FOOD AND DRUG ADMINISTRATION

DRUG SAFETY NEWSLETTER

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Our First FDA Drug Safety Newsletter!

We are proud to announce our first FDA Drug Safety Newsletter. The Food and Drug Administration (FDA) protects public health by ensuring the quality, safety, and efficacy of drug products. To achieve this, emerging issues and safety information concerning medicines must be communicated to everyone. Healthcare professionals must be updated on medicine safety, as they prescribe, dispense, administer and provide advise on the proper use of medicines; and report incidents of adverse drug reactions (ADR). It is also necessary that patients receive the correct information and are given proper counseling. Everyone must be informed, making sure that no one is left behind, because at some point in our lives, we need these medicines may it be for prevention, diagnosis, mitigation, treatment or cure of our diseases.

To keep you updated, FDA Drug Safety Newsletter shall be released quarterly. We will provide you with information on emerging issues on the use of medicines, new safety updates, and practical advice.

Dr. Samuel A. Zacate
Director General

In this issue:

Pharmacovigilance Corner

FDA monitors the safety of medicines through different pharmacovigilance (PV) activities such as ADR reporting, signal detection, and timely communication.

PV is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. (WHO, 2002)

NO MEDICINE IS 100% SAFE

The FDA Center for Drug Regulation and Research (CDRR) is in-charge of ensuring the quality, safety, and efficacy of medicinal products. We do this through (1) licensing of drug establishments, (2) registration of drug products, and (3) post-marketing surveillance (PMS) activities such as PV where we monitor the ADR of medicines.

PV activities start from the detection of side effects. Then assessment of the cases is done to understand the behavior of the medicine. To prevent future harm, necessary information and advice to healthcare professionals and the public is provided. It is essential that the side effects are reported to the FDA for us to evaluate the safety of medicines, making sure that the benefits always outweigh the risks.

No medicine is 100% safe. Although the FDA has already evaluated and tested the medicines through its registration process before it becomes available to the public, some side effects may only be recognized after it has been marketed and used in a wide range of the population. That is why reporting of the side effects is important. It will help us understand the behavior of the medicines and know how our body reacts to it.

On-going Safety Assessments

One of the functions of the PV Section is to monitor the use of medicines that might have an impact on its safety. The following are the safety assessment that is currently investigated:

- Domperidone drug classification, prescription (Rx) or over-the-counter (OTC), due to increased risk of cardiac adverse reaction
- Topical steroid classification (Rx or OTC) due to risk of misuse and abuse
- Bupivacaine and reports of serious ADRs from hospitals
- Vitamin B6 and risk of peripheral neuropathy

Results of the assessments will be updated in the succeeding issues of Drug Safety Newsletter and shall be posted at the FDA website.

Cohort Event Monitoring (CEM) of Molnupiravir

Molnupiravir is an oral antiviral medicine with a good pharmacokinetic profile. It is an RNA-dependent RNA polymerase (RdRp) inhibitor that plays an important role in replication of SARS-CoV-2. Currently, it is one of the medicines issued with Emergency Use Authorization (EUA) for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults 18 years old and above with a positive SARS-COV-2 diagnostic test and who are at risk for developing severe illness.

Molnupiravir is a novel drug and its popularity for the treatment of COVID-19 disease has gained high interest to monitor its safety profile. Thus, the World Health Organization (WHO) initiated a CEM for Molnupiravir. CEM is an active surveillance activity where we ensure timely collection of data by monitoring patients who had taken Molnupiravir to identify adverse events that are likely to be associated with it.

Philippines is one of the countries that expressed its intention to participate in the study. Led by principal investigator (PI) Dr. Regina Berba from the Philippine College of Physicians, the PV Section will be providing assistance on the needs of the study related to PV.

Pharmacovigilance Inspection

The PV Section, in partnership with the Regulatory Field Office (RFO) inspectors, is preparing to conduct PV inspection. This is to assess Market Authorization Holders (MAHs), and outsourced person or organization's functional PV system.

