PAIN MANAGEMENT

UNDERSTANDING PAIN
You know what it’s like to feel pain. Its unpleasantness can take many forms, whether it’s the smart of a burn, the daily ache of arthritis or a throbbing headache. What you might not be aware of is the science behind why you hurt. Pain involves a complex interaction between specialized nerves, your spinal cord and your brain. Always remember that the experience of pain varies from one person to another. Pain is both physical and emotional. It involves learning and memory. How you feel and react to pain depends on what’s causing it, as well as many personal factors.

TYPES OF PAIN
Pain may be classified as being either acute or chronic - and their differences are significant

ACUTE PAIN
- Comes on suddenly and often resolves quickly
- Can usually be diagnosed and treated
- Results from disease, inflammation, or injury to tissues
- Is often a symptom of a recent event, such as an injury

CHRONIC PAIN
- May last a long time, sometimes several months or longer
- May be associated with a disease
- May be more difficult to treat than acute low back pain

Table: Types of pain

PAIN EVALUATION

COMPARATIVE PAIN SCALE CHART (Pain Assessment Tool)

<table>
<thead>
<tr>
<th>Pain Free</th>
<th>Very Mild</th>
<th>Discomforting</th>
<th>Tolerable</th>
<th>Distressing</th>
<th>Very Distressing</th>
<th>Intense</th>
<th>Very Intense</th>
<th>Usuriously Horrible</th>
<th>Excruciating</th>
<th>Unbearable</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Pain</td>
<td>Minor Pain</td>
<td>Moderate Pain</td>
<td>Severe Pain</td>
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<tr>
<td>Feeling perfectly normal. Napping, annoying, but doesn’t interfere with most daily living activities. Patient able to adapt to pain psychologically and with medication or devices such as cushions.</td>
<td>Interferes significantly with daily living activities. Requires lifestyle changes but patient remains independent. Patient unable to adapt pain.</td>
<td>Disabling; unable to perform daily living activities. Unable to engage in normal activities. Patient is disabled and unable to function independently.</td>
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Three main types of pathophysiology can be considered to result in chronic pain:

1. Pain resulting from damage to sensitive or infected nerves.
2. Pain resulting from damage to nondamaged or infected nerves.
3. Pain resulting from a disorder or disease, such as diabetes, that causes nerve damage.

More than 1 type of pain may be present in a given patient.
Cannabis: A painkiller

Ganja, weed, cannabis, marijuana – or in its many other names – is illegal to be consumed or used in its raw form.

How it works as a painkiller?
Cannabis triggers a complex set of experiences in humans including euphoria, heightened sensitivity to external experience, and relaxation. The primary non-psychoactive compound of cannabis, cannabidiol (CBD), has recently been shown to possess considerable therapeutic potential for treating a wide range of disorders such as chronic pain, nausea, epilepsy psychosis and anxiety. CBD in therapeutics is used within a large therapeutic window, ranging from 2.85 to 50 mg/kg/day, meaning that its therapeutic dose is still unclear.

Benefits versus Harms
The potential benefits of cannabis-based medicine (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) in chronic neuropathic pain might be outweighed by their potential harms. The quality of evidence for pain relief outcomes reflects the exclusion of participants with a history of substance abuse and other significant comorbidities from the studies, together with their small sample sizes.

Is cannabis addictive?
Unlike the main psychoactive ingredient of cannabis, Δ9-tetrahydrocannabinol (THC), CBD lacks addictive properties and euphoric effects, thus representing an interesting pharmacological compound to be further investigated for potential therapeutic utility.

Clinical studies indicate that cannabidiol (CBD), the primary non-addictive component of cannabis that interacts with the serotonin (5-HT) 1A receptor, may possess analgesic and anxiolytic effects. However, its effects on 5-HT neuronal activity, as well as its impact in models of neuropathic pain, are unknown.

Cannabis in Malaysia
Cannabis is classified as a highly dangerous drug across the world, including Malaysia. Malaysian Association for the Study of Pain (MASP) president Dr Mary Cardosa says more clinical trials are needed to determine its use in a variety of conditions, including neuropathic pain, or pain caused by damage, injury or dysfunction of nerves. National Anti-Drugs Agency director-general Datuk Seri Zulkifli Abdullah said there was room in the Dangerous Drugs Act 1952 for the cultivation of cannabis for said purposes, with the condition that prior permission is obtained. He added that its cultivation should be strictly controlled so it is not misused for other purposes.
People become vegetarians for many reasons, including health, religious convictions, concerns about animal welfare or the use of antibiotics and hormones in livestock, or a desire to eat in a way that avoids excessive use of environmental resources. Becoming a vegetarian has become more appealing and accessible, thanks to the year-round availability of fresh produce, more vegetarian dining options, and the growing culinary influence of cultures with largely plant-based diets.

