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S&A PHARMA NEWSLETTER

EDITORIAL

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Founding Partner

Healthcare is a basic necessity of every individual; it should always be up to date on healthcare challenges. At present, the world is facing multiple challenges in regulating health sector in terms of therapy availability, quality drug distribution channel, reports of fake/spurious drugs and increasing rate of drug-resistant pathogens. Regulatory authorities with their comprehensive updated guidelines keep regulating these challenges globally, however extra efforts are needed from the organizations and governments to combat the challenges in tandem.

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

In the present issue, we start with a discussion on the Central Government's notification putting all implantable medical devices along with some diagnostic medical devices as drugs, which bring these devices under regulatory framework and will ensure safety. Going forward, this edition addresses DoP's draft quality control orders (QCOs) on six Medical Devices, which recommends mandatory BIS standardizations for these devices. This issue then, discusses the ICMR collaboration with Pfizer for the purpose to achieve the unified goal of reducing AMR. The next article covers the National Pharmaceutical Pricing Authority's decision to categorize 42 non-scheduled Anti-cancer drugs under price control. Next, the newsletter addresses the proposed amendment in Cosmetics Rule, 2018 seeking submission of product composition details from Cosmetics Manufacturers before licensing their product. Further, this edition addresses the proposed amendment in Drug and Cosmetics Rule, 1945 where Central Government amendment is intended to regulate irrational naming practice of branded medicine to avoid chances of medication errors.

From the international arena, we talk about recent regulatory reforms concerning various health issues and the health reports focusing on improving health in countries. Here, we discuss a new guidance on certain medical devices issued from European Medicine Agency, which introduce new roles and responsibilities for Agency and national competent authorities for these devices.

We wrap up this issue with a note on PRAC recommendation to suspend fenspiride, a cough relieving medicine suspected to cause risk of QT prolongation and torsades de pointes.

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

Thank you.

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Contents

Central Government notifies all implantable devices as drugs

On February 08, 2019, the Central Government announced[1] that all *Implantable Medical Devices* along with *CT scan Equipment, MRI Equipment, Defibrillators, Dialysis Machine, PET Equipment, X-Ray Machine, and Bone Marrow Cell Separator* are defined as drug under the Drugs and Cosmetics Act, 1940 (the 'Act'). This inclusion will be effective from 1st April 2020. Once effective, the national regulatory body Central Drug Control Standard Organization (CDSCO) will become the approving authority for sale, manufacture and import licenses of these medical devices.

The Central Government in pursuance of sub-clause (iv) of clause (b) of section 3 of the Act and after consultation with the Drugs Technical Advisory Board (DTAB) has categorized these medical devices as drugs.

***[Section 3 Definition**.—In this Act, unless there is anything repugnant in the subject or context, ……..(b) —drug includes….(iv) such devices* intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, as may be specified from time to time by the Central Government by notification in the Official Gazette, after consultation with the Board;]*

Medical device regulation in India

Medical device sector is still emerging in India and is dominated by imports. According to a report *Medical Device Sector Survey: Make In India*, the Medical Devices industry in India is presently valued at USD 5.2 billion and contributes 4-5% to the USD 96.7 billion Indian health care industry. Currently, India is counted among the top 20 global medical devices market and is the 4th largest medical devices market in Asia after Japan, China and South Korea.

At present majority of medical devices are unregulated, only notified medical devices are regulated as Drugs under the Act and Rules made thereunder. There are 27 categories of devices which were notified as drugs till 2018 including blood pressure monitoring devices, digital thermometers and glucometers that were last notified in December 2018. With this announcement government has brought all implantable devices and some diagnostic equipment into the regulatory framework which is an important step from patient safety perspective.

Moreover, the government has also notified the Medical Device Rules, 2017. The Rules provide risk-based classification of medical devices for the medical devices industry.

