KEMENTERIAN KESIHATAN MALAYSIA
HOSPITAL BEAUFORT

PHARMACY BULLETIN

IN THIS ISSUE

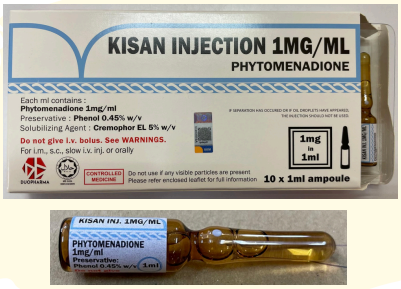
EDITORIAL TEAM

PHYTOMENADIONE (VITAMIN K) INJECTION

Differences & Administration Method

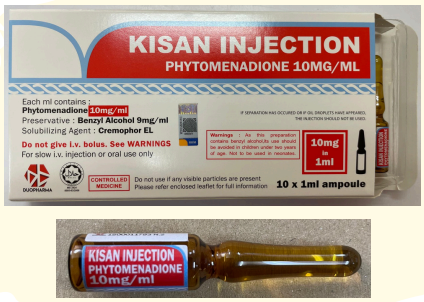
By Farkhanah Rahmi

Phytonadione or vitamin K1, is a water-insoluble vitamin that is indicated for the treatment of various coagulation disorders due to a lack of or a decrease in factors II, VII, IX & X. The interplay of these factors in the coagulation leads to the formation of thrombin and then fibrin that is responsible for clot stabilization. There are two strengths of vitamin K in the hospital.



Phytomenadione 1mg/ml Injection

Phytomenadione 10mg/ml Injection



Brand Name & Strength	Kisan 10mg/ml Injection	Kisan 1mg/ml Injection
Reconstitution	Not required	Not required
Dilution	IV infusion • Dilute 0 – 20 mg in 50ml diluent [4] Dilute 21 – 50mg in 100ml diluent [4]	Not required
Compatible Diluent	• Normal saline 0.9% [3,4] • Dextrose 5% [3,4] • Dextrose 5% in Normal saline 0.9% [3,4]	Same with diluent used for Kisan 10mg/ml (only when dilution is indicated) [5]
Administration	• Oral [2,3] • IM, SC [2,3] • Slow IV [2,3] • IV infusion [4]	• Oral [3,5] • IM, SC [3,5] • Slow IV [3,5]
Storage & Stability	• Administer immediately after dilution [2] • Photosensitive; protect from light [2]	• Photosensitive; protect from light [5]
Remarks	• Should be avoided in children under two years of age [2] • Not to be used in neonates [2]	• Should be used for neonates [5]

Recommended Administration for Phytomenadione (Vitamin K) 10mg/ml Injection

ORALLY

- Use an insulin syringe with a filter needle to draw up 1mg of vitamin K [3]
- Dilute with Water for Injection and drink immediately
- Unpleasant after taste can be avoided by drinking sufficient fluid after the dose [2,4,5]

IV Infusion / Slow IV

- Administer 0 - 20mg over 30 minutes [4]
- Administer 21 - 50mg over 60 minutes [4]
- For Slow IV, administer not exceeding 1mg/minute [2,3]
- IV injection must be reserved for potentially fatal haemorrhage & situations where other routes not feasible [2]

Subcutaneous / Intramuscular

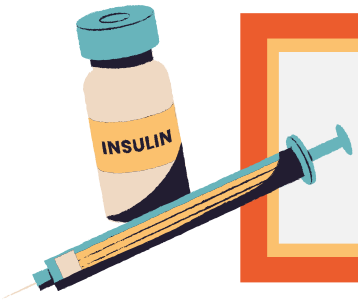
- Administer undiluted [2,3]
- Subcutaneous injection is the preferred parenteral route [2,3]
- Intramuscular injection should be avoided due to the risk of hematoma formation [2,3]

Severe reactions, including fatalities, have occurred during and immediately after INTRAVENOUS & INTRAMUSCULAR injection of Vitamin K. A reminder on proper method of administration for Vitamin K injections; must be infused by VERY SLOW INTRAVENOUS INJECTION and NOT BY BOLUS, at a rate not exceeding 1ml/minute.

Phytomenadione 1mg/ml Injection & Phytomenadione 10mg/ml Injection are Look Alike Sound Alike (LASA) Medications!!

