Dupixent	dupilumab	3/28/2017	To treat adults with moderate-to-severe eczema (atopic dermatitis)
12.	Ocrevus	ocrelizumab	3/28/2017	To treat patients with relapsing and primary progressive forms of multiple sclerosis
13.	Austedo	deutetrabenazine	4/3/2017	For the treatment of chorea associated with Huntington's disease
14.	Ingrezza	valbenazine	4/11/2017	To treat adults with tardive dyskinesia
15.	Brineura	cerliponase alfa	4/27/2017	To treat a specific form of Batten disease
16.	Alunbrig	brigatinib	4/28/2017	To treat patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib
17.	Rydapt	midostaurin	4/28/2017	To treat acute myeloid leukemia
18.	Tymlos	abaloparatide	4/28/2017	To treat osteoporosis in postmenopausal women at high risk of fracture or those who have failed other therapies
19.	Imfinzi	durvalumab	5/01/2017	To treat patients with locally advanced or metastatic urothelial carcinoma
20.	Radicava	edaravone	5/05/2017	To treat patients with amyotrophic lateral sclerosis (ALS)
21.	Kevzara	sarilumab	5/22/2017	To treat adult rheumatoid arthritis

22.	Baxdela	delafloxacin	6/19/2017	To treat patients with acute bacterial skin infections
23.	Bevyxxa	betrixaban	6/23/2017	For the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness
24.	Tremfya	guselkumab	7/13/2017	For the treatment of adult patients with moderate-to-severe plaque psoriasis
25.	Nerlynx	neratinib maleate	7/17/2017	To reduce the risk of breast cancer returning
26.	Vosevi	sofosbuvir, velpatasvir and voxilaprevir	7/18/2017	To treat adults with chronic hepatitis C virus
27.	Idhifa	enasidenib	8/01/2017	To treat relapsed or refractory acute myeloid leukemia
28.	Mavyret	glecaprevir and pibrentasvir	8/03/2017	To treat adults with chronic hepatitis C virus
29.	Besponsa	inotuzumab ozogamicin	8/17/2017	To treat adults with relapsed or refractory acute lymphoblastic leukemia
30.	Vabomere	meropenem and vaborbactam	8/29/2017	To treat adults with complicated urinary tract infections
31.	benznidazole	benznidazole	8/29/2017	To treat children ages 2 to 12 years old with Chagas disease
32.	Aliqopa	copanlisib	9/14/2017	To treat adults with relapsed follicular lymphoma
33.	Solosec	secnidazole	9/15/2017	To treat bacterial vaginosis
34.	Verzenio	abemaciclib	9/28/2017	To treat certain advanced or metastatic breast cancers
35.	Calquence	acalabrutinib	10/31/2017	To treat adults with mantle cell lymphoma
36.	Vyzulta	latanoprostene bunod ophthalmic solution	11/02/2017	To treat intraocular pressure in patients with open-angle glaucoma or ocular hypertension.
37.	Prevymis	letermovir	11/08/2017	To prevent infection after bone marrow transplant
38.	Fasenra	benralizumab	11/14/2017	For add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype
39.	Mepsevii	vestronidase alfa-vjbk	11/15/2017	To treat pediatric and adult patients with an inherited metabolic condition called mucopolysaccharidosis type VII (MPS VII), also known as Sly syndrome.
40.	Hemlibra	emicizumab	11/16/2017	To prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A who have developed antibodies called Factor VIII (FVIII) inhibitors.
41.	Ozempic	semaglutide	12/05/2017	To improve glycemic control in adults with type 2 diabetes mellitus
42.	Xepi	ozenoxacin	12/11/2017	To treat impetigo
43.	Rhopressa	netarsudil	12/18/2017	To treat glaucoma or ocular hypertension

44.	Macrilen	macimorelin acetate	12/20/2017	For the diagnosis of adult growth hormone deficiency
45.	Steglatro	ertugliflozin	12/20/2017	To improve glycemic control in adults with type 2 diabetes mellitus
46.	Giapreza	angiotensin II	12/21/2017	To increase blood pressure in adults with septic or other distributive shock

Conclusion:

Novel drugs are innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient care and public health.

USFDA's first drug approval for the treatment of Eosinophilic Granulomatosis with Polyangiitis (formerly known as Churg-Strauss Syndrome)

On December 12, 2017, the U.S. Food and Drug Administration expanded the approved use of Nucala (mepolizumab) to treat adult patients with Eosinophilic Granulomatosis with PolyAngiitis (EGPA), a rare autoimmune disease that causes vasculitis, an inflammation in the wall of blood vessels of the body. This new indication provides the first FDA-approved therapy - specifically to treat EGPA.

The approval of Nucala is granted to GlaxoSmithKline on the basis of clinical trial data spanning 52-weeks , which showed that patients receiving 300 mg of Nucala achieved a significantly greater accrued time in remission compared to the patients receiving placebo[32].

About Eosinophilic Granulomatosis with Polyangiitis (EGPA)

According to the National Institute of Health (NIH)[33], EGPA is a rare condition characterized by asthma with high levels of eosinophils (a type of white blood cells that help fight infection), and inflammation of small- to medium-sized blood vessels. The inflamed vessels can affect various organ systems including the lungs, gastrointestinal tract, skin, heart and nervous system. The exact cause of eosinophilic granulomatosis with polyangiitis is unknown, but it is thought to be an autoimmune disorder. It is estimated that approximately 0.11 to 2.66 new cases per million people are diagnosed each year, with an overall prevalence of 10.7 to 14 per million adults.

About Mepolizumab (Nucala)

Nacula is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) produced by recombinant DNA technology in the ovarian cells of Chinese hamster. It is a targeted biological therapy developed to treat diseases which are driven by inflammation linked to higher-than-normal eosinophils being present in the blood.

Nucala was previously approved in 2015 to treat patients age 12 years and older with a specific subgroup of asthma (severe asthma with an eosinophilic phenotype) in addition to their current asthma medicines. At present, Mepolizumab 100mg is approved for the treatment of patients with severe eosinophilic asthma in over 40 countries including the EU, US and Japan and has been prescribed to over 18,000 patients in the US. Mepolizumab 300mg is now approved in the US for the treatment of adult patients with EGPA. Nucala is administered subcutaneously into the upper arm, thigh or abdomen once in every four weeks by a health care professional[34].

32 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm588594.htm

33 https://rarediseases.info.nih.gov/diseases/6111/eosinophilic-granulomatosis-with-polyangiitis

34 https://www.gsk.com/en-gb/media/press-releases/gsk-achieves-approval-for-nucala-mepolizumab-for-the-treatment-of-eosinophilic-granulomatosis-with-polyangiitis-egpa-for-adults-in-the-us/

USFDA approval of Ogivri is the first Biosimilar approval for cancer drug Herceptin

On December 1, 2017, the United States Food and Drug Administration (USFDA) gave approval to Ogivri (trastuzumab-dkst), as a Biosimilar to Herceptin (trastuzumab) for the treatment of patients with breast or metastatic stomach cancer whose tumors overexpress the HER2 gene (HER2+). Ogivri, approved as a Biosimilar and not as an interchangeable product, is the first Biosimilar approved in the United States for the treatment of breast cancer or stomach cancer, and on the second Biosimilar approved in the United States for the treatment of cancer.