Guidelines on PV inspections will be released prior to its implementation. Selected MAHs will be notified prior to inspection. The PV inspection is planned to be implemented in 2024.

The PV Team together with the RFO inspectors completed the Pharmacovigilance Inspections Training Course offered by the WHO.

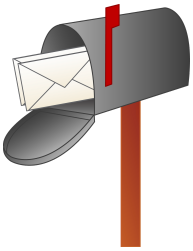
What to do in case you experience an ADR?

Adverse Drug Reaction (ADR) can either be serious or non-serious. Non-serious or mild ADRs, such as headache, fever, or body pains, usually resolve after a day or two and can be treated with over-the-counter medicines such as Paracetamol and Ibuprofen. For serious ADRs and ADRs that do not resolve or worsen after a few days, immediately seek the advice of your Healthcare Professional (HCP).

Always report any suspected ADR. You may ask the assistance of your HCP or you may choose any of the following reporting channels.

Online reporting
Step 1: Visit the Online Adverse Drug Reaction Reporting or scan the QR code.
Step 2: Fill in all available information and be as complete as possible.
Step 3: Review the information then click Send report.
Step 4: A prompt will appear that your report has been sent. You have the option to download your report.

Reporting through email
Step 1: Download the FDA Suspected Side Effects Reporting Form.
Step 2: Fill in all available information and be as complete as possible.
Step 3: Save, print, or scan the accomplished form.
Step 4: Send it to pharmacovigilance@fda.gov.ph
Step 5: An acknowledgement email will be sent to you once the report is received.



Reporting via direct mail
Step 1: Download the FDA Suspected Side Effects Reporting Form.
Step 2: Fill in all information available. Information shall be as complete as possible.
Step 3: Save and print the accomplished form.
Step 4: Mail to the following address:

Pharmacovigilance Section
Product Research and Standards Development Division
Center for Drug Regulation and Research
FOOD AND DRUG ADMINISTRATION
Civic Drive, Filinvest City, Alabang, Muntinlupa City 1781

or

FDA Regional Field Office near you. Check the FDA website for the directory.

Step 5: An acknowledgement email will be sent to you once the report is received.

Reporting through telephone
Step 1: Call us at (02) 8809 5596.
Step 2: Somebody will receive your call and ask you for all the needed information with reference to the FDA Suspected Side Effects Reporting Form.

Note: **All information provided are treated with utmost confidentiality**. You may be contacted if additional information is needed. You may also walk-in to our FDA Action Center (FDAC).

Newly Approved Medicines Corner

This section includes New Chemical Entities (NCEs) - these are the newly approved medicines with an active substance that has not been previously registered for any pharmaceutical use in the country.

Below is a list of all newly approved medicines for 2022:

PRODUCT NAME	REGISTRATION NUMBER	INDICATION
Neratinib maleate (Nerlynx) 40 mg Film-Coated Tablet	DR-XY48091	Antineoplastic Agent (Protein Kinase Inhibitor) For the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy.
Roxadustat (Evrenzo) 50 mg Film-Coated Tablet	DR-XY48343	Antianemic Preparation For the treatment of adult patients with symptomatic anemia associated with Chronic Kidney Disease (CKD).
Roxadustat (Evrenzo) 20 mg Film-Coated Tablet	DR-XY48344	Antianemic Preparation For the treatment of adult patients with symptomatic anemia associated with Chronic Kidney Disease (CKD).
Ofatumumab (Bonspri) 20 mg/0.4 mL Solution for Injection	BR-1418	Immunosuppressant For the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features.
Tildrakizumab (Ilumya) 100 mg/mL Solution for Injection	BR-1419	Interleukin Inhibitor For the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
Fexuprazan hydrochloride (Fexuclue) 40 mg Film-Coated Tablet	DR-XY48448	Potassium-Competitive Acid Blocker (P-CAB) For the treatment of erosive esophagitis (EE).

The safety of NCE products are closely monitored by the PV Section.

Everyone is encouraged to report any suspected ADRs especially on newly approved medicines in order to improve their safety profile.