References:

1. Kalus JS. Pharmacologic interventions for reversing the effects of oral anticoagulants. AM J Health Syst Pharm.2013;70(10)(suppl 1)
2. Product Leaflet [Kisan 10mg/ml: Duopharma (M) Sdn.Bhd
3. McGraw-Hill's IV Drug Handbook. (2009
4. GlobalRPH. Phytonadione (Vitamin K): Intravenous Dilution Database [Internet]
5. Product Leaflet [Kisan 1mg/ml: Duopharma (M) Sdn.Bhd



PROPER INSULIN NEEDLES DISPOSAL

by Cassandra Eva Charles

Healthcare workers who are exposed to used needles are at increased risk of needle stick injury and potential serious infections with blood borne pathogens such as hepatitis B virus, hepatitis C virus, or HIV.

A lot of patients don't know proper sharps disposal. Some of them flush their needles down the toilet or bury them, both of which are dangerous.

Disposal of the Sharps

Patients are encouraged to dispose used needles using these methods to prevent needle stick injuries:

1 **Dispose at the Healthcare Center**

Patients can take their own sharps containers filled with used needles to appropriate collections sites: hospitals, health clinics or pharmacies for proper disposal. All the sharps MUST be disposed properly in yellow sharp bins in hospitals and health clinics

2 **Self-disposal**

Put used needles/cartridges/lancets directly into a thick plastic or metal container with a tight cap or lid.

Label (Sharp or *Jarum*) on the containers.

Keep the container out of reach of small children and pets.

When the container is full, tightly secure the lid and reinforce it with heavy-duty tape before throwing it in the trash. Be sure not to put it in the recycling bin.

TYPES OF CONTAINERS TO USE

Patients can use containers that is:

- Made of thick plastic, so needles can't poke through.
- Have a small opening on top with a puncture-resistant lid that screws on tightly to prevent spills.
- Upright and stable during use
- Examples: plastic bleach bottle, plastic liquid detergent bottle.

Do not use containers that can break or puncture easily such as:

- Glass containers
- Light-weight plastic containers e.g. mineral water bottles
- Plastic bags

References:

1. Handle With Care: How To Throw Out Used Insulin Syringes and Lancets At Home. Retrieved October 23, 2023, from https://www.prescott-az.gov/wp-content/uploads/2016/03/disposal_safety_tips.pdf
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3. Kimberly. (2017). Discarding Sharps. Easy ways to trash your needles, lancets, and other sharps safely. diabetesforecast.org J. Retrieved April 15, 2024, from https://diabetes.org/sites/default/files/2023-10/ddrc-discarding-sharps-2018.pdf

SODIUM VALPROATE IN WOMEN OF CHILDBEARING POTENTIAL

by Noor Nabilah Binti Shamsudin

USE OF SODIUM VALPROATE IN PREGNANCY

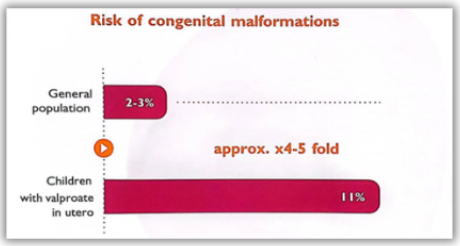
FDA

PREGNANCY CATEGORY D

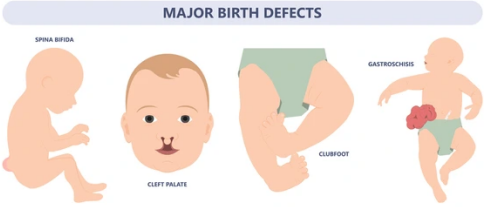
FDA has issued a reminder to healthcare professionals that valproate use during pregnancy is harmful for the unborn child. Both valproate monotherapy and valproate polytherapy including other antiepileptics are frequently associated with abnormal pregnancy outcomes. Children exposed in utero to valproate have a higher risk for congenital malformations and neurodevelopmental disorders. The risks are dose-related.

