PHARMACY BULLETIN

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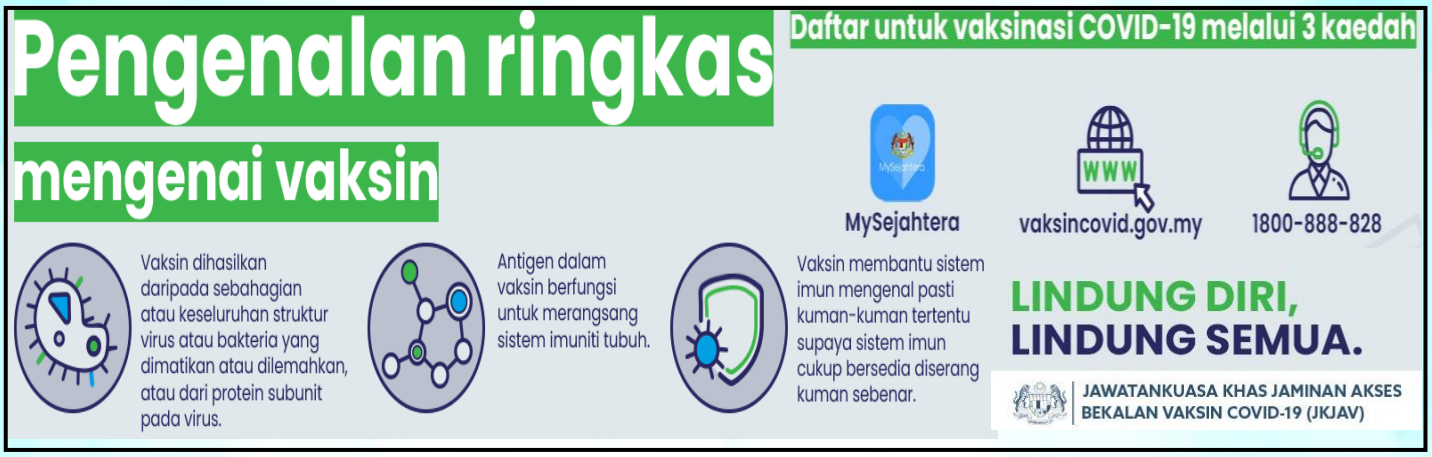

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Highlight: COVID-19 & PFIZER-BIONTECH COVID-19 VACCINE (COMIRNATY®)

Prepared by: *Ng Hwee San*

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2. It is predominantly a respiratory illness that can affect other organs.

Symptoms can range from mild to severe and may appear 2 to 14 days after exposure to the virus:		Seek medical care immediately if having any of these emergency warning signs for COVID-19:
• fever or chills • cough • shortness of breath • fatigue • muscle or body aches • headache	• new loss of taste or smell • sore throat • congestion or runny nose • nausea or vomiting • diarrhea	• Trouble breathing • Persistent pain or pressure in the chest • New confusion • Inability to wake or stay awake

The Pfizer-BioNTech COVID-19 Vaccine (COMIRNATY®) is authorized for use under an Emergency Use Authorization for active immunization to prevent COVID-19 in individuals 16 years of age and older.

Dosage Form	Suspension for injection
Type of vaccine	mRNA
Dosage	2 doses (0.3mL each), 21 days apart
Administration	Intramuscular
Does not contain	Eggs, Preservatives, Latex

Mechanism of action

The modRNA in the Pfizer-BioNTech COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

Common Side Effects (COMIRNATY)

- Pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, and fever.
- Usually start within a day or two of getting the vaccine, which typically lasted several days.

All Malaysian citizens aged 18 and over who are certified eligible by a medical practitioner can receive COMIRNATY vaccine, **except**:

Contraindications:

- Individuals with known history of a severe allergic reaction (e.g., anaphylaxis) after a previous dose of this vaccine or allergy to any component of the Pfizer-BioNTech COVID-19 Vaccine.

