PMDA Updates

March, 2021

News

1. Message from Director of Center for Regulatory Science

Dr. SUZUKI

I am Dr. SUZUKI Hiroshi. I was appointed as the Director of Center for Regulatory Science (RS) of PMDA in April 2020. I am also serving as Director of Department of Pharmacy, The University of Tokyo Hospital, Faculty of Medicine, The University of Tokyo, and I would like to fill the gap between the medical/research practice and regulatory research.

I expect RS Center to function as a bridge of hope between medical care and advanced technology for patients. To this end, I am planning to train personnel to have the latest technical knowledge and wisdom in their field of expertise and promote regulatory science, which is the basis for scientific decision-making on efficacy and safety of medical products. Our research activities include pharmacoepidemiological investigations utilizing electronic real-world data (RWD) such as the National Database of Health Insurance Claims and Specific Health Checkups of Japan and MID-NET, research on safety measures, horizon scanning, and research on modeling and simulation methodologies for drugs. As the recent activities for the utilization of RWD, we have established a couple of consultation categories for utilization of registry data in FY 2019, and prepared two draft guidelines, "Basic principle for utilization of registry data for regulatory submission" and "Points to consider for ensuring the data reliability", which were open for public consultation in December 2020. Based on comments gathered by the consultation, these guidelines were updated and published on 23 March.

PMDA try to improve RS, promote the quality of review and safety measures, create guidelines that will contribute to the development of innovative medical products, and actively disseminate information to other countries/regions. In addition, from the perspective of human resource development, we would like to promote joint research activities with academia and further develop "The Science Board", which is a high-level consultative body established as an external advisory body in 2012 to discuss scientific aspects of medical products review. In this way, we will compile reports on the evaluation of advanced technologies as results of horizon scanning, and make efforts to contribute to the international cooperation among regulatory authorities.

2. PMDA-ATC Pharmacovigilance Webinar 2021

From February 1 to 4, 2021, PMDA held an online seminar entitled "PMDA-ATC Pharmacovigilance Webinar 2021", as the Center of Excellence (CoE) Workshop in the Asia-Pacific Economic Cooperation, Life Sciences Innovation Forum, Regulatory Harmonization Steering Committee (APEC-LSIF-RHSC). This webinar was designed for regulatory officials in charge of pharmacovigilance (PV) from overseas regulatory authorities. Total of 26 regulators from 15 economies (Azerbaijan, India, Indonesia, Korea, Malaysia, Myanmar, Nigeria, Philippines, Saudi Arabia, Singapore, Sri Lanka, Taiwan, Tanzania, Thailand and Uganda) participated in the webinar.

Recorded lectures and case study materials were prepared by the staff members from PMDA, U.S.FDA, Japan Pharmaceutical Manufacturers Association (JPMA) and academic institutions, and provided in advance of the webinar, as the preliminary training materials.

The recorded lectures covered such topics as overview of PV systems in the US, EU and Japan and international harmonization, evaluation of benefit/risk balance, pharmacoepidemiology, end-to-end labeling process, and communication of safety risk information. The lectures were then followed by the live question and answer sessions on the 1st and the 2nd day, where the participants actively engaged in the discussion.

On the 3rd and the 4th day, the participants were divided into five groups and engaged in the case studies using the mock data for discussion on safety specifications and risk minimization activities.

Top row: Speakers in the opening and the closing ceremonies, from left in order of appearance, Mr. UZU Shinobu (Director of the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs, PMDA), Dr. NAKASHIMA Nobumasa (Associate Executive Director for International Programs, PMDA), Mr. ONIYAMA Yukio (Director of the Office of Pharmacovigilance I, PMDA), Dr. FUJIWARA Yasuhiro (Chief Executive, PMDA), Dr. SATO Junko (Director of the Office of International Programs, PMDA)
Lower rows: Some of the participants at the webinar

Please refer to the following web site for the details of PMDA-ATC Pharmacovigilance Webinar 2021.
https://www.pmda.go.jp/english/symposia/0201.html