The higher the dose, the higher the risk, however all doses carry a risk

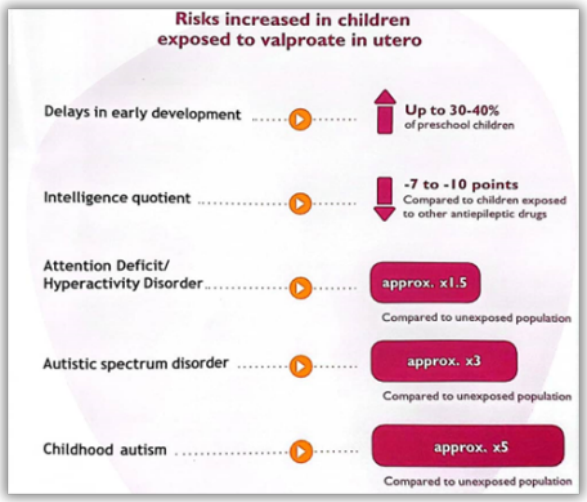
1. CONGENITAL MALFORMATIONS



Data derived from two meta-analysis including registries[1] and cohort studies[2] have shown that about 11% of children of epileptic women exposed to valproate monotherapy during pregnancy had major congenital malformations than for the general population, for whom the risk is equal to about 2-3%. The risk is greatest at higher doses (above 1g daily). Available evidence[3] does not show that folate supplementation prevents birth defects due to valproate exposure.



2. NEURODEVELEPMENTAL DISORDERS



Studies in preschool children show that up to 30-40% of children with a history of valproate exposure in utero experience delays in their early development such as talking and walking later, lower intellectual abilities, poor language skills (speaking and understanding) and memory problems. Besides, intelligent quotient (IQ) measured in school aged children (age 6 years old) with a history of valproate exposure in utero was on average 7-10 points lower than children exposed to other antiepileptic drugs. Available data from a population-based study show that children with a history of valproate exposure in utero are at increased risk on autistic spectrum disorder (approximately 3-fold) and childhood autism (approximate 5-fold) compared to the unexposed population in the study. Available data from another population-based study show that children with a history of valproate exposure in utero are at increasing risk of developing symptoms of attention deficit/hyperactivity disorder (ADHD) approximately 1.5 fold compared to the unexposed population in study.

ROLE OF HEALTHCARE PROVIDERS

SPECIALIST

1. Diagnosis
2. Treatment initiation ONLY IF other treatments are ineffective or not tolerated and negative pregnancy test.
3. Explain the risks of congenital malformations and neurodevelopmental disorders when using valproate during pregnancy and ensure patient understanding.
4. Provide counselling on effective contraception and pregnancy prevention-mandatory use of effective contraception (preferably an intra-uterine device, or implant, or 2 complementary forms including a barrier method)

- Even if patient has amenorrhea
- Without interruption during the entire valproate treatment duration
- Regardless of sexual activity status.

5. Annual treatment review, and ad-hoc treatment review as required.
6. Discontinuation if necessary or switching to alternative treatment prior to conception if planning to pregnant-contraception should only be stopped after complete valproate cessation and valproate should be discontinued gradually over few weeks with close monitoring to reduce early recurrence and a fast cross tapering of alternative while discontinuing valproate is recommended.
7. In case of exposed pregnancy, refer patient to gynecologist/obstetrician for appropriate pregnancy monitoring (including prenatal monitoring to detect the possible occurrence of neural tube defects and other malformations) and counselling regarding exposed pregnancy.

GENERAL PRACTITIONER

1. Refer patient to the relevant specialist to confirm diagnosis of epilepsy or bipolar disorder and to initiate treatment ONLY IF other treatments are ineffective or not tolerated and negative pregnancy test.
2. Ensure appropriate treatment continuation.
3. Remind the patient of the annual visit to the specialist.
4. Provide full information about the risks of using valproate during pregnancy and ensure patient understanding.
5. Provide counselling on effective contraception and pregnancy prevention.
6. Refer the patient to their specialist when a patient consults for pregnancy.
7. Refer patient to their specialist for switching and discontinuation or if their condition worsens.

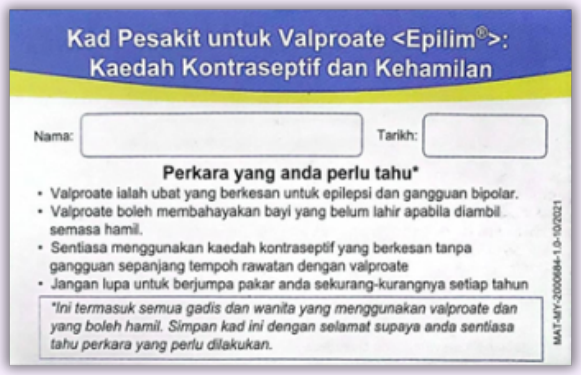
MIDWIFE / NURSE

1. Provide counselling on effective contraception and pregnancy prevention counselling.
2. Provide full information about the risks of using valproate during pregnancy and ensure patient understanding.
3. Refer the patient to their specialist when a patient consults for pregnancy.