The FDA defines Biosimilar as a biological product that is 'highly similar' to and has 'no clinically meaningful differences' from an existing FDA-approved reference product[35]. A manufacturer developing a proposed biosimilar demonstrates that its product is highly similar to the reference product by extensively analyzing (i.e., characterizing) the structure and function of both the reference product and the proposed biosimilar. State-of-the-art technology is used to compare characteristics of the products, such as purity, chemical identity, and bioactivity. The manufacturer uses results from these comparative tests, along with other information, to demonstrate that the biosimilar is highly similar to the reference product. The manufacturer must also demonstrate that its proposed biosimilar product has no clinically meaningful differences from the reference product in terms of safety, purity, and potency (safety and effectiveness). This is generally demonstrated through human pharmacokinetic (exposure) and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.

The approval of Ogivri is based on the review of evidence that included data from extensive structural and functional characterization, animal study, human pharmacokinetic and pharmacodynamic, clinical immunogenicity and other clinical safety and effectiveness that demonstrates Ogivri is Biosimilar to Herceptin[36]. The USFDA granted approval of Ogivri to Mylan GmbH, the first biosimilar from Mylan and Biocon´s joint portfolio approved in the United States. Mylan anticipates potentially being the first company to offer a biosimilar to Herceptin. Mylan and Biocon's biosimilar for Herceptin is also under review by regulatory authorities in Australia, Canada, Europe and several additional markets. It is already approved in 19 countries around the world, including India, thus providing increased access to this more affordable biologic for cancer patients.

About Ogivri (Trastuzumab)

Trastuzumab is a HER2/neu receptor antagonist indicated for the treatment of HER2 overexpressing breast cancer; HER2-overexpressing metastatic gastric or gastro-esophageal junction adenocarcinoma and metastatic stomach cancer[37,38].

About HER2 overexpression

The HER2 (human epidermal growth factor receptor 2) is a gene that plays a role in the development of breast cancer. HER2 gene makes HER2 proteins. HER2 proteins are receptors on breast cells. Normally, HER2 receptors help control how a healthy breast cell grows, divides, and repairs itself. But in about 25% of breast cancers, the HER2 gene doesn't work properly and makes too many copies of itself (known as HER2 gene amplification).

35 https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm

36 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587378.htm

37 https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103792s5250lbl.pdf

All these extra HER2 genes propel breast cells to produce too many HER2 receptors (HER2 protein overexpression), making breast cells grow and divide uncontrollably[39].

Note -

Mylan and Biocon are exclusive partners on a broad portfolio of biosimilar and insulin products. Biosimilar for Herceptin is one of the six biologic products co-developed by Mylan and Biocon for the global marketplace.

39 http://www.breastcancer.org/symptoms/diagnosis/her2

US FDA issues final rule on safety and effectiveness for certain active ingredients in over-the-counter health care antiseptic hand washes and rubs in the medical setting

On December 19, 2017, the United States Food and Drug Administration has finalized a rule, first proposed in 2015, regarding use of Triclosan and 23 other active ingredients, not generally recognized as safe and effective (GRASE), in over-the-counter (OTC) healthcare antiseptic products like hand washes and rubs, surgical hand scrubs and rubs, and patient antiseptic skin preparations used by healthcare personnel.

As no additional safety and effectiveness data were provided to the FDA to support monograph conditions for these 24 active ingredients[40], the FDA has ruled that products containing these active ingredients, intended for use in OTC healthcare antiseptics by health care professionals in a hospital setting or in other health care situations outside the hospitals, are not allowed to be marketed without undergoing pre-market review. Healthcare antiseptic drug products containing one or more of these non-GRASE active ingredients will be considered new drugs for which approved new drug applications (NDAs) are required for marketing. Manufacturers will have one year to comply with this final rule either by reformulating (revising or changing formulas) their products or removing them from the market. Based on the rule, manufacturers have already started removing these ingredients from their products. Of the 24 active ingredients listed by the FDA as non-GRASE, Triclosan is the only active ingredient currently being used in any marketed healthcare antiseptic product. Therefore, most healthcare antiseptics, currently marketed, will not be impacted by this final rule.

Speaking on this matter, the FDA Commissioner Scott Gottlieb said that "Ensuring the safety and effectiveness of over-the-counter healthcare antiseptics has been a priority for the FDA, not only because these products are an important component of infection control strategies in health care settings, but also because of the role these products may play in contributing to antimicrobial resistance if they're not manufactured or used appropriately." The final rule has been published in the Federal Register of the United States titled as "Safety and Effectiveness of Health Care Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use[41]."

Final Rule Covers Only Healthcare Antiseptics

The final rule describes 'Healthcare Antiseptics' as "drug products that are generally intended for use by healthcare professionals in a hospital setting or other healthcare situations outside the hospital. Patient antiseptic skin preparations, which are products that are used for preparation of the skin prior to surgery (i.e., preoperative) and preparation of skin prior to an injection (i.e., pre-injection), may be used by patients outside the traditional health care setting. Some patients (e.g., diabetics who manage their disease with insulin injections) self-inject medications that have been prescribed by a healthcare professionals for use at home or at other locations and use patient preoperative skin preparations prior to injection".

In this final rule, the term 'healthcare antiseptics' includes the following products:

- Hand washes for Healthcare personnel
- Hand rubs for Healthcare personnel
- Surgical hand scrubs

40 https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm589474.htm

41 https://www.federalregister.gov/documents/2017/12/20/2017-27317/safety-and-effectiveness-of-health-care-antiseptics-topical-antimicrobial-drug-products-for

- Surgical hand rubs
- Patient antiseptic skin preparations (i.e., patient preoperative and pre-injection skin preparations)

Ingredients Not Generally Recognized as Safe and Effective

Under the final rule the list of following ingredients has been classified as Not Generally Recognized as Safe and Effective (non-GRASE), because no additional safety or effectiveness data have been submitted to support a GRAS/GRAE determination for the non-deferred health care antiseptic active ingredients described in this rule.