COMIRNATY Vaccine

USE IN SPECIFIC POPULATIONS	Risk Summary
Pregnancy	Available data are insufficient to inform vaccine-associated risks in pregnancy.
Lactation	Data are not available to assess the effects on the breastfed infant or on milk production/excretion.
Pediatric Use	Emergency Use Authorization of vaccine does not include use in individuals younger than 16 years of age.

References:

1. *Pfizer Inc. (2021). Fact Sheet For Healthcare Providers Administering Vaccine (Vaccination Providers). Retrieved from: https://www.fda.gov/media/144413/download*
2. *COVID-19 Malaysia, Kementerian Kesihatan Malaysia. (2021). Soalan Lazim (FAQ) Berkenaan VAKSIN COVID-19 Keluaran PFIZER (COMIRNATY®). Retrieved from: http://covid-19.moh.gov.my/vaksin-covid-19/faq/faq-vaksin-covid-19-pfizer-comirnaty*
3. *Centers for Disease Control and Prevention (2021, January 25) Information about the Pfizer-BioNTech COVID-19 Vaccine. Retrieved from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/differentvaccines/PfizerBioNTech.html#:~:text=Based%20on%20evidence%20from%20clinical,works%20in%20real%2Dworld%20conditions.*

Medication safety: AEFI –ADVERSE EVENTS FOLLOWING IMMUNISATIONS COVID-19 VACCINE

Prepared by: Syafizawati binti Ghazali

WHO definition of AEFI:
Any untoward medical event occurring after immunization and does not necessarily have a casual relationship with the usage of the vaccine.

COVID-19 vaccine:
can cause undesirable side effects or adverse events following immunization which can range from mild to severe and from common to rare.

However, not every vaccine consumer will have AEFI and mostly reported as mild where recovery may takes a few days with or without treatment.

Frequently reported mild AEFI are as follows:

pain, redness and swollen at the site of injection.
dizziness, muscle ache and joint pain
nauseous, chills, feverish
feeling fatigue

What to do if having fever?
Fever usually occur 48 hours after immunization and recovers without treatment.
Seek treatment immediately at nearest healthcare centre if

having fever after or more than 48hours of immunization
stay with positive COVID-19 patients in short period of time
staying with someone who has COVID-19 symptoms
having COVID-19 symptoms

Generally, vaccine usage is safe and constantly monitored by MOH. IF AEFI happens, it can be reported by health personnel, the company and the public. The report received will be reviewed and evaluated in terms of the vaccine's relationship with the AEFI.

AEFI Online Reporting (NPRA official website at *www.npra.gov.my*)

1) Vaccine recipient

• Vaccine recipient can report AEFI using Consumer side effect reporting form (*Pelaporan Kesan Sampingan Ubat untuk Pengguna > ConSERF)* to National Centre for Adverse Drug Reactions Monitoring.

• Reporting through MySejahtera. MySejahtera has been updated. *(Icon Vaksinasi COVID-19 is added).* Vaccine recipient can access the AEFI reporting only if they have undergone the vaccination process.

2) AEFI identifying facilities

• Report AEFI using the Report on Suspected Adverse Drug Reaction form (Borang Pelaporan ADR Revision-01) to National Centre for Adverse Drug Reactions Monitoring

***AEFI identifying facilities (PPV, Government health facilities other than PPV, Private facility)*

- The identities of Reporter, Patient and Institution will remain confidential.
- AEFI reports submitted can assist in monitoring the adverse effects and safety of vaccines available in the market.

References:
1. *COVID-19 Malaysia, Kementerian kesihatan Malaysia. (2020, December 31). Soalan Lazim Berkaitan Vaksin Covid-19. Retrieved from: https://www.infosihat.gov.my/images/media_sihat/INatain_lain/faqvaksin/mobile/index.html (Accessed on 16th February 2021)*
2. *National Pharmaceutical Regulatory Agency, Ministry of Health, Malaysia. Reporting Adverse Drug Reactions and Adverse Events Following Immunisation. Retrieved from: https://www.npra.gov.my/index.php/en/health-professionals/reporting-adr.html (Accessed on 16th February 2021)*

Know your medicine:
REMDESIVIR

Prepared by: Tan Woei Yan

Remdesivir is a broad spectrum antiviral.The active form of remdesivir acts as a nucleoside analog which binds to the RNA-dependent RNA polymerase (RdRp) of coronaviruses including SARS-CoV-2, inhibiting viral replication through premature termination of RNA transcription.