PHARMACIST

1. Ensure that the patient card is provided every time valproate is dispensed and that the patient understands its content.
2. Remind the patient of the safety messages including the need of effective contraception.
3. Advise the patient not to stop valproate medication and to urgently contact their doctor when planning or in the case of suspected pregnancy.
4. Dispense valproate in the original package with an outer warning. Unpacking should be avoided. In the situations where this cannot be avoided, always provide a copy of the package leaflet, patient card and the outer box if available.

Kad Pesakit Valproate



Kad Pesakit untuk Valproate <Epilim®>:
Kaedah Kontraseptif dan Kehamilan

Nama: Tarikh:

Perkara yang anda perlu tahu*

- Valproate ialah ubat yang berkesan untuk epilepsi dan gangguan bipolar.
- Valproate boleh membahayakan bayi yang belum lahir apabila diambil semasa hamil.
- Sentiasa menggunakan kaedah kontraseptif yang berkesan tanpa gangguan sepanjang tempoh rawatan dengan valproate
- Jangan lupa untuk berjumpa pakar anda sekurang-kurangnya setiap tahun

Ini termasuk semua gadis dan wanita yang menggunakan valproate dan yang boleh hamil. Simpan kad ini dengan selamat supaya anda sentiasa tahu perkara yang perlu dilakukan.

MAT-MY-2000684-1.0-102021

As a Patient, What Should You Do?

1. If you are taking valproate and are able to become pregnant:
- Always use effective contraception (birth control).
- Do not stop using the contraception at any time.

2. If you are taking valproate thinking about having a baby :
- Speak first to your doctor before stopping your contraception.
- Never stop taking valproate unless your doctor tells you because your condition may become worse.

3. If you are taking valproate and have become pregnant :
- Do not stop taking valproate because your epilepsy or bipolar disorder may become worse.
- Talk promptly to your doctor about your options and what you need to know. Your doctor will explain if you need to switch to another treatment and how.

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1. Meador K, Reynolds MW, Creans S, Fahrbach K, Probst C. Pregnancy outcomes in women with epilepsy: a systematic review and meta analysis of published pregnancy registries and cohorts. Epilepsy Res. 2008; 81(1): 1-13.
2. Weston J, Bromley R, Jackson CF, Adab N, Clayton-Smith J, Greenhalgh J, Hounsome J, McKay AJ, Tudur Smith C, Marson AG. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD010224
3. Jentink J, Bakker MK, Nijenhuis CM, Willfert B, de Jong-Van den Berg LT. Does folic acid use decrease the risk of spina bifida after in utero exposure to valproic acid? Pharmacoepidemiol Drug Saf. 2010 Aug;19(8):803-7.
4. Bromley RL, Mawer G, Love J, Kelly J, Purdy L, McEwan L et al. Early cognitive development in children born to women with epilepsy: a prospective report. Epilepsia 2010 October; 51(10):2058-65.
5. Cummings et al. Neurodevelopment of children exposed in utero to lamotrigine, sodium valproate and carbamazepine. Arch Dis Child 2011;96: 643-647
6. Meador K et al. Cognitive function at 3 years of age after fetal exposure to antiepileptic drugs. NEJM 2009; 360(16): 1597-1605
7. Thomas S.V et al. Motor and mental development of infants exposed to antiepileptic drugs in utero. Epilepsy and Behaviour 2008 (13):229-236
8. Meador KJ, Baker GA, Browning N, Cohen MJ, Bromley Rl, Clayton-Smith J, Kalayjian LA, Kanner A, Liporace JD, Pennell PB, Privitera M, Loring DW; NEAD Study Group. Fetal antiepileptic drug exposure and cognitive outcome at age 6 years (NEAD study); a prospective observational study. Lancet Neurol. 2013; 12(3):244-52
9. Christensen J et al. Prenatal Valproate Exposure and Risk of Autism Spectrum Disorders and Childhood Autism. JAMA 2013; 309(16):1696-1703
Christensen J, Pederson L, Sun Y, Dreier JW, Brikell I, Dalsgaard S. Association of prenatal exposure to valproate and other antiepileptic drugs with risk for attention deficit/hyperactivity disorder in offspring. JAMA New Open. 2019:2(1) e186606