Thus, the following active ingredients are not GRAS/GRAE for use as a healthcare antiseptic:

1. Chlorhexidine gluconate
2. Cloflucarban
3. Fluorosalan
4. Hexachlorophene
5. Hexylresorcinol
6. Iodophors (Iodine-containing ingredients)
7. Iodine complex (ammonium ether sulfate and polyoxyethylene sorbitan monolaurate)
8. Iodine complex (phosphate ester of alkylaryloxy polyethylene glycol)
9. Iodine tincture USP
10. Iodine topical solution USP
11. Nonylphenoxypoly (ethyleneoxy) ethanoliodine
12. Poloxamer—iodine complex
13. Undecoylium chloride iodine complex
14. Mercufenol chloride
15. Methylbenzethonium chloride
16. Phenol
17. Secondary amyltricresols
18. Sodium oxychlorosene
19. Tribromsalan
20. Triclocarban
21. Triclosan
22. Triple dye
23. Combination of calomel, oxyquinoline benzoate, triethanolamine, and phenol derivative
24. Combination of mercufenol chloride and secondary amyltricresols in 50 percent alcohol

Compliance Date

Under the final rule, manufacturers will have one year to remove the 24 ingredients from their products. Of the 24, FDA says triclosan is the only one currently marketed and that going forward manufacturers will need to submit a new drug application (NDA) before marketing antiseptics containing any of the other listed ingredients. Accordingly, OTC healthcare antiseptic drug products containing these active ingredients will require approval under an NDA (New Drug Application) or ANDA (Abbreviated New Drug Application) prior to marketing.

Ingredients Deferred by the FDA for review

In response to requests from industry, the FDA has deferred final rulemaking for one year, subject to renewal, on following six specific active ingredients that are the most commonly used in currently marketed OTC healthcare antiseptic products:

- alcohol (ethanol),
- isopropyl alcohol,
- povidone-iodine,
- benzalkonium chloride,
- benzethonium chloride, and
- chloroxylenol (PCMX)

The deferment has been provided to manufacturers with more time to complete the scientific studies necessary to fill the data gaps identified so that the agency can make a safety and efficacy determination about these ingredients. In addition, the final rule does not affect healthcare antiseptics that are currently marketed under new drug applications and abbreviated new drug applications.

The monograph or non-monograph status of these six ingredients will be addressed, either after completion and analysis of ongoing studies to address the safety and effectiveness data gaps of these ingredients or at a later date, if these studies are not completed.

Conclusion

This action on part of the FDA is an ongoing, comprehensive review of OTC antiseptic active ingredients to ensure that these ingredients remain safe and effective for use.

US FDA Issues Guidance for Industry on Product Name Placement, Size, and Prominence in Promotional Labeling and Advertisements

The US Food and Drug Administration (FDA) in December 2017, issued guidance for industry on prescription drug product name placement, size, prominence and frequency in promotional labeling and advertisements for human prescription drugs[42].

This guidance clarifies the requirements for product name placement, size, prominence, and frequency in promotional labeling and advertisements for prescription drugs. The disclosure of the product name in promotional labeling and advertisements is important for proper identification and to ensure safe and effective use. This guidance also articulates the circumstances under which FDA intends to refrain from taking enforcement action regarding these requirements.

The recommendations in this guidance pertain to product names in traditional print media promotional labeling and advertisements (e.g., journal advertisements, detail aids, brochures), audiovisual promotional labeling (e.g., videos shown in a health care provider's office), broadcast advertisements (e.g., television advertisements, radio advertisements), and electronic and computer-based promotions (e.g., internet, social media, emails, CD-ROMs, DVDs).

In this guidance, FDA has further clarified issues relating to the direct conjunction of the proprietary and established names, as well as the frequency of use of the established name on printed pages or spreads, in running text or columns, in the audio portion of audiovisual promotions, and in electronic media.

FDA Commissioner Scott Gottlieb said that "Promotional material that drug makers share with patients and providers can be a helpful tool for encouraging patients to seek medical care and raising awareness about new and different treatment options. The FDA plays an important role in helping to make sure these presentations are truthful, balanced, and non-misleading, and we need to study promotional material to constantly improve our oversight over these activities". He further said, "A key to our oversight is recognizing claims in prescription drug promotion that have the potential to deceive or mislead consumers and health care professionals. We also need to have clear rules for how sponsors can present certain information, even elements as straightforward as the product name, and do so without introducing features that could mislead patients. These new efforts are part of an ongoing policymaking process aimed at making sure our practices protect consumers and help ensure that the information provided to them is useful for protecting their health"[43].

The FDA has also released a Federal Register Notice, concerning FDA's proposal to study the ability of consumers and healthcare professionals to spot and report deceptive prescription drug promotion practices. The ability to spot deceptive prescription drug promotion in the marketplace has important public health implications. Patients may use information from drug promotions, such as information about a product's efficacy and risks, when exploring treatment options and making treatment choices. Likewise, health care professionals may consider information from promotional materials when making prescription decisions. In cases where such information is false or misleading, consumers may ask for and health care professionals may prescribe specific drugs that they would not otherwise request or prescribe, respectively. Once completed, the proposed studies will provide data on whether consumers and health care professionals can identify claims as false or misleading, and whether they would be willing to report deceptive drug promotion to the FDA. Although both studies will assess consumers

42 https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM375784.pdf

43 https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm588419.htm

and health care professionals, one study will focus on the degree of deception in an advertisement while the second study will focus on implicitly vs explicitly deceptive claims[44].

44 https://s3.amazonaws.com/public-inspection.federalregister.gov/2017-26704.pdf

US FDA proposes new, risk-based enforcement priorities to protect consumers from potentially harmful, unproven homeopathic drugs

FDA continues to find that some homeopathic drugs are manufactured with active ingredients that can create health risks while delivering no proven medical benefits

On December 18, 2017, the United States Food and Drug Administration proposed a new, risk-based enforcement approach to drug products labeled as homeopathic[45]. To protect consumers who choose to use homeopathic products, this proposed new approach would update the FDA's existing policy to better address situations where homeopathic treatments are being marketed for serious diseases and/or conditions but where the products have not been shown to offer clinical benefits. It also covers situations where products labeled as homeopathic contain potentially harmful ingredients or do not meet current good manufacturing practices[46].

Under the law, homeopathic drug products are subject to the same requirements related to approval, adulteration and misbranding as any other drug product. However, prescription and nonprescription drug products labeled as homeopathic have been manufactured and distributed without FDA approval under the agency's enforcement policies since 1988.

Speaking on the matter FDA Commissioner Scott Gottlieb said that "In recent years, we've seen a large uptick in products labeled as homeopathic that are being marketed for a wide array of diseases and conditions, from the common cold to cancer. In many cases, people may be placing their trust and money in therapies that may bring little-to-no benefit in combating serious ailments, or worse – that may cause significant and even irreparable harm because the products are poorly manufactured, or contain active ingredients that are not adequately tested or disclosed to patients. Our approach to regulating homeopathic drugs must evolve to reflect the current complexity of the market, by taking a more risk-based approach to enforcement. We respect that some individuals want to use alternative treatments, but the FDA has a responsibility to protect the public from products that may not deliver any benefit and have the potential to cause harm."