The impact of this notification

- The notified Medical Devices come under regulatory framework. It will ensure that medical devices and implants used in India are safe and tested.
- These notified Medical Devices may also come under the purview of Drug Price Control Order (DPCO), 2013 as it qualify the definition of drug required for price regulation.

Conclusion:

A large segment of devices still fall under unregulated category; the government needs to regulate medical devices as a product group on the basis of safety and performance rather than regulating device by device. Moreover, forming a separate medical device policy is recommended which could regulate the medical devices sector in the country.

1 http://www.egazette.nic.in/WriteReadData/2019/197157.pdf

DoP proposes mandatory Quality Control Orders (QCOs) for certain Medical Devices

On February 15, 2019, the Department of Pharmaceuticals (DoP), Ministry of Chemicals and Fertilizers issued six draft Quality Control Orders (QCOs)[2], after consulting with the Bureau of Indian Standards (BIS) to ensure safety and effectiveness of these medical devices:

1) Medical Electrical Equipment (Quality Control) Order, 2018
2) Sphygmomanometers (Quality Control) Order, 2018
3) Clinical Electrical Thermometers (Quality Control) Order, 2018
4) Blood Glucose Monitoring System (Quality Control) Order, 2018
5) Gloves (Quality Control) Order, 2018
6) Surgical Blades (Quality Control) Order, 2018

The QCOs, drafted using powers vested under sub-sections (1) and (2) of Section 16 read with Section 17 and sub-section 3 of the Bureau of Standards Act, 2016 ('BIS Act'), are open for stakeholders' comments/ suggestions till 15th April 2019.

The QCOs also propose:

i. Compulsory use of Standard Mark for Goods or articles specified in the QCOs shall conform to the corresponding Indian Standard given therein and shall bear the Standard Mark under a license from the BIS Regulations, 2018. The draft QCOs also suggest that nothing in these Orders shall apply in relation to goods or articles meant for export, which conform to any specification required by the foreign buyer.

ii. The BIS shall be the certifying and enforcing authority for the goods/articles specified in QCOs. In addition, an officer not below the rank of General Manager, Distinct Industries Center in Department of Industries of the State Government shall also be the enforcing authority.

iii. Any person who contravenes the provisions of this Order shall be punishable under the provisions of the BIS Act. The latest version of Indian Standards including the amendments issued thereof, as published and notified by the Bureau from time to time, shall be applicable from the date as notified by the Bureau.

Conclusion:

The draft orders, once finalized will make BIS the certifying and enforcing authority for these medical devices. However, making voluntary ISI marking mandatory for only few medicals devices instead of regulating all medical devices will not offer imperative solution to medical device sector.

2 http://pharmaceuticals.gov.in/sites/default/files/Draft%20Quality%20Control%20Order%20dated%2015.02.2019.pdf

Pfizer and ICMR come together to tackle Antimicrobial Resistance (AMR) in the country

Antimicrobial Resistance (AMR) is a major global challenge and is getting the attention of all relevant stakeholders. Factors such as inappropriate and irrational use of antimicrobial agents among others have led to the increase in AMR. To address this issue, Indian Council of Medical Research (ICMR) has initiated a series of activities under its AMR surveillance network with tertiary care hospitals to collect national data, guide treatment practices and rationalize antibiotic use in the country. This challenging program needs to be further built up on multiple levels of health care and expand these activities to private nursing homes and district hospitals.

The Ministry of Health & Family Welfare (MoHFW) identified AMR as one of the top 10 priorities for the ministry's collaborative work with World Health Organization (WHO). The health ministry has launched National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017 – 2021[3]. The strategic objectives of NAP-AMR are aligned with the global action plan based on national needs and priorities, and in addition to the top 5 priorities of GAP-AMR, India has a sixth priority that is India-specific dealing with India's leadership on AMR – including international, national and sub-national collaborations on AMR.