NPRA SAFETY UPDATES

For healthcare professionals

PARACETAMOL : Reports of Fixed Drug Eruptions

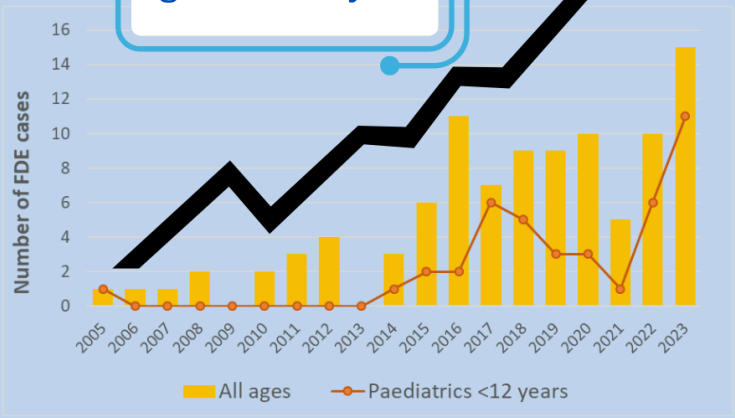
Paracetamol is **very rarely** associated with **fixed drug eruptions** (FDEs).

99
total reports in Malaysia*

41%
in children aged below 12 years

WHAT'S NEW?

Increasing trend particularly involving children aged below 12 years



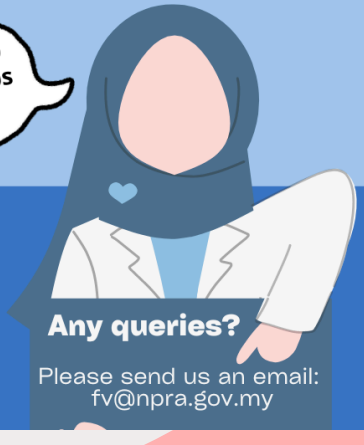
*** From Jan 2005 - Mar 2024**

PLEASE REMIND PATIENTS (OR THEIR CAREGIVERS) :

✔ to watch out for these early signs and symptoms of FDE: skin reddening, blisters, rash.

✔ to STOP using the medicine immediately and seek medical attention if these signs and symptoms occur.

Your reports will help the NPRA to take steps to reduce the risk.



REPORT

Where to report?

scan here to download the ADR form

Please report **any adverse events** to the **NPRA**.

Any queries?
Please send us an email:
fv@npra.gov.my

National Pharmaceutical Regulatory Agency
Ministry of Health, Malaysia

FOR PATIENTS' REFERENCE

WHEN GIVING

PARACETAMOL

commonly used medicine for reducing fever and pain

LIKE ALL MEDICINES, PARACETAMOL CAN CAUSE SIDE EFFECTS

Very rarely, it may cause severe skin reactions, including in children

STAY ALERT

Watch out for these early signs and symptoms

skin reddening

blisters

rash

eye irritation

WHAT TO DO?

If any of these signs and symptoms occur, STOP using the medicine immediately and seek medical attention right away.

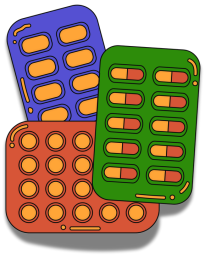
WHERE TO REPORT?

Please **report ANY side effects** experienced.
You may report :

- through your pharmacist or doctor, **OR**
- directly to NPRA by **post or email** at fv@npra.gov.my. Scan the QR code to download the reporting form.