The FDA's proposed approach prioritizes enforcement and regulatory actions against unapproved drug products labeled as homeopathic that have the greatest risk-potential to harm patients. Under this approach, many homeopathic products will likely fall outside the risk-based categories described in the new draft guidance and will remain available to consumers. The FDA intends to focus its enforcement authority on the following kinds of products:

- ***Products with reported safety concerns*** **-** For example, MedWatch reports or other information submitted to the Agency can indicate or signal a potential association between the product and an adverse event, medication errors, or other safety issues.
- ***Products that contain or claim to contain ingredients associated with potentially significant safety concerns*** **-** For example, potentially significant safety concerns are raised by products that contain or purport to contain:
    - An infectious agent with the potential to be pathogenic;

45 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm589243.htm

46 https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM589373.pdf

- A controlled substance, as defined in the Controlled Substances Act, 21 U.S.C. 812;
- Multiple ingredients that, when used in combination, raise safety concerns due to possible interactions, synergistic effects, or additive effects of the various ingredients; and,
- Ingredients that pose potential toxic effects, particularly when those ingredients are concentrated or in low dilution presentations (e.g., 1X, 2X, or 1C), or are not adequately controlled in the manufacturing process.

- ***Products for routes of administration other than oral and topical -*** For example, unapproved injectable drug products and unapproved ophthalmic drug products pose a greater risk of harm to users due to their routes of administration (e.g., bypassing some of the body's natural defenses, differences in absorption) and the potential risk of harm from contamination.
- ***Products intended to be used for the prevention or treatment of serious and/or life-threatening diseases and conditions -*** Unapproved products for serious and/or threatening diseases and conditions raise public health concerns, in part, because they may cause users to delay or discontinue medical treatments that have been found safe and effective through the NDA (New Drug Application) or BLA (Biologics License Application) approval processes.
- ***Products for vulnerable populations -*** For example, patient populations such as immunocompromised individuals, infants and children, the elderly, and pregnant women may be at greater risk for adverse reactions associated with a drug product, even if it contains only small amounts of an ingredient, due to their varying ability to absorb, metabolize, distribute, or excrete the product or its metabolites. These populations may also be at greater risk of harm as a result of foregoing the use of medical treatments that have been found safe and effective through the NDA or BLA approval processes or under the OTC (Over-the-Counter, Non-Prescription) Drug Review.
- ***Products that do not meet standards of quality, strength or purity as required under the law -*** For example, if a product purports to be or is represented as a product recognized in an official compendium but its strength, quality, or purity differs from the standards set forth in that official compendium (defined by 21 U.S.C. 321 as the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, official National Formulary, or any supplement to any of them), or if there are significant violations of current good manufacturing practice requirements.

Examples of products that may be subject to the enforcement priorities in the draft guidance are infant and children's products labeled to contain ingredients associated with potentially significant safety concerns, such as belladonna and nux vomica; and products marketed for serious conditions, such as cancer and heart disease.
While the FDA considers comments to the draft guidance, it intends to examine how the agency is implementing its current compliance policy. Given the concerns about the proliferation of potentially ineffective and harmful products labeled as homeopathic, the FDA will consider taking additional enforcement and/or regulatory actions, consistent with the current enforcement policies, which also align with the risk-based categories described in the draft guidance, in the interest of protecting the public.

Homeopathy is an alternative medical practice developed in the late 1700s, based on two main principles: that a substance that causes symptoms in a healthy person can be used in diluted form to treat illness (known as "like-cures-like"); and the more diluted the substance, the more potent it is (known as the "law of infinitesimals"). Homeopathic drug products are prepared from a variety of sources, including plants, minerals, chemicals and human and animal excretions or secretions. These products are typically sold in pharmacies, retail stores and online.

Until relatively recently, homeopathy was a small market for specialized products. Over the last decade, the homeopathic drug market has grown exponentially, resulting in a nearly $3 billion industry that exposes more

patients to potential risks associated with the proliferation of unproven, untested products and unsubstantiated health claims. During this time, the FDA has seen a corresponding increase in safety concerns, including serious adverse events, associated with drug products labeled as homeopathic. In addition, the agency has also found an increasing number of poorly manufactured products that contain potentially dangerous amounts of active ingredients that can create additional risks.

In September 2016, the FDA warned against the use of homeopathic teething tablets and gels containing belladonna, a toxic substance that has an unpredictable response in children under two years of age, after the products were associated with serious adverse events, including seizures and deaths, in infants and children[47]. An FDA lab analysis later confirmed that certain homeopathic teething tablets contained elevated and inconsistent levels of belladonna[48]. A similar issue occurred in 2010, when Hyland's Teething Tablets were found to contain varying amounts of belladonna. An FDA inspection of this product's manufacturing facility indicated substandard control in the product's manufacturing.

The FDA has issued warnings related to a number of other homeopathic drug products over the past several years. These include certain homeopathic zinc-containing intranasal products that may cause a loss of sense of smell[49]; homeopathic asthma products that have not been shown to be effective in treating asthma; and various homeopathic drug products labeled to contain potentially toxic ingredients, like nux vomica which contains strychnine[50] (a highly toxic, well-studied poison often used to kill rodents).

Janet Woodcock, director of the FDA's Center for Drug Evaluation and Research said that the "Homeopathic products have not been approved by the FDA for any use and may not meet modern standards for safety, effectiveness and quality. The draft guidance is an important step forward in the agency's work to protect patients from unproven and potentially dangerous products."

In April 2015[51], the FDA held a public hearing to obtain inputs from stakeholders about the current use of drug products labeled as homeopathic, as well as the agency's regulatory framework for these products. The FDA sought broad public feedback on its enforcement policies related to drug products labeled as homeopathic. As a result of the agency's evaluation, which included consideration of the information obtained from the public hearing and the more than 9,000 comments received to the agency's public docket, the FDA has determined that it is in the best interest of the public health to issue a new draft guidance that proposes a comprehensive, risk-based enforcement approach to drug products labeled as homeopathic and marketed without FDA approval.

The FDA is not alone in reexamining its approach to homeopathy. In November 2016, the Federal Trade Commission (FTC) announced a new enforcement policy[52] explaining that they will hold efficacy and safety claims for over-the-counter homeopathic drugs to the same standard as other products making similar health claims. Notably, the FTC said that companies must have competent and reliable scientific evidence for health-related claims, including claims that a product can treat specific conditions.

The FDA encourages public comments on the draft guidance during the 90-day comment period.

47 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm523468.htm

48 https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm230762.htm

49 https://wayback.archive-it.org/7993/20170113083935/http:/www.fda.gov/ForConsumers/ConsumerUpdates/ucm166931.htm

50 https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2017/ucm586501.htm

51 https://www.fda.gov/Drugs/NewsEvents/ucm430539.htm

52 https://www.ftc.gov/news-events/press-releases/2016/11/ftc-issues-enforcement-policy-statement-regarding-marketing

Conclusion:

The US Food and Drug Administration (FDA) through this new draft guidance outlines how it will take a new risk-based enforcement approach to drug products labeled as homeopathic. The agency says it will begin prioritizing enforcement actions against such homeopathic products with reported safety concerns, products intended for preventing or treating serious or life-threatening diseases and products aimed at vulnerable populations, among others.

World Health Organization (WHO) advises Dengue Vaccine (Dengvaxia) to be used only in people previously infected with dengue

On December 13, 2017, following a consultation with the Global Advisory Committee on Vaccine Safety, the World Health Organization (WHO) determined that the dengue vaccine CYD-TDV, sold under the brand name Dengvaxia, prevents disease in majority of vaccine recipients but it should not be administered to people who have previously not been infected with dengue virus[53].