One of the strategic objectives of NAP-AMR focuses on strengthening India's leadership on AMR through international collaborations to ensure India's contributions towards global efforts to contain AMR, national collaborations to facilitate collaborations among vertical disease control programmes and national stakeholders, and state level collaborations to ensure action at the ground level against AMR.

Pfizer and ICMR collaboration on AMR

ICMR under the sixth priority NAP-AMR has decided to collaborate with Pfizer for the purpose to achieve the unified goal of reducing AMR[4]. This will be an important and high profile activity and will be used to help determine the status of AMR in India.

In this view, ICMR invites Expression of Interest (EOI) from reputed, eligible and experienced firms offering Project Management Consultancy (PMC) Services to set up a Project Management Unit (PMU) in accordance with the Scope of Work (SoW) for a period of two (2) years commencing from date of start.

About AMR

AMR is a broad term for resistance in different types of microorganisms such as bacteria, viruses, fungi and parasites and encompasses resistance to antibiotics such as antibacterial, antiviral, anti-parasitic and anti-fungal drugs. AMR occurs naturally but is facilitated by the misuse or overuse of antibiotics. Examples of misuse include when they are taken by people with viral infections like colds and flu, and when they are given as growth promoters in animals or used to prevent diseases in healthy animals. AMR is present in every country making it a top ten serious threat to global public health that requires action across all government sectors and society.

3 http://www.searo.who.int/india/topics/antimicrobial_resistance/nap_amr.pdf

4 https://www.icmr.nic.in/sites/default/files/whats_new/Scope_of_work.pdf

India puts 42 non-scheduled cancer drugs under price control

On February 27, 2019, the National Pharmaceutical Pricing Authority or NPPA (hereinafter also referred as 'Authority') capped trade margins of 42 non-scheduled cancer drugs to curb profiteering on vital medicines notified in the Standing Order[5]. NPPA, an independent body of Department of Pharmaceuticals, (DoP) functions inter-alia fixation and revision of retail/ceiling prices of scheduled drug formulations under the Drugs (Prices Control) Order, 2013 (DPCO) aims to ensure that essential drugs are available to all at affordable prices.

Authority usually follows price capping for the National List of Essential Medicines (NLEM) which are adopted on the basis of essentiality and further listed in the First Schedule of DPCO as scheduled medicines[6]. Apart from this, Authority also monitors non-scheduled medicines by ensuring that the annual price increase shall not be more than 10 percent.

Now, the Authority for the first time has decided to undertake 'Trade Margin Rationalization Approach' for the matter of price control. The authority, in the exercise of the powers of extraordinary circumstances vested in provisions of Para 19 of the DPCO[7], has recommended 42 non-scheduled Anti-Cancer medicines for price control on pilot basis. The Government has put a cap on trade margin of 30% and also -

- Directs manufacturers to fix their retail price based on price at first point of sale of product (hereinafter referred as Price to Stockist), using this formula:

  Retail price of the product = Price to Stockist (PTS) x {1 + (0–TM)}

  Where TM = Trade Margin not exceeding 30, Where PTS = PTS for the month of June 2018

- This price cap will be applicable on the non-scheduled formulations containing any of the 42 drugs listed in the table below (whether individual or in combination, irrespective of dosage strength, dosage form and /or route of administration):

Sl. No.	Name of the Drug
1	Azacitidine
2	Bendamustine Hydrochloride
3	Bortezomib
4	Crizotinib
5	Cytarabine
6	Dasatinib
7	Decitabine
8	Doxorubicin HCI Pegylated Liposomal Injection
9	Enzalutamide
10	Epirubicin
11	Eribulin mesylate

5 http://nppaindia.nic.in/ceiling/press27February19/Notification-25.02.2019%20(Final).pdf

6 http://164.100.47.193/lsscommittee/Chemicals%20&%20Fertilizers/16_Chemicals_And_Fertilizers_45.pdf