DO YOU KNOW THAT?
Vegetarians are people who don’t eat meat, poultry, or seafood. But people with many different dietary patterns call themselves vegetarians, including the following:

- **Vegans (total vegetarians):** Do not eat meat, poultry, fish, or any products derived from animals, including eggs, dairy products, and gelatin.
- **Lacto-ovo vegetarians:** Do not eat meat, poultry, or fish, but do eat eggs and dairy products.
- **Lacto vegetarians:** Eat no meat, poultry, fish, or eggs, but do consume dairy products.
- **Ovo vegetarians:** Eat no meat, poultry, fish, or dairy products, but do eat eggs.
- **Partial vegetarians:** Avoid meat but may eat fish (pesco-vegetarian, pescatarian) or poultry (pollo-vegetarian).

**Health Benefits of a Vegan Diet**

**Heart disease:**
A lower risk for cardiac events (such as a heart attack) and death from cardiac causes. Vegans, compared with omnivores, consume substantially greater quantities of fruit and vegetables. A higher consumption of fruit and vegetables, which are rich in fiber, folic acid, antioxidants, and phytochemicals, is associated with lower blood cholesterol concentrations, a lower incidence of stroke, and a lower risk of mortality from stroke and ischemic heart disease. Vegans also have a higher consumption of whole grains, soy, and nuts, all of which provide significant cardioprotective effects.

**Cancer**
Hundreds of studies suggest that eating lots of fruits and vegetables can reduce the risk of developing certain cancers, and there’s evidence that vegetarians have a lower incidence of cancer than non-vegetarians do. Fruit and vegetables are known to contain a complex mixture of phytochemicals that possess potent antioxidant and antiproliferative activity and show additive and synergistic effects. The phytochemicals interfere with several cellular processes involved in the progression of cancer. Red meat and processed meat consumption are consistently associated with an increase risk of colorectal cancer. Those in the highest quintile of red meat intake had elevated risks, ranging from 20% to 60%, of esophageal, liver, colorectal, and lung cancers than did those in the lowest quintile of red meat intake.

**Type 2 diabetes**
Research suggests that a predominantly plant-based diet can reduce the risk for type 2 diabetes. In studies of Seventh-day Adventists, vegetarians’ risk of developing diabetes was half that of non-vegetarians, even after taking BMI into account.

**Lose weight**
Many observational studies show that vegans tend to be thinner and have lower body mass indexes (BMIs) than non-vegans. In addition, several randomized controlled studies the gold standard in scientific research that vegan diets are more effective for weight loss than the diets they are compared to non-vegan diet.

References: https://academic.oup.com/ajcn/article/89/5/1627S/4596952#110695950
Outpatient Pharmacy

- T. Atenolol 100mg VS T. Amiodarone 200mg
- T. Chlorpheniramine 4mg VS T. Bromhexine 8mg
- T. Metformin XR 500mg VS T. Metformin 500mg and Glibenclamide 2.5mg
- T. Olanzapine 10mg VS C. Omeprazole 20mg

Inpatient Pharmacy

- IV Amoxicillin 1g & Clavulanate 200mg VS IV Vancomycin 500mg
- IV Metoclopramide 10mg/ml VS IV Amiodarone 150mg/3ml
**Indication**: Treatment of endometriosis

**Dosage**: one tablet daily without any break, taken preferable at the same time each day, can be taken with or without food

**Management of missed tablets**: Take one tablet only, as soon as she remembers and continue the next day at her usual time. If vomiting occurs within 3-4 hours after tablet taking, take one tablet only.

**Contraindications**: active venous thromboembolic disorder, diabetes mellitus with vascular involvement, arterial and cardiovascular disease, presence or history of liver tumors, undiagnosed vaginal bleeding, known or suspected sex hormone-dependent malignancies

Reference: Visanne Product leaflet
Lamotrigine: Risk of Hemophagocytic Lymphohistiocytosis (HLH)

Background of Safety Issue

The United States Food and Drug Administration (US FDA) warned that lamotrigine can cause a very rare but serious reaction called Hemophagocytic Lymphohistiocytosis (HLH), that excessively activates the body's infection-fighting immune system. HLH typically presents as a persistent fever and it can lead to severe problems with blood cells and affects organs such as the liver, kidneys, and lungs. The Japan Pharmaceuticals and Medical Devices Agency (PMDA) also issued out a similar alert following one reported case of HLH.

Diagnosis is often complicated because early signs and symptoms such as fever and rash are not specific. HLH may also be confused with other serious immune-related adverse reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS). The time to onset can occur within 4 weeks after initiation of lamotrigine.