This recommendation was based on new evidence communicated by the vaccine manufacturer (Sanofi Pasteur), indicating an increase in incidence of hospitalization and severe illness in vaccinated children never infected with dengue.

The WHO Global Advisory Committee on Vaccine Safety considered the company's new results from the analysis of clinical trial data, which indicate an increased risk of severe dengue disease, in people who have never been infected affects about 15% of the vaccinated individuals. The magnitude of risk is in the order of about 4 out of every 1000 seronegative patients vaccinated who developed severe dengue disease during the five years of observation; whereas the risk of developing severe dengue disease in non-vaccinated individuals has been calculated as 1.7 per 1000 over the same period of observation. By contrast, for the 85% who have had dengue disease before immunization, there is a reduction of 4 cases of severe dengue per 1 000 who are vaccinated.

To minimize illness for seronegative vaccinated people, WHO recommends enhancing measures that reduce exposure to dengue infection among populations where the vaccine has already been administered. For vaccine recipients who present with clinical symptoms compatible with dengue virus infection, access to medical care should be expedited to allow for proper evaluation, identification, and management of severe forms of the disease.

Background

Dengue is a mosquito-borne viral infection causing a severe flu-like illness and, sometimes causing a potentially lethal complication called severe dengue. The incidence of dengue has increased 30-fold over the last 50 years. Up to 50-100 million infections are now estimated to occur annually in over 100 endemic countries, putting almost half of the world's population at risk[54]. The dengue virus (DEN) comprises four distinct serotypes (DEN-1, DEN-2, DEN-3 and DEN-4) which belong to the genus Flavivirus, family Flaviviridae.

Distinct genotypes have been identified within each serotype, highlighting the extensive genetic variability of the dengue serotypes. Among them, "Asian" genotypes of DEN-2 and DEN-3 are frequently associated with severe disease accompanying secondary dengue infections.

The disease is endemic in more than 100 countries in WHO's African, American, Eastern Mediterranean, South-East Asian and Western Pacific regions; wherein the Americas, South-East Asia and Western Pacific regions are the most seriously affected.

There is no specific dengue treatment and prevention is primarily limited to vector control measures. A safe and effective dengue vaccine would therefore, represent a major advance in the control of the disease.

53 http://www.who.int/medicines/news/2017/WHO-advises-dengvaxia-used-only-in-people-previously-infected/en/

54 http://www.who.int/denguecontrol/disease/en/

Sanofi Pasteur, the vaccines division of Sanofi, was the first pharmaceutical company to develop and market a vaccine for Dengue known as Dengvaxia® (earlier known as CYD-TDV). It is the first vaccine to be licensed in the world for the prevention of dengue. It is a live attenuated tetravalent vaccine made using recombinant DNA technology and is administered in three phases separated by six-month intervals. It became commercially available in 2016 and is currently licensed in 19 countries (Argentina, Australia, Bangladesh, Bolivia, Brazil, Cambodia, Costa Rica, El Salvador, Guatemala, Honduras, Indonesia, Malaysia, Mexico, Paraguay, Peru, The Philippines, Singapore, Thailand and Venezuela)[55].

New analysis evaluated long-term safety and efficacy

Earlier on November 29, 2017, Sanofi announced that it will ask health authorities to update information provided to physicians and patients on its dengue vaccine Dengvaxia® in countries where it is approved. The request was based on a new analysis of long-term clinical trial data, which found differences in vaccine performance based on prior dengue infection[56].

Based on up to six years of clinical data, the new analysis evaluated long-term safety and efficacy of Dengvaxia in people who had been infected with dengue prior to vaccination and those who had not been infected. The analysis confirmed that Dengvaxia provides persistent protective benefit against dengue fever in those who had prior infection. For those not previously infected by dengue virus, however, the analysis also found that in the longer term, more virulent and severe form of disease could occur following vaccination upon a subsequent dengue infection.

Proposed Label Update

Based on the new analysis, Sanofi will propose that national regulatory agencies update the prescribing information, known as the label in many countries, requesting that healthcare professionals assess the likelihood of prior dengue infection in an individual before vaccinating. Vaccination should only be recommended when the potential benefits outweigh the potential risks (in countries with high burden of dengue disease). For individuals who have not been previously infected by dengue virus, vaccination should not be recommended.

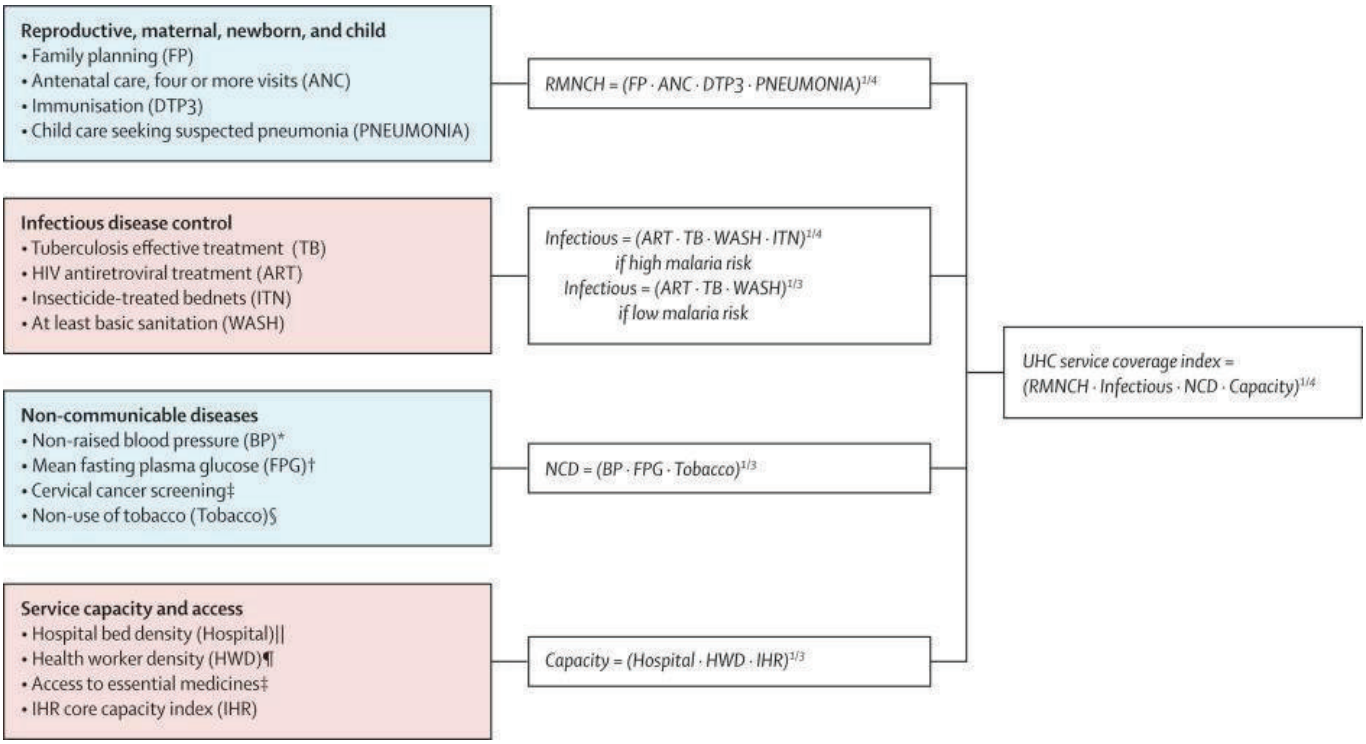
55 http://dengue.info/dengue-vaccine-registered-in-19-countries/