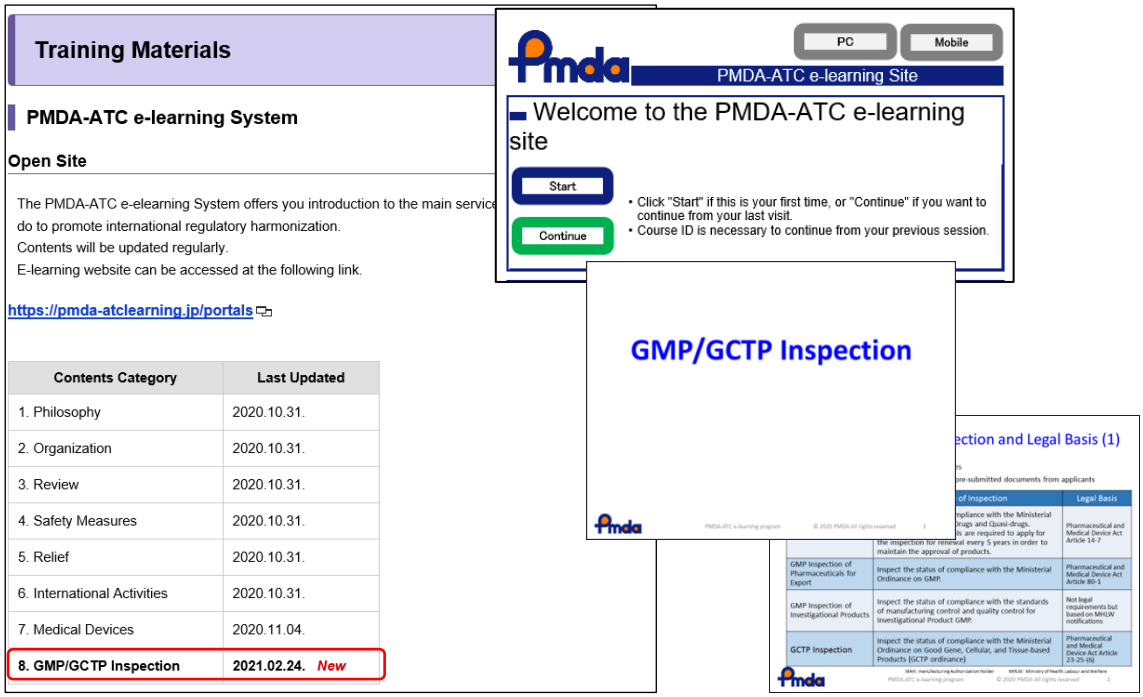
3. PMDA-ATC e-learning Contents information updated

PMDA has been providing with the PMDA-ATC e-learning system since January 2020. In this system, we are pleased to announce that the new content on Good Manufacturing Practice (GMP)/ Good Gene, Cellular, and Tissue-based Products Manufacturing Practice (GCTP) Inspection is released. E-learning website can be accessed at the following link.

https://pmda-atclearning.jp/portals

The above URL will be closed at the end of March and all the contents will move to YouTube from April, 2021. The e-learning website can be accessed at the following link from April, 2021.

https://www.pmda.go.jp/english/int-activities/training-center/0003.html



English Translations of Review Reports

The followings are current information about English version of review reports on PMDA website.

Pharmaceuticals

https://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0001.html

Brand Name	Non-proprietary Name	Posting date
Skyrizi [Initial Approval]	risankizumab (genetical recombination)	March 2
Erleada [Initial Approval]	apalutamide	March 10

English translations of Notifications and Administrative Notices

The following are English version of Notifications and Administrative Notices newly published on PMDA website.

https://www.pmda.go.jp/english/review-services/regulatory-info/0003.html

Issue Date	Document Type & No.	Title	Posting date
Dec 21, 2020	PSEHB/PED Notification No. 1221-1	Guidelines for Analysis Reports Involving Physiologically based Pharmacokinetic Models	February 24, 2021
Mar. 8, 2019	PSEHB/PED Notification No. 0308-1 PSEHB/MDED Notification No.0308-1	Guidelines on Cancer Immunotherapy Development	March 11, 2021

Safety Information

Pharmaceuticals and Medical Devices Safety Information No. 380 (February 24, 2021)

1. Revision of Precautions for Lidocaine Hydrochloride/Adrenaline Injections concerning Patients for Whom Anaesthesia Is Intended for Ears or Digits as Contraindication in Conduction or Infiltration Anaesthesia
2. Important Safety Information
   (1) Pomalidomide
3. Revision of Precautions (No. 320)
   Alemtuzumab (genetical recombination) (1 other)
4. List of Products Subject to Early Post-marketing Phase Vigilance

https://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0018.html

Pharmaceuticals Revisions of PRECAUTIONS (February 25, 2021)