Product Recall Corner

FDA ensures that registered drug products that pose health risk and considered not safe are removed from the market.

Recall is the method of withdrawing or correcting unsafe or hazardous health products from the distribution chain that may present a health hazard to the consumer or user.

Below is the list of all recalled medicines for 2022:

PRODUCT NAME	DOSAGE STRENGTH	BATCH/LOT NUMBER	REASON OF RECALL	STATUS OF RECALL
Irbesartan (Aprovel) Film-Coated Tablet DRP-5716	150 mg	AA271 AA193	Detection of impurities	Ongoing
Irbesartan (Aprovel) Film-Coated Tablet DRP-5715	300 mg	AA645		
Irbesartan + Amlodipine (Aprovasc) Film-Coated Tablet DR-XY45509	150 mg/5 mg	AMXA006 AMXA007 AMXA008 AMXA009		
Irbesartan + Amlodipine (Aprovasc) Film-Coated Tablet DR-XY45507	300 mg/5 mg	AMXA003		
Irbesartan + Amlodipine (Aprovasc) Film-Coated Tablet DR-XY45508	300 mg/10 mg	AMXA002		
Irbesartan + Hydrochlorothiazide (Co-Aprovel) Film-Coated Tablet DRP-002	300 mg/12.5 mg	AA550		
Ciclosporin (Ikervis) Ophthalmic Emulsion DR-XY46077	1 mg/mL	1L14S	Crystallization of Active Pharmaceutical Ingredient (API)	Completed
Salbutamol (as Sulfate) (Ventolin) Tablet DRP-6319	2 mg	20H003 20H004 20L001 21C001 21C002 21E004	Detection of nitrosamine compounds above allowable limit	Completed
Gliclazide (Azukon MR) Prolonged - Release Tablet DRP-3777	30 mg	BU79H001	Out-of-Specification result	Ongoing
Mupirocin (Mupizee) Ointment DR-XY46245	20 mg/g (2% w/w)	820-346 820-413	Out-of-Specification result	Ongoing
Cloxacillin (as sodium) Philclox Capsule DRP-7969	500 mg	203131413	Out-of-Specification result	Completed

PRODUCT NAME	DOSAGE STRENGTH	BATCH/LOT NUMBER	REASON OF RECALL	STATUS OF RECALL
Atracurium besilate (Atrium) Solution for Injection DRP-7642	10 mg/mL	1320259	Out-of-Specification result	Completed
Simvastatin (Philstat) Film-Coated Tablet DRP-7965	20 mg	2011558	Out-of-Specification result	Completed
Gadoteric Acid (Dotarem) Solution for Injection DR-XY26429	0.5 mmol/mL (equi. to 279.32 mg/mL)	20GD080A	Defect in packaging material	Completed
Vancomycin hydrochloride Powder for IV Infusion DR-XY12581	500 mg (500,000 IU)	H036913AAR H036913AAR1	Issues on shelf life	Ongoing
Quinapril hydrochloride (Accupril) Filn-Coated Tablet DRP-2002	5 mg	FN6525 DM5044	Detection of nitrosamine compounds above allowable limit	Ongoing
Quinapril hydrochloride (Accupril) Filn-Coated Tablet DRP-3104	20 mg	EA9305		
Gliclazide (Azukon MR) Prolonged-Release Tablet DRP-3777	30 mg	BU79G001 BU79G002 BU79G006 BU79G007 BU79G008 BU79G009 BU79G017 BU79G018 BU79G019 BU79G020 BU79G021 BU79G022 BU79H005 BU79H006 BU79H007 BU79H009 BU79H010	Issues on shelf life	Ongoing
Gliclazide Prolonged-Release Tablet DRP-3777-02	30 mg	BU79G009 BU79G019 BU79H010		
Paracetamol (Dolexpel) Tablet DR-XY2296	500 mg	21AT01 22AT01 22AT02 22AT03 22AT04	Out-of-Specification result	Completed
Ascorbic Acid (Myrevit-C) Syrup HRP-083	100 mg/5 mL	WKN206 WKN207 WKN208	Out-of-Specification result	Completed