Adverse Drug Reaction Reports

Since year 2000, NPRA has received 272 reports and 496 adverse events suspected to be associated with lamotrigine use. Out of these reports, no case of HLH had been reported to NPRA.

Advice for Healthcare Professionals

- Evaluate patients and consider diagnosis of HLH based on the symptoms if patients are taking lamotrigine.
- Discontinue lamotrigine if the diagnosis of HLH has been confirmed.
- Advise patients to see the doctor should any symptoms such as fever, skin rash, and neurological symptoms such as shaking and confusion develop while taking lamotrigine.

Ceftriaxone: Disturbed consciousness, convulsions or involuntary movements

Background

The National Pharmaceutical Regulatory Agency (NPRA) received information from the Pharmaceuticals and Medical Devices Agency (PMDA), Japan, on reports of disturbed consciousness, convulsions or involuntary movements associated with the use of ceftriaxone.

PMDA has published important safety information regarding revision of the precautions in the package insert of ceftriaxone products. Disturbed consciousness (such as loss of consciousness and decreased level of consciousness), convulsions or involuntary movements (such as choreoathetosis and myoclonus) may occur with ceftriaxone use. These neuropsychiatric symptoms have been reported in numerous patients with severe renal disorder.

The pathophysiological mechanisms of cephalosporin-associated neurotoxicity have yet to be fully understood. It is believed that beta-lactam associated encephalopathy is related to the competitive inhibition of y-aminobutyric acid in brain tissues. Considering that ceftriaxone penetrates efficiently into the central nervous system, it is thought that it may trigger increased neural excitability, even at normal dosages.

Adverse Drug Reaction Reports

Since year 2000, the NPRA had received a total of 1,747 reports with 3,106 adverse events suspected to be related to ceftriaxone-containing products. Of these, there were six (6) reports involving loss of consciousness and five (5) reports involving seizure/convulsions.

Advice for Healthcare Professionals:

- Patients receiving ceftriaxone, particularly those with severe renal disorder, should be carefully monitored for disturbed consciousness, convulsions, or involuntary movements.
- If any of these symptoms are observed, appropriate measures such as discontinuing administration should be taken.
**Beta-Lactam antibiotics: Severe Cutaneous Adverse Reactions (SCARs)**

**Background**

Health Canada has reviewed the potential risk of Severe Cutaneous Adverse Reactions (SCARs) with beta-lactam antibiotics after receiving information from a manufacturer that included reports of SCARs with the use of amoxicillin-clavulanic acid in Canada. Following this, Health Canada will be working with the manufacturers to update the product information of beta-lactam antibiotics with the information related to SCARs.1

**Adverse Drug Reaction Reports**

Since year 2000, the NPRA has received a total of **833 ADR reports related to SCARs** for beta-lactam antibiotics2.

**Advice for Healthcare Professionals**

1. Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams.
2. Before initiating therapy with any beta-lactam antibiotics, careful inquiry should be made regarding previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents.
3. If an allergic reaction occurs, the beta-lactam antibiotic must be discontinued immediately and appropriate alternative therapy instituted.
4. Advise patients to stop the antibiotic and seek medical assistance immediately if they experience any of the following symptoms: skin reddening, blisters, rash, fever, sore throat or eye irritation.

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**Acetazolamide: A new contraindication during pregnancy**

**Background of Safety Issue**

The National Pharmaceutical Regulatory Agency (NPRA) received information from the French National Agency for Medicines and Health Products Safety (ANSM), on the new contraindication of acetazolamide during the first trimester of pregnancy. In the 2nd and 3rd trimesters of pregnancy, its use is restricted to situations of absolute necessity (for example in the emergency treatment of glaucoma and absence of safer alternatives) and requires special monitoring.

Despite limited data, ANSM confirmed the signal of malformative effects and toxicity in the fetus since acetazolamide is a known animal teratogen, and the malformation is consistent with its mechanism of action.

**Adverse Drug Reaction Reports**

Since year 2000, the NPRA has received a total of **28 reports** with **51 adverse events** suspected to be related to acetazolamide-containing products. Among the reports, the most reported adverse reactions were hypoesthesia (3), rash (3) and rash maculo-papular (3). To date, no ADR related to teratogenicity or malformation following the use of acetazolamide has been reported to the NPRA.

**Advice for Healthcare Professionals**

a) Acetazolamide should not be used in pregnancy, especially during the first trimester. It may only be used in pregnancy if the potential benefit justifies the potential risk. Consider other available alternatives.

b) Carry out specialised prenatal follow up and assessment in the newborn in case of exposure during pregnancy (ultrasound, monitoring of amniotic fluid volume, hydro-electrolytic assessment, etc.).