National Pharmaceutical Regulatory Agency
Ministry of Health, Malaysia

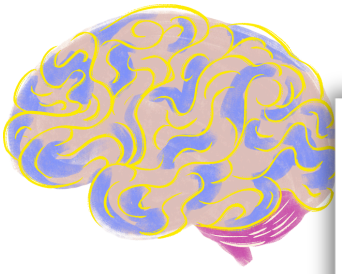
NPRA SAFETY ALERTS

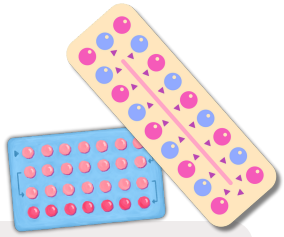


1. Hydroxychloroquine (HCQ) is commonly used to treat various rheumatic diseases. In Malaysia, HCQ has been approved by the Drug Control Authority (DCA) for conditions such as rheumatoid arthritis, juvenile chronic arthritis, discoid and systemic lupus erythematosus (SLE), & dermatological conditions caused or aggravated by sunlight.
2. European Medicines Agency (EMA) & the Japan Pharmaceuticals and Medical Devices Agency (PMDA) had requested updates to the hydroxychloroquine (HCQ) product information to include the risk of acute febrile neutrophilic dermatosis (Sweet's syndrome).
3. Sweet's syndrome; acute febrile neutrophilic dermatosis, manifests as fever & erythematous papules, plaques, or nodules. Histopathologic examination typically reveals a dense neutrophilic dermal infiltrate without evidence of vasculitis. Sweet syndrome can be divided into 3 subtypes: classic, malignancy-associated, and drug-induced.
4. NPRA has received 242 reports documenting 446 adverse events suspected to be linked to HCQ. Among these, the most commonly reported adverse events include electrocardiogram QT prolonged (29 reports), pruritus (29), rash (28), and rash maculo-papular (15). Notably, no local cases of Sweet's syndrome have been reported as being associated with the administration of HCQ products.
5. Advice for healthcare professionals:

- Be aware of the potential risk of Sweet's syndrome associated with HCQ use.
- Advise patients to monitor for any skin reactions, such as plum-coloured, raised, & painful sores, especially on the arms, hands, fingers, face, and neck, accompanied by fever, following treatment with HCQ. Remind them to seek immediate medical attention if these symptoms occur.
- If signs and symptoms suggestive of Sweet's syndrome develop, refer the patient to a dermatologist for diagnosis confirmation and further management. In cases where HCQ is the suspected culprit, immediately discontinue HCQ, and consider an alternative therapy.
- Report all suspected adverse events associated with HCQ-containing products to the NPRA.

NPRA SAFETY ALERTS





1. **Progestogens, also known as gestagens, can be either natural or synthetic (referred to as progestins) compounds that bind to progesterone receptors and mimic effects of progesterone.**
2. **They are used to treat various gynaecological conditions, such as endometriosis, fibroids, prolonged or heavy periods, and menstrual cycle disorders. Additionally, they are applied in hormone replacement therapy, including menopausal hormone therapy, as well as in obstetrics for conditions like luteal insufficiency-related sterility and recurrent abortions.**
3. **Meningiomas are typically slow-growing, non-cancerous tumours that can still exert pressure on nearby brain tissue, potentially necessitating surgical interventions.**
4. **There are no local cases of meningioma have been received among the submitted reports up until 26/08/2024.**
5. **Advice for healthcare professionals:**

- **While the NPRA is still reviewing this status issue, be aware of the potential risk of meningioma when initiating any progestogens:**
- **Cyproterone acetate and chlormadinone are known risk factors for meningioma, particularly with cumulative high doses.**
- **A recent French epidemiological study identified an excess risk of meningioma with prolonged use (≥ 1 year) of medroxyprogesterone acetate (injectable).**
- **Be attentive to any previous progestogen use when prescribing new progestogens. Avoid using progestogens with reported risks of meningioma in patients with a history of meningioma or existing meningioma.**
- **In exceptional cases, progestin treatment may be considered after a thorough evaluation in a multidisciplinary consultation, weighing the individual benefit-risk ratio and the availability of alternatives.**
- **Always prescribe progestogen at the minimum effective dose and for the shortest duration necessary.**
- **Educate patients to contact their doctor immediately if they experience a change in vision (seeing double or blurriness), hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures, or weakness in their arms or legs.**
- **Vigilantly monitor high-risk patients for signs and symptoms of meningiomas in line with clinical practice. Consider a brain Magnetic Resonance Imaging (MRI) if meningioma is suspected.**
- **If a meningioma is diagnosed, consider discontinuing treatment with these progestogens permanently.**
- **Report all suspected adverse events associated with progestogens-containing products to the NPRA.**