PRODUCT NAME	DOSAGE STRENGTH	BATCH/LOT NUMBER	REASON OF RECALL	STATUS OF RECALL
Ascorbic Acid (Myrevit-C) Syrup (Oral Drops) HRP-096	100 mg/mL	WMN057 WMN125A XCN122	Out-of-Specification result	Completed
Bromhexine hydrochloride (Pulmohex) Tablet DRP-5719	8 mg	1D146 1D237 1E202 1G250	Issues on Good Manufacturing Practice (GMP)	Completed
Hyoscine-N-Butylbromide (Hyospan) Syrup DRP-388-01	1 mg/mL (5 mg/5 mL)	2F119	Issues on Good Manufacturing Practice (GMP)	Completed
Doxofylline (Ansimar) Syrup DR-XY31275	100 mg/5 mL (2 g/100 mL)	A1809	Defect in packaging material	Completed
Ibuprofen (Medicol Advance) Capsule DR-XY41760	400 mg	E002266	Defect in packaging material	Ongoing
Oxytocin (Exerta) Solution for Injection DRP-4985-03	10 IU/mL	1108 1414	Under-filled ampules	Ongoing
Vancomycin hydrochloride Powder for IV Infusion DR-XY12581	500 mg (500,000 IU)	J026913AAR J026913AAR1 J026913AAR2 J026913BAR J026913BAR1	Out-of-Specification result	Ongoing
Iron + Vitamin B-complex (Sangobion Kids) Syrup DR-XY32945	-	All batches (preventive)	Detection of Ethylene Glycol above allowable limit in one (1) batch of the product	Ongoing

What to do in case you took a recalled medicine?

If the medicine you are taking is being recalled, don't panic! Do the following:

- 

Stop taking the medicine immediately.
- 
Contact your HCP for possible alternatives or replacement of your medicine.
- 
Observe for possible ADRs and report.

For more information, visit the FDA website for the issued FDA Advisories on product recall.

Counterfeit Medicines Corner

FDA safeguards the public by evaluating suspected counterfeit medicines through product verification.

Counterfeit medicines refer to medicinal products with the following characteristics: (1) correct ingredients but not in the correct amount, (2) wrong ingredients, (3) without active ingredients, (4) with sufficient quantity of active ingredient, which results in the reduction of the drug's safety, efficacy, quality, strength or purity. It is a medicine which is deliberately and fraudulently mislabeled with respect to identity and/or source or with fake packaging, and can apply to both branded and generic products. (R.A. No. 8203)

The WHO simplified this definition as those medicines that are substandard, falsified, and unregistered. Substandard or Out-of-Specification (OOS) products are those that fail to meet their quality standards/specification. Falsified medicines are those that are deliberately or fraudulently misrepresent their identity, composition, or source. While Unregistered products are those that have not gone evaluation and approval of the FDA. (WHO, 2018)

Counterfeit medicines continue to pose a threat to public health. With the rise of online selling platforms, the proliferation and distribution of counterfeit medicines became seamless. Online buyers continue to purchase through these platforms due to lower prices, in addition to the discounts given and convenience it provides. These buyers do not realize the health hazard of counterfeit medicines (see Dangers of Buying Medicines from Online Unlicensed Establishment on the next page).

In 2022, the FDA verified 447 counterfeit medicines. 78.97% (353) are OTC medicines, 15.66% (70) are prescription medicines, and 5.37% (24) are household remedy products. The top counterfeited medicines are:

1. Biogesic®
2. Neozep® Forte
3. Bioflu®
4. Alaxan® FR
5. Tuseran® Forte
6. Solmux®
7. Medicol® Advance
8. Decolgen® Forte, Flanax® Forte
9. Diatabs®
10. Dolfenal®