56 http://mediaroom.sanofi.com/sanofi-updates-information-on-dengue-vaccine/

Half the world lacks access to essential health services: A report by World Bank and WHO

On December 13, 2017, the World Bank and World Health Organization (WHO) released the Universal Health Coverage (UHC): 2017 Global Monitoring Report; simultaneously published in Lancet Global Health, suggests that half of the world lacks access to essential health services.

The Universal Health Coverage (UHC) says health services for all, which means everyone can obtain the health services they need without suffering financial hardship. However, the UHC report looks at how many people globally lack access to essential health services and how many are pushed into poverty or spending too much of their household budgets on health care expenses. Further, the calculation of universal health coverage service index is accomplished on the basis of national levels of coverage of 16 indicators, which are broadly categorized under four major groups as described in the flow chart given below -



IHR=International health regulations

Fig 1 – 16 indicators in four major groups

The UHC 2017 Global Monitoring report advocates that, more than 7.3 billion, though having access to some of health services, do not receive all of the essential services they need. In terms of financial protection, 800 million people spend at least 10 percent of their household budgets on health expenses for themselves, a sick child or another family member. For almost 100 million people these expenses are high enough to push them into extreme poverty, forcing them to survive on just $1.90 or less a day. But the report also shows some good news; the 21st century has seen an increase in the number of people able to obtain some key health services. In addition, fewer people are now being tipped into extreme poverty than at the turn of the century.

However, progress is highly uneven as there are wide gaps in the availability of basic healthcare services in Sub-Saharan Africa and Southern Asia. In some other regions with slightly better services as in Eastern Asia, Latin America and Europe, a growing number of people are spending at least 10 percent of their household budgets on out-of-pocket health expenses[57].

Overall many countries are making progress towards UHC. Countries can take actions to move more rapidly towards it, or to maintain the gains they have already made. In countries where health services have traditionally been accessible and affordable, governments are finding it increasingly difficult to respond to the ever-growing health needs of the populations and the increasing costs of health services[58].

Universal Health Coverage Forum 2017: Tokyo Declaration on Universal Health Coverage Adopted

The Japan International Cooperation Agency (JICA) co-hosted the Forum with the World Bank; the World Health Organization (WHO); the United Nations Children's Fund (UNICEF); UHC2030*1; the Ministry of Finance, the Ministry of Foreign Affairs; and the Ministry of Health, Labour and Welfare of Japan. High-level government officials from various countries, representatives of international agencies and experts — including the Japanese Prime Minister and the United Nations' Secretary General— gathered together and adopted the Tokyo Declaration on Universal Health Coverage, a commitment to achieve universal health coverage (UHC) by 2030. As an outcome of the Forum, the Tokyo Declaration on Universal Health Coverage was adopted. Pillars of the declaration as a commitment to achievement of UHC by 2030 include strengthening global momentum, accelerating country-led process and innovation[59].

India and Universal Health Coverage (UHC)

In India, the Government has taken concrete steps to reduce the Out of Pocket Expenditure (OOPE) to achieve UHC, wherein some of the health programs and missions listed below play a major role-

1. **Mission Indradhanush/intensified mission indradhanush** is one of the largest global public health initiatives launched in 2014. In its four phases till date, MI has successfully reached over 25 million children in over 528 districts.
2. **The Pradhan Mantri Dialysis Program** has been launched under the National Health Mission (NHM) provided to States/UTs for provision of free dialysis services to the poor, where 1.43 lakhs patients have availed free services from 1,069 Dialysis units and under Free Drugs and Diagnostics Program.
3. **Affordable Medicine and Reliable Implants for Treatment** (**AMRIT**) is a pharmacy outlets programme, where nearly 47 Lakh patients have benefitted from AMRIT Pharmacies through purchase of subsidized medicines. A total of more than 5000 drugs and other consumables are being sold at up to 50% discounts.
4. **Health and Wellness Centres (HWCs)** is the plan, as per the Ministry, to transform 1.5 lakh Sub-health Centres to Health and Wellness Centres (HWCs) to expand the basket of services of primary care and make it comprehensive.
5. **National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS)** is the Government initiated universal screening of common NCDs programme to provide free diagnostic facilities and free drugs for NCD patients attending the NCD clinics at the District and CHC levels. In FY 2017-18, over 1.92 crore people had been screened till the 2nd Quarter.
6. **Online Registration System (ORS)** is a framework to link various hospitals for online registration, payment

57 http://www.who.int/mediacentre/news/releases/2017/half-lacks-access/en/

58 http://www.who.int/mediacentre/factsheets/fs395/en/

59 http://www.who.int/universal_health_coverage/tokyo-decleration-uhc.pdf

of fees and appointment, online diagnostic reports, online enquiry for availability of blood etc. As on date, around 124 hospitals including Central hospitals like AIIMS, RML Hospital; SIC, Safdarjung Hospital; NIMHANS; Agartala Government Medical College; JIPMER etc. are on board ORS.

7. **National Vector Borne Disease Control Programme (NVBDCP)** was launched to control and eliminate Malaria, Japanese encephalitis (JE) and kala-azar.

8. **Labour Room Quality Improvement Initiative (LaQshya)**: There is enough evidence that supports the fact that improving the quality of care in Labour rooms is central to maternal and neonatal survival. LaQshya is expected to improve the quality of care that is being provided to the pregnant mother in the Labour Room and Maternity Operation Theatres, thereby preventing the undesirable adverse outcomes associated with childbirth.

9. **Operational Guidelines for Obstetric High Dependency Units (HDUs) and Intensive Care Units (ICUs)** is another important aspect related to maternal mortality is availability of critical care for complicated cases. For this, the Government of India had released Guidelines for setting up of Obstetric High Dependency Units (HDUs) and Intensive Care Units (ICUs) in 2016.

10. **Safe Delivery Application:** The Safe Delivery Application is a mHealth tool that can be used for health workers who manage normal and complicated deliveries in the peripheral areas. The application has Clinical Instruction films on key obstetric procedures which can help the health workers translate their learnt skills into practice[60].

Conclusion -

The goal of achieving universal health coverage is the main focus of health system reforms around the world. In this view, the Government of India, to achieve Universal health coverage has recently increased the budget of the Health Ministry for 2017-18 up to 27.7%, and is planning to launch new improvised health programs to achieve UHC target.