Approval:
US FDA approved remdesivir in treating hospitalized adult and pediatric patients (aged ≥12 years & weighing at least 40 kg) with COVID- 19 and also available through FDA Emergency Use Authorization for emergency use by licensed healthcare providers to treat suspected or confirmed COVID-19 hopitalized pediatric patients weighing 3.5kg to <40kg or aged <12 years weighing at least 3.5 kg.
Should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care.

Evidence of Efficacy:
A phase 3, multinational, double-blind, randomized, placebo-controlled trial (Adaptive Covid-19 Treatment Trial, ACTT-1) showed that patients who received Remdesivir had a significantly faster recovery time (~ 10 days) compared to placebo group (~ 15 days).

Before initiating Remdesivir and during treatment:
Assess **prothrombin time** and perform **eGFR** & **hepatic laboratory test.**

Dosage and Administration:
Single loading dose (200mg) at Day 1 followed by once daily maintenance dose (100mg) at Day 2, administer via intravenous infusion over 30-120 minutes. Not recommended in patient with eGFR <30ml/min.

Recomended duration of treatment :
For patients not requiring invasive mechanical ventilation is 5 days. (may be extended up to total of 10 days if no clinical improvement.) For patients requiring invasive mechanical ventilation is 10 days.

Adverse Effects:

- Nausea (most common)
- Incresed level of liver enzymes (ALT, AST)
- Hypersensitivity reactions (rashes, shortness of breath; swelling of face, lips or throat, fever, shivering.)
- Increase in prothrombin time

Drug Interaction:
Concomitant use of **Chloroquine** or **hydroxychloroquine** should be avoided as these drugs antagonized the antiviral activity of remdesivir.

USE IN SPECIFIC POPULATIONS	SAFETY SUMMARY
Pregnancy	Available data from published case reports and compassionate use of Remdesivir in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
Peadiatric	Safety and effectiveness have not been established in pediatric patients aged <12 years or weighing <40 kg.
Geriatric	No differences in responses between the elderly and younger patient. No dosage adjustment is required (over the age of 65 years)

Warnings and Precautions:

- **Hypersensitivity** (infusion related or anaphylactic reaction) have been observed during and following administration. Close medical supervision is required during and following administartion and discontinue immediately if hypersensitivity reactions is occured.
- **Increased risk of transaminase elevations** have been observed. Consider discontinuingif ALT levels increase to greater than 10 times the upper limit of normal and discontinue if ALT elevation is accompanied by signs or symptoms of liver inflammation.

Brand Name: Veklury

References:

1. *Cennimo D.J. (2021, February 22). What is the role of the antiviral Drug remdesivir in the treatment of coronavirus disease 2019 (COVID-19)? Medscape. Retrieved from https://www.medscape.com/answers/2500114-197451/what-is-the-role-of-the-antiviral-drug-remdesivir-in-the-treatment-of-coronavirus-disease-2019-covid-19 (Accessed on February 22, 2021)*
2. *United States Food and Drug Administration. (2020, October 22). FDA's approval of Veklury (remdesivir) for the treatment of COVID-19—The Science of Safety and Effectiveness. Retrieved from: https://www.fda.gov/drugs/drug-safety-and-availability/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness (Accessed on February 22, 2021)*
3. *National Institutes of Health. (2021, February 23). COVID-19 Treatment Guidelines. Retrieved from: https://www.covid19treatmentguidelines.nih.gov/ (Accessed on February 23, 2021)*
4. *Rubin D, Chan-Tack K, Farley J, Sherwat A. (2020, December 31). FDA approval of remdesivir — a step in the right direction. N Engl J Med 2020;383:2598-2600. DOI: 10.1056/NEJMp2032369*

Adverse Drug Reaction – CLOZAPINE: RISK OF SERIOUS BOWEL COMPLICATIONS CAUSED BY CONSTIPATION

Prepared by: Diviyasri A/P S. Soundra Rajan

Background:

- Clozapine is an atypical antipsychotic agent which is indicated in treatment-resistant schizophrenia.
- A very common ADR of clozapine is constipation and if left untreated, it may lead to serious complications, including complete bowel obstruction due to its higher potency anticholinergic activity.
- The time to onset for serious bowel events were between 3 days to 6 months after clozapine administration.