Pursuant to the provisions of Republic Act No. 8203 or the "Special Law on Counterfeit Drugs" and by virtue of the Presidential Proclamation No. 2082 s. 2010, the third (3rd) week of November is declared as the National Consciousness Week Against Counterfeit Medicines (NCWACM). The FDA, together with public and private partners, celebrated NCWAC last 14-18 November 2022 with the theme **"Technology and Regulation at the forefront of Fighting Counterfeit Medicines - Maging Mapanuri, MAGKAISA! Labanan Pekeng Medisina!"**

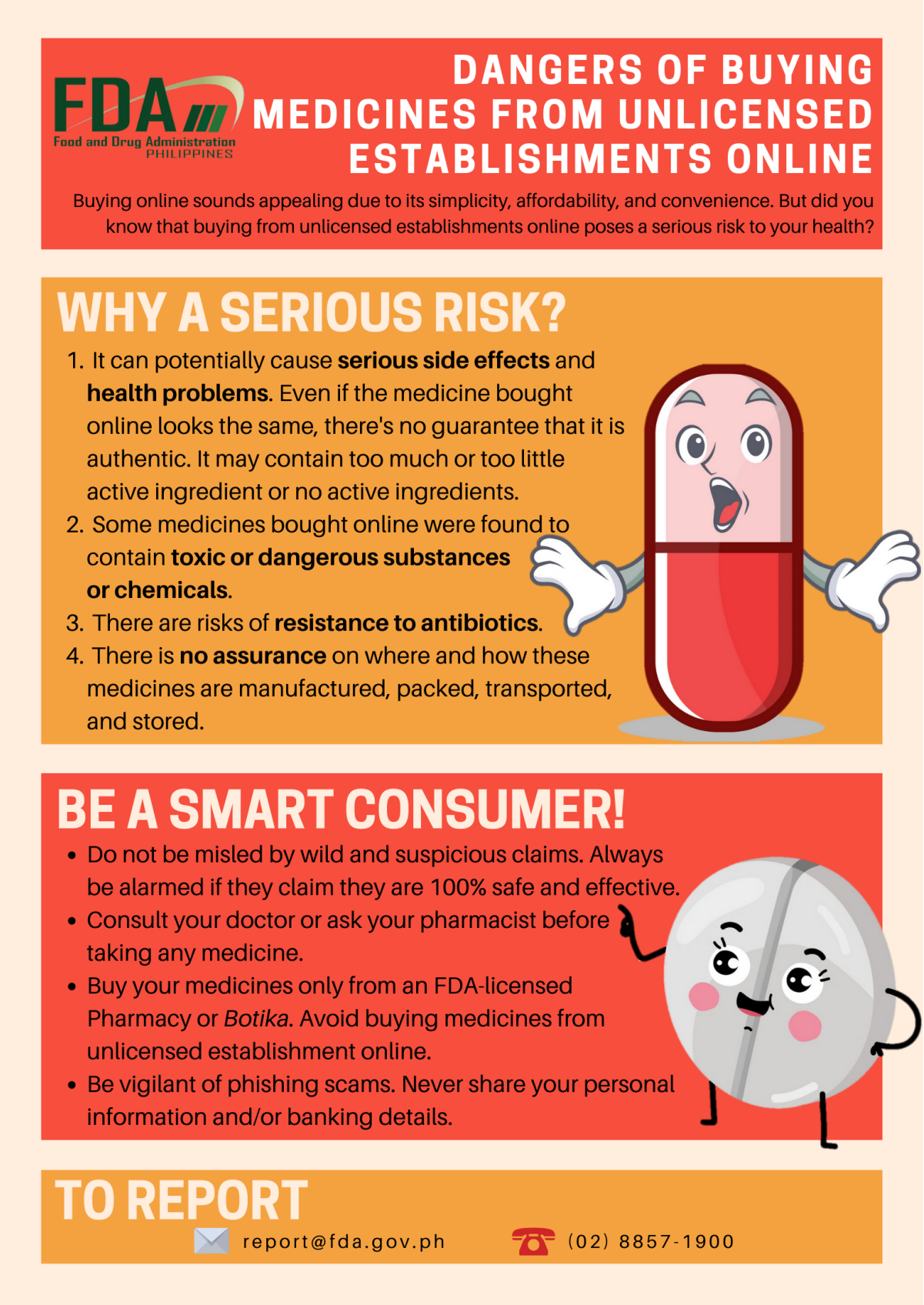
Our fight against counterfeit medicines should now be stronger more than ever. Be one with us in combating counterfeit medicines!