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**References:**

Epilim® (Sodium Valproate): Important new restrictions on use

Description:
Children exposed in utero to valproate are at risk of serious developmental disorders (in up to 30-40% of cases) and congenital malformations (in approximately 10% of cases). Previously in 2015, the warnings and restrictions on the use of valproate medicines in women and girls were strengthened, to minimise the risk of malformations and developmental problems in babies exposed to valproate in the womb.

Recently, a Direct Healthcare Professional Communication (DHPC) letter has been issued by Sanofi-Aventis (Malaysia) Sdn. Bhd, in agreement with the NPRA to highlight new contraindications, strengthened warnings and measures to prevent valproate exposure during pregnancy.

New contraindications:
In epilepsy:
- valproate is contraindicated in pregnancy unless there is no suitable alternative treatment.
- valproate is contraindicated in women of childbearing potential, unless the conditions described in the DHPC letter are fulfilled.

In bipolar disorder:
- valproate is contraindicated in pregnancy.
- valproate is contraindicated in women of childbearing potential, unless the conditions described in the DHPC letter are fulfilled.

Patients are advised not to stop taking sodium valproate without first discussing it with their doctor.


UPDATED PRODUCT LEAFLET

<table>
<thead>
<tr>
<th>Medications</th>
<th>Warnings</th>
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<tbody>
<tr>
<td>Pemotrexed</td>
<td>- Nephrogenic diabetes insipidus (hypernatremia)</td>
</tr>
<tr>
<td></td>
<td>- Renal tubular acidosis</td>
</tr>
<tr>
<td>Products containing filgrastim, pegfilgrastim and lenograstim</td>
<td>- Aortitis</td>
</tr>
<tr>
<td>Domperidone with potent CYP3A4 inhibitor (contraindicated)</td>
<td>- QT interval prolongation</td>
</tr>
<tr>
<td>Clarithromycin and domperidone (contraindicated)</td>
<td>- QT interval prolongation</td>
</tr>
<tr>
<td></td>
<td>- Cardiac arrhythmias</td>
</tr>
</tbody>
</table>

Changes in the Shape of Medication
⇒ Levodopa 200mg, Benserazide 50mg

Reference: ROCHE (MALAYSIA) SDN BHD
CANCELLATION OF REGISTERED COMPLEMENTARY AND ALTERNATIVE PRODUCT

- Zn Seven
- Minyak Gamat Plus
- Minyak Anjib, Cécair, 60 Ml
- Bam Resdong
- Petani Plus
- Products the contain Methyl Salicylate
- Products the contain Sildenafil
- Nan Bao (Capsule)
- Balm Umm

CANCELLATION OF NOTIFIED COSMETICS PRODUCTS

- Tati Ultra Night Cream
- Deeja Wrinkle Cream
- Asdanne Whitening Freckle Day Cream
- Fulenze- Whitening Freckle Day Cream
- Robisis-Anti-Acne Whitening Day &
- Tati Ultra Treatment
- Deeja Dream Cream

*Updated on 28th Feb 2019, extracted from NPRA website*
On 28th February 2019, pharmacy department conducted Quality Use of Medicines-consumer (QUMC) programme at Sekolah Kebangsaan Kulim, Kedah. 188 students and 34 teachers took part in the programme. The objectives of this program are to:

- Increase awareness on a proper use of medication
- Outline the differences between dosage forms and types of medication that are available in Hospital Kulim
- Educate on the right way of medication storage
- Educate students and teachers on how to practice 5R in handling their medication.

Pharmacist, Mdm Najihah bt Abdul Razak delivered a talk on “Know Your Medication” to students, followed by quiz session.

Later on, a talk on “Antibiotics Awareness” was delivered by Pharmacist Miss Fatin ‘Ainaa bt Mohamed Anwar. There was also exhibition on medicines and medication-related devices that attracted attention from students and teachers.

In conjunction with Chinese New Year 2019, a celebration was held in Pharmacy Department of Hospital Kulim on 19th February. The event was officiated by our beloved Chief Pharmacist Madam Haniza. We also celebrated birthday for our colleagues whose birthday falls on January, February or March. It was a wonderful afternoon filled with laughter and food with excellent colleagues.

Group photos with pharmacists and teachers from SK Kulim.
JOKES OF THE DAY

MR. DIFINI, HAVE YOU SEEN YOUR CATHETER? I LEFT IT RIGHT HERE BY THIS JUICE POUCH.

“I have solved your medical mystery, but unfortunately I am not able to decrypt my own handwriting..."

“I’m glad that you’re eating more fresh fruit and vegetables, but be careful to chew more thoroughly.”

“Well, it looks like you’ve picked up a rhinovirus!”