7 **Para 19 Fixation of ceiling price of a drug under certain circumstances** – *'Notwithstanding anything contained in this order, the Government may, in case of extra-ordinary circumstances, if it considers necessary so to do in public interest, fix the ceiling price or retail price of any Drug for such period, as it may deem fit and where the ceiling price or retail price of the drug is already fixed and notified, the Government may allow an increase or decrease in the ceiling price or the retail price, as the case may be, irrespective of annual wholesale price index for that year'.*

Sl. No.	Name of the Drug
12	Erlotinib HCl
13	Estramustine phosphate
14	Everolimus
15	Exemestane
16	Fulvestrant
17	Irinotecan HCl Trihydrate
18	Lapatanib
19	Leuprolide acetate depot for Inj.
20	Lomustine
21	Mitoxantrone
22	Nilotinib
23	Plerixafor
24	Carfilzomib
25	Cladribine
26	Triptorelin
27	Pomalidomide
28	Osimertinib
29	Pegasperagase
30	Regorafenib
31	Ribociclib
32	Clofarabine
33	Sunitinib
34	Olaparib
35	Olaratumab
36	Paclitaxel (Protein-bound particles)
37	Cabazitaxel
38	Bevacizumab
39	Lenalidomide
40	Pegfilgrastim
41	Mitomycin
42	Pemetrexed

- Further, the Government has also directed manufacturers to provide the information in respect of the non-scheduled formulations containing drugs mentioned in the above table, irrespective of whether there is any change in MRP or not, by March 06, 2019.

Why Trade Margin Rationalization Approach?

The Government has been examining options for rationalization of prices in this segment in a graded manner. One major factor that contributes to high drug prices in India, is the unreasonably high trade margins. Trade

margin is the difference between the price at which the manufacturers sell the drugs to stockist / distributors (price to stockist) and the final price to patients (maximum retail price).

The policy note '*Making Market Work for Affordable Healthcare*' published by Competition Commission of India (CCI) says "One major factor that contributes to high drug prices in India is the unreasonable high trade margin. The high margins are in form of incentive and an indirect marketing tool employed by drug companies." Subsequently, the expert committee report on *'High Trade Margin in the sale of drugs'* inter-alia stated that 'It is neither the desire nor is it possible for the government to interfere in the day to day business activities of the industry. The committee observed capping of trade margins necessary and recommends that intra trade margins could be decided by the industry subject to a cap to be notified by the Government from time to time.

The Government then decided to undertake the matter of price control through a 'Trade Margin Rationalization Approach'. And therefore, in order to bring in regulation of drugs in the 'non-scheduled' segment the Government undertook a Pilot for Proof of Concept by capping prices of selected anticancer drugs, identified by the MoHFW as being essential for the treatment of this disease.

Why only cancer drugs for price control?

The Authority noted that 'Cancer is one of the leading causes of adult illness and death due to chronic and non-communicable diseases (NCD) in India. As per WHO estimate, there are approximately 18 million cases globally and 1.5 million in India alone. There were 8 lakhs cancer deaths in India in 2018. The number of new cases is estimated to double in India in 2040. The financial burden associated with cancer can force patients and households to acute misery and even insolvency. It is also noted that out of pocket (OOP) expenditure on cancer hospitalization is about 2.5 times of overall average hospitalization expenditure. It is estimated that almost more than 50% cancer patients avail the private sector facilities and out of pocket expenses in the healthcare including cancer care is about around 65%.

At present NLEM has 376 medicines out of which 59 drugs are already under the category of antineoplastic/ immunosuppressive, hormones & anti-hormones and medicines used for palliative care. Pricing of these medicines are controlled through DPCO as amended from time to time.

A disease centric approach on cancer assumes salience because of specific national policy commitments to ensure universal access to healthcare at affordable prices. Cancer patients in India incur heavy out-of-pocket expenditures. The cancer drugs need to be affordable so that whenever required the treatment can be provided at the earliest in the early stages when the cancer treatment is curable. The Authority noted that availability and affordability of cancer drugs will give impetus to treatment outcomes and will bring down the cost of common anti-cancer drugs thereby increasing affordability and accessibility of these drugs. The authority offers seven days period to drug manufacturers to recalculate the prices and inform back to NPPA.