What to do in case you suspect you bought a counterfeit medicine?

- ✓  Do not take the product.
- ✓  Report to the FDA through:
  Telephone: (02) 8857 1900
  Email: ereport@fda.gov.ph
  Or you may also contact the legitimate product owner (pharmaceutical company)
- ✓  If you took the medicine, observe any possible ADRs and report.

Dangers of Buying Medicines from Unlicensed Establishments Online

Know the risks of buying online, especially to unlicensed establishments, through FDA Advisory No. 2019-154. You may check if an establishment is licensed and if a medicine is registered with the FDA through our verification portal. You may also check the ABCDE's on Buying Health Products Online.



COVID-19 Vaccines Corner

COVID-19 vaccines have played a big role in shaping the COVID-19 pandemic. Vaccines work by stimulating an immune response from the body.

The following are the vaccines issued with Emergency Use Authorization (EUA) by the FDA:

- Pfizer-BioNTech COVID-19 mRNA Vaccine (nucleoside modified) [Comirnaty]; Tozinameran + Famtozinameran [Comirnaty Original/Omicron BA.4-5]
- AstraZeneca COVID-19 Vaccine (ChAdOx1-S [recombinant]) [Vaxzevria]
- COVID-19 Vaccine (Vero Cell), Inactivated [CoronaVac]
- Gam-COVID-Vac [Sputnik V & Sputnik Light]
- COVID-19 Vaccine (Ad26.COV2-S [recombinant]) [Janssen COVID-19 Vaccine]
- COVID-19 Vaccine (Whole Virion Inactivated Corona Virus vaccine) [Covaxin]
- Moderna COVID-19 mRNA Vaccine (nucleoside modified) [Spikevax]; Elasomeran + Imelasomeran [Spikevax Bivalent Original/Omicron BA.1]
- Inactivated COVID-19 Vaccine (Vero Cell) [COVID-19 Vaccine Sinopharm BIBP/Wuhan]
- COVID-19 Vaccine (SARS-CoV-2 rS Protein Nanoparticle [Recombinant]) [Covovax]

COVID-19 vaccination rollout started as soon as the first vaccine became available in the country. Initially under the banner, *Resbakuna Kasangga ang Bida* to now, *PinasLakas*, the vaccination program has more than 169.9 million doses administered (as of 28 December 2022). 73.7 million Filipinos are now fully vaccinated or have completed their primary series. Primary series are administered in two (2) doses except for Janssen COVID-19 Vaccine and Sputnik Light which are administered as a single dose.

Data on COVID-19 vaccines below is based on its approved and recommended use as of 31 December 2022.

Table 1. Age eligibility and interval of primary series of COVID-19 vaccines

VACCINE	ELIGIBILITY	PRIMARY SERIES
Inactivated Vaccines		
CoronaVac (Sinovac)	6 y/o and up	4 weeks apart
Sinopharm	18 y/o and up	21-28 days apart
Covaxin	18 y/o and up	28 days apart
Viral Vector Vaccines		
Vaxzevria (AstraZeneca)	18 y/o and up	4-12 weeks apart
Sputnik V (Gamaleya)	18 y/o and up	3 weeks apart
Sputnik Light (Gamaleya)	18 y/o and up	Single dose
Janssen	18 y/o and up	Single dose
mRNA Vaccines		
Comirnaty (Pfizer)	5 y/o and up	21 days apart
Spikevax (Moderna)	6 y/o and up	28 days apart
Protein Subunit Vaccine		
Covovax	12 y/o and up	21 days apart

*May change as new data comes in

On booster doses

Due to the virus' ability to undergo rapid genetic changes that produces new strains and the waning immunity from the primary dose series, booster doses were used to maintain protection against COVID-19 disease. Booster doses are given either as homologous or heterologous. Homologous dose refers to the administration of the same vaccine brand as the primary series.