60 http://pib.nic.in/newsite/erelease.aspx?relid=174239

European Medicines Agency (EMA): Recommends Approval of seven medicines in its December 2017 Meeting

Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 11-14 December 2017
Seven medicines recommended for approval, including an advanced therapy

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) recommended seven medicines for approval at its December 2017 meeting, including two orphan medicines, one of which is also an advanced therapy medicinal product (ATMP).

The seven new drugs recommended for approval are:

1. **Alofisel (darvadstrocel), for the treatment of complex perianal fistulas in patients with Crohn's disease:** The CHMP recommended granting a marketing authorisation for the ATMP Alofisel (darvadstrocel), for the treatment of complex perianal fistulas in patients with Crohn's disease. Alofisel has an orphan designation.

   Crohn's disease is a long-term condition that causes inflammation of the digestive system or gut. Apart from affecting the lining of the bowel, inflammation may also go deeper into the bowel wall. Perianal fistulas are common complications of Crohn's disease and occur when an abnormal passageway develops between the rectum and the outside of the body. These can lead to incontinence (a lack of control over the opening of the bowels) and sepsis (blood infection). Complex fistulas are known to be more treatment resistant than simple fistulas. There is currently no cure for Crohn's disease, so the aim of treatment is to stop the inflammatory process, relieve symptoms and avoid surgery wherever possible. Crohn's disease can affect people of all ages, with a higher incidence in the younger population.

   The active substance of Alofisel is darvadstrocel. Darvadstrocel contains expanded adipose stem cells which, once activated, impair proliferation of lymphocytes and reduce the release of pro-inflammatory cytokines at the inflammation sites. This immunoregulatory activity reduces inflammation and may allow the tissues around the fistula tract to heal.

   The applicant for Alofisel (Darvadstrocel) is Tigenix, S.A.U.

2. **Crysvita (burosumab), a medicine for the treatment of X-linked hypophosphataemia:** The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended granting a conditional marketing authorisation, in the European Union, for Crysvita (burosumab), a medicine for the treatment of X-linked hypophosphataemia (XLH) with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons.

   XLH is an inherited disorder characterized by low levels of phosphate in the blood. The phosphate is abnormally processed in the kidneys, which causes a loss of phosphate in the urine (phosphate wasting) and leads to soft, weak bones (rickets). In most cases, the signs and symptoms of hereditary hypophosphataemic rickets begin in early childhood. Characteristic features include bowed or bent legs, short stature, bone pain, and severe dental pain.

   The CHMP recommended conditional approval for the medicine. This is one of EU's regulatory mechanisms to facilitate early access to medicines that fulfil unmet medical need. Conditional approval allows the Agency to recommend a medicine for marketing authorisation in the interest of public health where the benefit of its immediate availability to patients outweighs the risk inherent in the fact that additional data is still required.

The Applicant for Crysvita (Burosumab) is Kyowa Kirin Limited.

3. **Ozempic (Semaglutide) for the treatment of type 2 diabetes:** The Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Ozempic, intended for the treatment of type 2 diabetes.

   The active substance of Ozempic is semaglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist. Like native GLP-1, semaglutide leads to an increase in glucose-dependent insulin secretion and a reduction in glucagon release.

   Ozempic is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:
   As monotherapy when metformin is considered inappropriate due to intolerance or contraindications
   In addition to other medicinal products for the treatment of diabetes.

   The applicant for Ozempic is Novo Nordisk A/S.

4. **Alkindi (Hydrocortisone) for the treatment of Replacement therapy of adrenal insufficiency in infants, children and adolescents:** The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended granting a paediatric-use marketing authorisation (PUMA) for Alkindi (hydrocortisone) for the treatment of primary adrenal insufficiency, a rare hormonal disorder, in infants, children and adolescents.

   Primary adrenal insufficiency is a condition where the adrenal glands (located just above the kidneys) do not produce enough cortisol, a steroid hormone (also known as the stress hormone because it is released in response to stress). Symptoms include weight loss, muscle weakness, fatigue, low blood pressure, low blood sugar, disturbances in sodium and potassium balance and sometimes darkening of the skin. Adrenal insufficiency can be life-threatening and usually requires life-long treatment to replace the missing cortisol.

   Alkindi is a paediatric-specific formulation of hydrocortisone, a glucocorticoid which is being routinely used over the last 50 years as a replacement therapy for the treatment of adrenal insufficiency in adults and children

   .

   The applicant for Alkindi is Diurnal LTD.

5. **Herzuma (Trastuzumab) for the Treatment of breast and gastric cancer:** The Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Herzuma, intended for the treatment of breast and gastric cancer.

   Herzuma will be available as a 150mg powder concentrate for solution for infusion. The active substance of Herzuma is trastuzumab, a monoclonal antibody that binds with high affinity and specificity to HER2 leading to the inhibition of proliferation of tumour cells that overexpress HER2.

   Herzuma is a biosimilar medicinal product. It is highly similar to the reference product Herceptin (trastuzumab), which was authorised in the EU on August 28, 2000.

   The applicant for Herzuma (Trastuzumab) is Celltrion Healthcare Hungary Kft.

6. **Anagrelide for the treatment of Reduction of elevated platelet counts in at risk essential thrombocythaemia patients:** The Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product

Anagrelide, intended for the reduction of elevated platelet counts in at risk essential thrombocythaemia patients.

The active substance of Anagrelide is anagrelide, an antineoplastic agent. The precise mechanism by which anagrelide reduces blood platelet count is unknown. Anagrelide is an inhibitor of cyclic AMP phosphodiesterase III.

Anagrelide Mylan is a generic and hybrid of Xagrid (0.5 mg hard capsules), which has been authorised in the EU since November 16, 2004.

The full indication is: "Anagrelide is indicated for the reduction of elevated platelet counts in at risk essential thrombocythaemia (ET) patients who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.

An at risk essential thrombocythaemia patient is defined by one or more of the following features:

> 60 years of age or
a platelet count > 1,000 x 10^9/l or
A history of thrombo-haemorrhagic events.

The applicant for Anagrelide Mylan is Mylan S.A.S.

7. **Efavirenz/Emtricitabine/Tenofovir disoproxil Krka for the Treatment of HIV infection:** The Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Efavirenz/Emtricitabine/Tenofovir disoproxil Krka, intended for the treatment of HIV infection.

   Efavirenz/Emtricitabine/Tenofovir disoproxil Krka contains as active substances - the antiretrovirals efavirenz, emtricitabine and tenofovir disoproxil (ATC code: J05AR06). The medicine will be available as film-coated tablets (600 mg/200 mg/245 mg). Efavirenz activity is mediated by noncompetitive inhibition of HIV reverse transcriptase, while emtricitabine and tenofovir disoproxil are substrates and competitive inhibitors of HIV reverse transcriptase. After phosphorylation, they are incorporated into the viral DNA chain, resulting in chain termination.