Risk increased when:

1) **Higher dose** of Clozapine is administered.
2) When Clozapine is **co-administer** with other **anticholinergic agents**.
3) Clozapine is **co-administer** with other drugs which is **known to cause constipation**.

Reports:

In US (FDA): Reviewed ten (10) local cases of constipation which lead to serious bowel problems resulting in hospitalisation, surgery and five (5) deaths.

In Malaysia (NPRA): Received a total of 312 ADR reports with 534 adverse events suspected to be related to clozapine products.

Adverse events related to serious bowel complications are tabulated below:

Medical Conditions	No. Cases Reported
Intestinal obstruction	6
Ileus paralytic	5
Gastric hypomotility	3
Faecaloma	2
Illeus	1
Subacute intestinal obstruction	1

US FDA & **NPRA** are requiring all product registration holders of clozapine containing products to update package insert with the risk of serious bowel complications.

Advice for Healthcare Professionals:

- Be aware on possible risk of serious bowel complications when clozapine was prescribed to patients.
- Assess patient's bowel function prior to clozapine initiation and avoid prescribing other anticholinergic drugs that may cause constipation.
- Advise patients to seek immediate medical attention if the patient experiences symptoms of potential bowel complications such as nausea and vomiting, bloating and abdominal distension or pain. Emphasize that prompt treatment is critical to prevent serious complications.
- Counsel patients and their caregivers to increase fiber dietary intake and fluids intake to prevent constipation.
- Monitor patients on the frequency and character of bowel movements.
- Consider prophylactic laxative treatment when starting clozapine in patients with a history of constipation or bowel obstruction.

References:

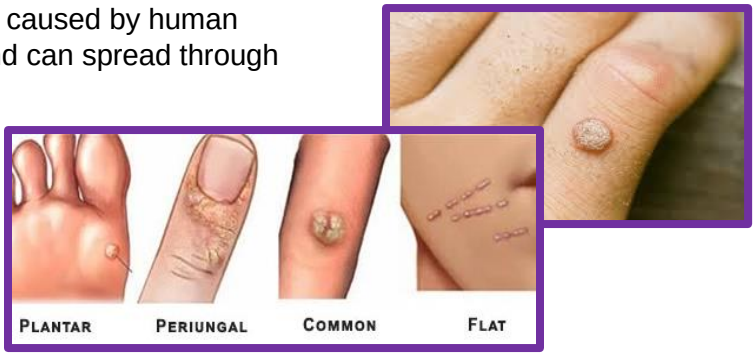
1. *National Pharmaceutical Regulatory Agency, Ministry of Health Malaysia. (2021, January 29). Clozapine: Risk of serious bowel complications caused by constipation. Retrieved from: https://www.npra.gov.my/index.php/en/industry-news-announcements/more-recent-updates/426-english/safety-alerts-main/safety-alerts-2021/1527189-clozapine-risk-of-serious-bowel-complications-caused-by-constipation.html (Accessed on: 15 February 2021)*
2. *United States Food and Drug Administration (US FDA). (2020, February 18). FDA strengthens warning that untreated constipation caused by schizophrenia medicine clozapine (Clozaril) can lead to serious bowel problems. Retrieved from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-strengthens-warning-untreated-constipation-caused-schizophrenia-medicine-clozapine-clozaril-can. (Accessed on: 15 February 2021)*

Counselling Point: TOPICAL PREPARATION (VIRAL SKIN INFECTIONS – WARTS)

Prepared by: Fam Hwei Teng

Warts are benign proliferations of skin and mucosa caused by human papillomavirus (HPV) which is highly contagious and can spread through contacts, most frequently affects the hands, feet (plantar warts) and the anogenital area.