Conclusion:

The latest move is expected to bring down prices of listed anti-cancer drugs for patients buying them at hospitals, and retail store, which generally bill them at MRP. However, it may not be effective for retail chains buying the drugs through wholesalers or stockiest that already give them large discounts.

Cosmetics manufacturers may submit product composition details before licensing their products

Central Government, in order to enhance the safety of the cosmetic products, has proposed the product composition details clause shall be mentioned in the approval issued by the licensing authority in the country. At present Maharashtra is practicing this format of approval for cosmetics. According to Drug Consultative Committee (DCC) meeting held on 31st Jan and 1st Feb 2019, the proposed draft will be incorporated in the final version of the Cosmetics Rules 2018, once finalized.

The Drugs and Cosmetics Act, 1940 ("Act') does not require product composition details for approval of cosmetic products. However, many incidences during sample investigation of approved products by Drug Inspectors have reported the presence of various traces of harmful elements that should not be a part of cosmetics. At such times, the manufacturers claims that they have submitted the composition details to the licensing authority but on the license submitted by these firms only the name of cosmetics is mentioned without its composition; placing the investigation officer under dilemma for taking proper action.

Now, the DCC has considered that complete composition details clause of cosmetics product shall be mentioned in the approval issued by the licensing authority in the country in following format for uniformity throughout the country -

S. No	Name of ingredient	Specification of ingredient	Percentage of ingredient	Purpose or function of ingredient

The Drug Controllers from Maharashtra have also highlighted this issue and suggested a provision to mention the percentage of restricted ingredients on product labels to make it easier for the field officer to detect violations. But the suggestion was rejected by DCC panel saying that "the composition of ingredients is reviewed as per prescribed standards while granting the manufacturing license".

Note: While deliberating the proposal it was informed that finalization of draft Cosmetics Rules, 2018 is under consideration and DCC recommended that the matter may be considered while finalizing the rules.[8]

Conclusion*:*

The Central Government via this provision will certainly bring a uniformity in licensing process all over the country and ease the inspection process of cosmetics product for field officer. Moreover, it will also enhance the safety of cosmetic products through the display of specification/percentage of its ingredients.

8 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/common_download.jsp?num_id_pk=ODI4

Central Government proposes amendment in D&C Rules to regulate brand names

On February 26, 2019 Central Government published draft amendment to the Drug & Cosmetic Rules, 1945[9] (the 'Rules') to include a clause where a manufacturer / applicant intending to market a drug under a brand name shall furnish an undertaking that the 'brand name or the trade name' used by them shall not lead to any confusion or deception in the market over look alike, sound alike (LASA) drugs.

At present, neither licensing authority nor trademark office regulates the brand name or trade name. There are probabilities of assigning similar trade names for different drugs which may create confusion to medical practitioners or patients over LASA drugs.

There are many LASA drugs in India that can result in medication errors. These errors could cause harm to patients or even death. Recently, the Hon'ble Delhi High Court directed the Drug Controller General of India (DCGI) and the state Food and Drug Administration (FDA) offices to implement an action plan to stop giving licenses to drugs with identical or near identical brand names or marks. The court issued the directive in a trademark infringement lawsuit involving Curewell Drugs and Pharmaceuticals and Ridley Sciences. Vitamin B capsules marketed by both the companies had the same brand name, Bevital, which had prompted Curewell to file the suit against Ridley.