On the other hand, heterologous dose means administration of a different vaccine brand/platform from primary series. You may refer to DOH Department Memorandum No. 2021-0492 for more information. Booster dose administration was shortened to at least three (3) months from the last dose of a primary two-dose vaccine, or at least 2-3 months after a primary single-dose vaccine based on DOH Press Release dated 21 December 2021.

Table 2. Information on additional doses of COVID-19 vaccines for fully vaccinated individuals

VACCINE	INTERVAL FIRST BOOSTER		INTERVAL SECOND BOOSTER		INTERVAL BIVALENT VACCINE	
Inactivated Vaccines						
CoronaVac (Sinovac) **[S]**	3 months apart from primary series	**S, AZ, SL, J, P, M**	4 months apart from first booster	**AZ, P, M**	At least 4-6 months apart from last prior dose of COVID-19 vaccine	**P, M**
Sinopharm **[SP]**		**SP, AZ, J, P, M**		**AZ, P, M**		**P, M**
Viral Vector Vaccines						
Vaxzevria (AstraZeneca) **[AZ]**	3 months apart from primary series	**AZ, SL, J, P, M**	4 months apart from first booster	**AZ, P, M**	At least 4-6 months apart from last prior dose of COVID-19 vaccine	**P, M**
Sputnik V (Gamaleya) **[SV]**		**AZ, P, M**		**AZ, P, M**		**P, M**
Sputnik Light (Gamaleya) **[SL]**	2 months apart from primary series	**AZ, J, P, M**		**AZ, P, M**		**P, M**
Janssen **[J]**		**J, AZ, P, M**		**AZ, P, M**		**P, M**
mRNA Vaccines						
Comirnaty (Pfizer) **[P]**	3 months apart from primary series	**P, AZ, SL, J, M**	4 months apart from first booster	**AZ, P, M**	At least 4-6 months apart from last prior dose of COVID-19 vaccine	**P, M**
Spikevax (Moderna) **[M]**		**M, AZ, SL, J, P**		**AZ, P, M**		**P, M**

*May change as new data comes in

The population eligible for second booster dose are individuals aged 18 to 49 y/o with comorbidities, adults aged 50 y/o and up, and frontline health workers. Vaccines are also given either as homologous or heterologous at four (4) months apart from first booster dose.

On bivalent booster dose

As the fight against COVID-19 pandemic continues, more resistant strains emerged that led to the development of bivalent vaccines targeting both the original strain of SARS-CoV-2 and specific omicron subvariants. The FDA has granted EUA to two bivalent vaccines: Comirnaty Original/Omicron BA.4-5 and Spikevax Bivalent Vaccine (Moderna). Both are allowed for individuals 12 y/o and up who have previously received at least a primary series. The recommended interval is at least 4-6 months apart from last prior dose of COVID-19 vaccine.

On extended shelf life

Shelf life or the expiration date reflects how long a medicine or vaccine retains its potency, purity, and quality at a given storage temperature. COVID-19 vaccine developers continue to study the stability of vaccines, thus, the application on extended shelf life. This is supported by stability studies, evaluated and approved by the FDA. Out of the nine (9) COVID-19 vaccines with EUA, seven (7) had their shelf life extended except for Covaxin and Sinopharm.

On Adverse Events Following Immunization (AEFIs)

AEFI is any untoward medical events after vaccination. These events are monitored by the FDA together with other public health partners. As of December 31, 2022, the FDA has received, analyzed, and evaluated 111,639 suspected AEFIs from COVID-19 vaccines, equivalent to 0.07% of the total doses administered (169,627,564). Reports of suspected adverse reaction to COVID-19 vaccines is posted in the FDA website and updated monthly.

Contact Us

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