Types of wart include common warts, flat warts, pigmented warts, plantar warts and genital warts.



Treatment of warts:

Medicines	Salicylic Acid 1-20%	Podophyllum 10-20% Paint	Imiquimod 5% cream
Prescriber category	**c**	**b**	**A***
Indication	Warts other than genital warts	External genital warts	External genital warts
Mode of action	• Potent keratolytic action and antiseptic action. • Soften and destroy the stratum corneum.	Prevent growth of wart tissue	Immune response modifier
Side effects	• Skin irritation • Skin ulceration (with higher concentration)	• Local irritation	• Burning sensation • Erosion • Erythema • Itching • Excoriation
Counselling point	• Apply carefully onto warts daily and protect surrounding skin, (eg with soft paraffin or specially designed plaster) • May need to continue up to 3 months. 	• Application must be done by trained personnel. • Avoid normal skin and open wound. • Strong irritant to the skin and mucous membrane. Special care must be taken to ensure application is restricted to the wart itself. • Apply 2 - 3 drops carefully to lesion after protecting surrounding area with vaseline. • Wash off after 6 hours or if feel burning sensation and repeat 2 - 3 times weekly or once weekly.	• Apply three times weekly up to 16 weeks. • Apply thin layer of cream to the wart and rub it until the cream vanishes. • Leave the cream for 6-10 hours then wash the area with mild soap and water. 

Reference:
1. *Pharmaceutical Services Programme, Ministry of Health, Malaysia. (2018). Topical Preparations Counselling Guide for Pharmacist, First Edition. Retrieved from: https://www.pharmacy.gov.my/v2/en/documents/topical-preparations-counselling-guide-pharmacist.html*

VISIT BY THE DIRECTOR GENERAL OF HEALTH MALAYSIA TO PSV AND PPV HOSPITAL PERMAI JB

Visit by the Director General of Health Malaysia, Tan Sri Dato' Seri Dr. Noor Hisham Bin Abdullah together with Health Director of Johor State, Dato' Dr. Aman Rabu; Director of Hospital Permai, Dr. Hj Norazam bin Haron; Director of Hospital Sultan Ismail, Dr. Khadijah binti Abu Bakar; Deputy Health Directors and Senior Officers of Johor State Health Department to the PSV and PPV Hospital Permai on 8 Mac 2021.

Pusat Simpanan Vaksin (PSV) HPJB

The vaccine supply for the first phase of the program arrived in Johor on Feb 21 and was stored at four Vaccine Storage Centers at Hospital Permai (Johor Bahru), Hospital Sultanah Nora Ismail (Batu Pahat), Hospital Temenggong Seri Maharaja Tun Ibrahim (Kulai) and Hospital Pakar Sultanah Fatimah (Muar).

Pusat Pemberian Vaksin (PPV) HPJB

Hospital Permai also served as one of the 10 PPV giving the COVID-19 vaccine for the first phase of program at Johor Bahru district.

Questions

Questions		TRUE	FALSE
1	COMIRNATY COVID-19 vaccine is indicated for active immunization to prevent coronavirus disease caused by SARS-CoV-2, in individuals 16 years of age or older.		
2	AEFI reports submitted can assist in monitoring the adverse effects and safety of vaccines available in the market. The identities of Reporter, Patient and Institution will remain confidential.		
3	The inactive form of remdesivir acts as a nucleoside analog which binds to the RNA-dependent RNA polymerase (RdRp) of coronaviruses including SARS-CoV-2, inhibiting viral replication through premature termination of RNA transcription.		
4	The time to onset for serious bowel complications caused by constipation was 1 year after clozapine administration.		
5	Warts are benign proliferations of skin and mucosa caused by human papillomavirus (HPV) which is highly contagious and can spread through contacts.		

LINDUNG DIRI,
LINDUNG SEMUA.

Bersama
Hentikan
Wabak
COVID-19