- Aspirin (preparations indicated for antipyresis, analgesia, anti-inflammation, prevention of thrombus/embolus formation, Kawasaki disease)
- Aspirin (preparations indicated for antipyresis, analgesia, anti-inflammation)
- Aspirin/dialuminate (330 mg)
- Ampiroxicam
- Piroxicam (oral dosage form)
- Isopropylantipyrine
- Isopropylantipyrine/acetaminophen/allylisopropylacetylurea/ anhydrous caffeine/ethenzamide
- Ibuprofen, celecoxib, naproxen, pranoprofen (oral dosage form), flurbiprofen axetil, loxoprofen sodium hydrate (oral dosage form), lornoxicam
- Etodolac, nabumetone, flurbiprofen (oral dosage form), mefenamic acid, esflurbiprofen/mentha oil
- Ketoprofen (injections)

- Ketoprofen (suppository)
- Zaltoprofen
- Dibucaine hydrochloride/sodium salicylate/calcium bromide, bucolome, flufenamate aluminum, mofezolac
- Sulpyrine hydrate
- Tiaprofenic acid
- Migrenin
- Salicylamide/acetaminophen/anhydrous caffeine/chlorpheniramine maleate, salicylamide/acetaminophen/anhydrous caffeine/promethazine methylenedisalicylate
- Ibuprofen piconol, glycol salicylate/l-menthol, methyl salicylate/dl-camphor/capsicum extract, methyl salicylate/dl-camphor/l-menthol, methyl salicylate/glycol salicylate/l-menthol/d-camphor/diphenhydramine/benzyl nicotinate, methyl salicylate/l-menthol/dl-camphor/glycyrrhetinic acid, suprofen
- Indometacin (agents for epidermis), ketoprofen (agents for epidermis), diclofenac sodium (agents for epidermis), piroxicam (agents for epidermis), felbinac, flurbiprofen (agents for epidermis), loxoprofen sodium hydrate (agents for epidermis), salicylic acid (dry powder, ointment, patches)
- Methyl salicylate
- Heparinoid/adrenal extract/salicylic acid
- Aspirin (preparations indicated for prevention of thrombus/embolus formation, Kawasaki disease), aspirin/dialuminate (81 mg), aspirin/lansoprazole, clopidogrel sulfate/aspirin
- Aspirin/vonoprazan fumarate
- Salbutamol sulfate

https://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0008.html

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
April 14	3rd Asian Network Meeting	Virtual
May 20-23	13th DIA China Annual Meeting	Suzhou
May 25, 31- June 3	ICH virtual meeting	Virtual

Reports from Overseas

Our officers deliver lively reports of their activities at their stationed overseas authorities.

EU-Medicines for all (EU-M4all)

The procedure called EU-Medicines for all or 'EU-M4all' is aimed to facilitate patient access to essential medicines primarily in low- and middle-income countries in cooperation with the World Health Organization [1)]. It was previously known as the Article 58 procedure as the legal basis is Article 58 of Regulation (EC) No 726/2004 of the European parliament and of the council.

So far, 11 medicines have received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) under the procedure, and 142 regulatory approvals have been granted in 91 countries, contributing to public health in these countries [2)]. The assessment reports under EU-M4all have been published on EMA website [3)].

Applicants may apply in parallel for an EU marketing authorisation under the centralised procedure and an opinion under EU-M4all for their medicine to be used inside and outside the EU [4)]. In January 2021, to promote the parallel submission EMA has issued a draft guidance for consultation [5)] and the guidance is planned to be finalised in the first quarter of 2021.

The EU-M4all brings many benefits [1)] and, of these, in my perspective, the involvement of experts from national regulatory authorities in targeted countries is one of the key elements. This helps to build capacity for regulatory agencies in the countries intending to use the medicine as well as to ensure local knowledge is taken into account during assessment. It is also noted that each national regulator takes the final decision on whether or not to use the medicine in the country. I think retaining and respecting the independence of participating regulatory agencies is of paramount importance for international collaboration including reliance approach.

1) https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/medicines-use-outside-european-union
2) https://doi.org/10.1080/17512433.2020.1724782
3) https://www.ema.europa.eu/en/medicines/opinions-medicines-use-outside-european-union
4) https://www.ema.europa.eu/en/documents/leaflet/eu-m4all-promoting-parallel-application-eu-m4all-opinion-centralised-marketing-authorisation_en.pdf
5) https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-parallel-application-eu-m4all-article-58-opinion-centralised-marketing-authorisation_en.pdf

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