The Government has proposed Drugs and Cosmetics (Amendment) Rules, 2019 wherein rule 71 A ***[for the renewal of the license for products or drugs other than those specified in [schedules c, c (1)]*** and rule 76 ***[manufacture for sale or for distribution drugs specified in Schedule C and C(1) excluding drugs specified in Schedule X or of Large Volume Parenterals, Sera and Vaccine and recombinant DNA (r-DNA) derived drugs]*** the following sub-rule shall be inserted, namely:-

> *"In case the applicant intends to market the drug under a brand name or trade name, the applicant shall furnish an undertaking to the licensing authority that such or similar brand name or trade name is not already in existence so that the brand name or the trade name to be used by the applicant shall not lead to any confusion or deception in the market."*

Conclusion:

The draft amendment in Drug and Cosmetic Act once finalized, will expect to control irrational naming practice of branded medicines and will increase the chances of patient safety by removing LASA factor.

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

Centre has drafted the first regulatory guidelines for evaluation of nano-pharmaceuticals in India

In February 2019, the Government of India introduced first draft regulatory guidelines for evaluation of nano-pharmaceutical products for therapeutic use in the country. The draft guidelines once finalized will speed up commercialisation of nanotechnology-based medical innovations by establishing transparent and predictable regulatory procedures. Nano-pharmaceutical, a combination of nanotechnology with pharmaceutical and biomedical science, is an emerging field focusing on targeted drug delivery for improved efficacy and safety of pharmaceuticals.

Scope of the Guidelines

The guidelines will be applicable to the nano-pharmaceuticals finished formulation and API of new molecule or an already approved molecule with altered dimensions, properties or phenomenon associated with the application of nanotechnology. However, these guidelines will not apply to conventional drugs which are present with incidental nanoparticles or microorganisms which are naturally present in drug products.[10]

Information Required for Evaluation of Nano-pharmaceuticals

Evaluation of nano-pharmaceuticals requires following data to be submitted to the regulatory authority, though the content of information will be decided from case to case basis -

- A brief introduction on nano-pharmaceuticals
- Chemical and pharmaceutical information
- Animal pharmacology
- Animal toxicology
- Human / Clinical pharmacology
- Therapeutic exploratory trials
- Therapeutic confirmatory trials
- Special studies
- Regulatory status in other countries
- Prescribing information
- Samples and testing protocol/

Note- These guidelines are developed along with the provision of the Schedule Y of Drugs and Cosmetics Rules, 1945, and with requirements for nano-pharmaceuticals. These guidelines provide guidance for specific requirements of chemical and pharmaceutical information, non-clinical data and clinical data relevant for any product developed based on nanotechnology. *The Schedule Y requirements are applicable to all the new drugs whether based on nanotechnology or not. However, due to complexity involved in the nano-technology based products, a 'case by case basis' approach should be adopted for evaluating their quality, safety and efficacy.*[11]

10 http://www.dbtindia.nic.in/wp-content/uploads/Modified-Guidelines-for-Evaluation-of-Nanopharmaceuticals-in-India-converted-2.pdf

11 http://www.dbtindia.nic.in/wp-content/uploads/Modified-Guidelines-for-Evaluation-of-Nanopharmaceuticals-in-India-converted-2.pdf

Conclusion:

General requirements and guidelines for manufacturing/import of any new nano-pharmaceuticals or to undertake clinical trial for same has already been specified in the Drugs and Cosmetics Rules, 1945. However, the complexity in nanotechnology necessitates the system of 'case by case approach' with involvement of varied expertise for successful development of nano-pharmaceuticals.

EMA publishes new guidelines for certain medical devices

On February 28, 2019, European Medicine Agency (EMA) (hereafter referred as 'Agency') published the first guidance on new rules for certain medical devices - the first of a series of guidance documents to help applicants to prepare for compliance with these new rules. The first guidance introduces new roles and responsibilities for EMA and national competent authorities (NCAs) in relation to certain types of medical devices and in-vitro diagnostics, demands efforts from the Agency with stakeholders including pharmaceutical and medical device industries, and notified bodies, to ensure a smooth transition to the new regulatory framework.

The new guidance document has been developed jointly by EMA and the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) in close collaboration with the European Commission.