   Efavirenz/Emtricitabine/Tenofovir disoproxil Krka is a generic of Atripla, which has been authorized in the EU since December 13, 2007.

   The applicant for Efavirenz/Emtricitabine/Tenofovir disoproxil Krka is KRKA, d.d., Novo mesto.

Negative opinion on new medicine

The CHMP adopted a negative opinion for Aplidin (plitidepsin). Aplidin was expected to be used to treat multiple myeloma.

Three recommendations on extensions of therapeutic indication

The Committee recommended extensions of indications for

a) **Taltz (Ixekizumab):** The CHMP adopted a new indication Psoriatic arthritis -

Taltz, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drug (DMARD) therapies.

The marketing authorisation holder for Taltz (Ixekizumab) is Eli Lilly Nederland B.V.

b) Truvada (Emtricitabine / Tenofovir disoproxil): The CHMP adopted an extension to an existing indication as follows -

Treatment of HIV-1 infection:

Truvada is indicated in antiretroviral combination therapy for the treatment of HIV-1 infected adults. Truvada is also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents

Pre-exposure prophylaxis (PrEP):

Truvada is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high risk.

The marketing authorisation holder for Truvada (Emtricitabine / Tenofovir disoproxil) is Gilead Sciences International Limited.

C) Yervoy (Ipilimumab): The CHMP adopted an extension to the existing indication as follows -

Yervoy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults, and adolescents 12 years of age and older.

The marketing authorisation holder for this medicinal product is Bristol Myers Squibb Pharma EEIG.

Outcome of review on Mycophenolate

The European Medicines Agency (EMA) has updated recommendations for contraception in men and women taking mycophenolate medicines which are used to prevent rejection of transplanted organs.

Mycophenolate medicines are known to increase the risk of malformations and miscarriages during pregnancy if the fetus is exposed to them in the womb.

The CHMP has concluded that current evidence does not indicate a risk of malformations or miscarriages during pregnancy when the father has taken mycophenolate medicines (used to prevent rejection of transplanted organs), although the risk of genotoxicity cannot be completely ruled out. For male patients, the CHMP now recommends that either the male patient or his female partner use reliable contraception (it is no longer required that they both use contraception).

The updated recommendations follow a periodic review of mycophenolate medicines by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), which considered the available clinical and non-clinical data.

Modified-release paracetamol-containing products to be suspended from European Union (EU) market

Recommendation endorsed due to the difficulty in managing overdose

On December 15, 2017, the European Medicines Agency's (EMA), Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)[61] has endorsed the recommendation to suspend marketing of products containing modified- or prolonged-release Paracetamol (designed to release Paracetamol slowly over a longer period than the usual immediate-release products). The recommendation was made by the Agency's experts in medicines safety, the Pharmacovigilance Risk Assessment Committee (PRAC).

Earlier, the Agency's experts in medicines safety, the Pharmacovigilance Risk Assessment Committee (PRAC) had recommended, that the advantages of a longer-acting product did not outweigh the complications of managing an overdose of the medicine, since the treatment procedures for immediate-release products are not appropriate for modified-release paracetamol products. In many cases, it may not be known whether an overdose of paracetamol involves immediate-release or modified-release products, making it difficult for caregivers to decide the overdose management.

CMDh noted the PRAC conclusion that practical measures to sufficiently reduce the risk to patients had not been identified. Furthermore, it had not proved possible to agree to a feasible and standardized way to adapt the management of overdose across the EU to cover both immediate- and modified-release paracetamol products. The CMDh therefore, endorsed the PRAC recommendation that the marketing authorizations for medicines containing modified-release paracetamol, alone or combined with the opioid medicine tramadol, should be suspended.

Because the CMDh's decision was agreed to by a majority vote, it will now be sent to the European Commission which will issue a final legally binding decision valid throughout the EU.

The review procedure of modified-release paracetamol by EMA:

The review of modified-release paracetamol was initiated on June 30, 2016, at the request of Sweden, under Article 31* of Directive 2001/83/EC.

↓

The review was carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), which gave its recommendations in September 2017[62].

↓

Following a request from companies involved in the review, the PRAC re-examined and confirmed its previous recommendation in December 2017[63].

↓

The PRAC recommendations were sent to Coordination Group for Mutual Recognition and Decentralised Procedures– Human (CMDh), as the CMDh position was adopted by majority vote.

↓

The CMDh position will now be sent to the European Commission, which will take an EU-wide legally binding decision.

61 http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/12/news_detail_002876.jsp&mid=WC0b01ac058004d5c1

62 http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/09/news_detail_002806.jsp&mid=WC0b01ac058004d5c1

63 http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/11/news_detail_002863.jsp&mid=WC0b01ac058004d5c1

*Article 31 referrals: In the European Union, this type of referral is triggered when the interest of the Union is involved, following concerns relating to the quality, safety or efficacy of a medicine or a class of medicines[64].

Background

The Agency's recommendations are based on a review of available data including a retrospective pharmacokinetic and clinical analysis of 53 cases of acute overdose with modified-release paracetamol by the Swedish Poison Information Centre, which found that the standard treatment protocol utilizing solely the Rumack-Matthew nomogram (or variations thereof) based on conventional paracetamol formulations may not be effective for overdoses with modified-release paracetamol formulations. The maximum plasma concentration may occur later, and high concentrations, in particular after large doses, may persist for several days. The usual protocols of sampling and treatment regimens used in the management of overdose with immediate-release formulations are therefore, not adequate. The dose of NAC may have to be increased and the optimal dosing has not been determined. These results confirm a similar Australian case series.

More about the medicine (Modified-release-paracetamol)

Products covered by this review contain paracetamol for modified-release and are intended to be taken by mouth and have a longer action. They are available in Belgium, Denmark, Finland, Greece, Iceland, Luxembourg, the Netherlands, Portugal, Romania, and Sweden under various names including Alvedon 665 mg, Panadol Artro, Panadol Extend, Panadol Retard 8 hours, Panodil 665 mg, Paratabs Retard and Pinex Retard.

Modified-release medicines containing paracetamol with the opioid painkiller tramadol are available under the names Diliban Retard or Doreta SR in Bulgaria, Czech Republic, Estonia, Hungary, Iceland, Latvia, Lithuania, Poland, Portugal, Romania, Slovakia, Slovenia and Spain, and these medicines are also covered by this review.

About CMDh & PRAC:

CMDh: Coordination Group for Mutual Recognition and Decentralised Procedures - Human - the group responsible for the examination and coordination of questions relating to the marketing authorisation of medicines for human use in two or more Member States in accordance with the mutual recognition or decentralised procedure.

PRAC: Pharmacovigilance Risk Assessment Committee - the committee that is responsible for assessing all aspects of the risk management of medicines for human use.

Conclusion:

The targeted medicines will remain suspended unless the companies that hold the marketing authorisations can provide evidence of appropriate and practical EU-wide measures to help prevent overdose with these products and adequately reduce its risks. However, immediate-release paracetamol products, which are not affected by this review, will continue to be available as before.

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64 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

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