Key points of new guidelines

This guidance document is prepared for the applicants to help them understand the scope of the Agency, its activities and should be read in conjunction with the new medical devices Regulation (EU) 2017/745, and the new In-vitro Diagnostic Medical Devices Regulation (EU) 2017/746. These regulations lay down roles and responsibilities for EMA and National Competent Authorities (NCA) for medicines, as follows:

- For medical devices incorporating a medicinal substance (with action ancillary to the device) the notified body shall seek a scientific opinion from either the NCAs or EMA. The notified body shall seek the opinion of EMA for medicinal products falling exclusively within the scope of centralized procedure, or those that incorporate human blood or plasma derivatives.
- For devices that are composed of substances or of combinations of substances that are systemically absorbed by the body in order to achieve their intended purpose, the notified body shall seek a scientific opinion from either the NCAs or the EMA.
- For companion diagnostics, the notified body shall seek a scientific opinion from either the NCAs or the EMA4.
- The European Commission may consult EMA when deliberating on the regulatory status of products in borderline cases involving medicinal products.
- For medicinal products with an integral medical device, there are new requirements to provide an opinion from a notified body.[12]

Note: This is the first guidance document of the series. EMA will publish further updates addressing other requirements for various categories of devices, including those made of substances that are systemically absorbed, products which are not clearly defined as medicinal products, known as 'borderline products', and in vitro diagnostic tests used to determine patients' eligibility for a specific medical treatment.

Conclusion:

This new guidance document published by EMA will help the applicants to carry out the obligations according to the new EU legislation on medical devices. This further introduces the new responsibilities of EMA and national competent authorities.

12 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/questions-answers-implementation-medical-devices-vitro-diagnostic-medical-devices-regulations-eu/745-eu-2017/746_en.pdf

Suspension of Fenspiride medicines due to potential risk of heart rhythm problems

On January 15, 2019European Medicine Agency (EMA)'s Pharmacovigilance Risk Assessment Committee (PRAC) recommended an EU-wide suspension of fenspiride medicines due to the risk of QT prolongation and torsades de pointes (abnormalities of the heart's electrical activity that may lead to heart rhythm disturbances)[13].

PRAC, in its February meeting, announced the suspension as a precautionary measure to protect patients while it reviews cases of heart rhythm problems which have been reported in patients who have taken these medicines in the past, and make recommendations on the action to be taken on marketing authorisations for fenspiride medicines across the EU.

The provisional suspension of fenspiride medicines is based on recent nonclinical studies (hERG channel binding and in vitro animal model studies) that showed that fenspiride has the potential to increase QT intervals in humans. This data was supportive of a previously suspected link between fenspiride and QT prolongation/ torsades de pointes in humans, which was based on a limited number of case reports.

The committee also informed patients and healthcare professionals that cough medicines containing fenspiride could cause sudden serious heart rhythm problems. It further advised them to stop using these medicines till the urgent EU safety review by authorities reaches a final conclusion. Healthcare professionals will be informed in writing about the suspension, and further information will be provided as needed and once the review has concluded.

About Fenspiride

Fenspiride medicines are available as syrup or tablets and used in adults and children from the age of 2 years to relieve cough resulting from lung diseases. In the EU, fenspiride medicines have been authorised via national procedures in Bulgaria, France, Latvia, Lithuania, Poland, Portugal and Romania and are available under various brand names (Elofen, Epistat, Eurefin, Eurespal, Fenspogal, Fosidal, Kudorp, Pneumorel, Pulneo, Еуреспал and Сиресп).

More about the Review Procedure

The review of fenspiride has been initiated at the request of France, under Article 107i of Directive 2001/83/EC. The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC). Since fenspiride medicines are all authorised nationally, once the PRAC concludes its review, its recommendations will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

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13 https://www.ema.europa.eu/en/news/suspension-fenspiride-medicines-due-potential-risk-heart-rhythm-problems

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