PHARMACY BULLETIN

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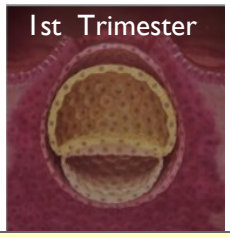
NITROFURANTOIN SAFETY UPDATES IN PREGNANCY .

Nitrofurantoin has been used for over half a century in the treatment of urinary tract infections. Asymptomatic bacteriuria commonly occurs during pregnancy and nitrofurantoin has been recommended as first line as *E.coli* is the most common pathogen. In 2009, Crider and colleagues published a population-based case–control study which showed a potential association between Nitrofurantoin exposure and adverse fetal effects. However the study had significant limitations which led to more recent studies. Here we highlight the current updates of Nitrofurantoin safety data in pregnancy.

REFERENCE			
ACOG Committee Opinion 717 (reaffirmed 2019) (American College of O&G)	Can be used if no other alternatives are available. Discuss risk/benefits and fetal/ maternal adverse reactions	May continue to be used as **1st line agent** for the treatment and prevention of UTI. Contraindicated in patients with G6PD deficiency as it can result haemolytic anaemia.	
Nordeng et al. Neonatal outcomes after gestational exposure to nitrofurantoin. Obstet Gynecol. 2013 (Norwegian Medical Birth Registry + Prescription Database)	The authors found no association between 1st trimester dispensing of nitrofurantoin and risk of major malfunctions.	Dispensing nitrofurantoin the **last 30 days** before delivery was associated with **increased risk of neonatal jaundice** (103 of 959 [10.8%]) compared with unexposed women (10,336 of 127,507 [8.1%], OR 1.31, 95% CI 1.02-1.70). No increased risk of hemolytic anemia was found compared with unexposed women in the control group	
Goldberg et al. Exposure to nitrofurantoin during early pregnancy and congenital malformations: a systematic review and meta-analysis. Journal of Obstetrics and Gynaecology Canada. 2015	Five cohort studies [9,275 exposed vs 1,491,933 unexposed infants] RR of 1.01 (95% CI 0.81 to 1.26); 3 case–control studies (39, 268 cases of major malformations and 129,394 controls) OR of 1.22 (95% CI 1.02 to 1.45). Teratogenicity risk for use during the first trimester cannot be ruled out.	This study only focused on Nitrofurantoin exposure during 1st trimester	
British National Formulary Edition 79. 2020	Nitrofurantoin as the first-choice antibiotic.	Nitrofurantoin is not recommended at term (38-42 weeks) in pregnancy because it may produce neonatal haemolysis. (if child has G6PD)	
UK NICE Guideline	First choice for lower UTI and asymptomatic bacteriuria. .	Avoid at term	

SUMMARY	1st TRIMESTER	2ND TRIMESTER	3RD TRIMESTER
NITROFURANTOIN	Use only if no alternatives	SAFE	SAFE. ACOG recommends as 1st line. But, caution near term.

UPDATES IN NAC USE : NAC **NOT** for CIN

Prevention of Serious Adverse Events Following Angiography

Take Home Points:

- Oral n-Acetylcysteine (NAC) is NOT superior to simple IV hydration for the prevention of Contrast-Induced Nephropathy (CIN)
- Latest edition of *Protokol Contrast Induced Nephropathy (CIN)* by Radiology , Medical (Nephro) and Pharmacy Department (disseminated via PROHUKM 11.9.2020) quotes PRESERVE trial- **no additional benefit of NAC in CIN**.

All Oral NAC will be sold in NF Pharmacy.

No more free supply for CIN procedures.

NAC 100mg sachet
RM 27/30's

NAC 600mg effervescent
RM 38/10's

RECALLED METFORMIN DUE TO NDMA

⇒ WHAT PRODUCTS HAVE BEEN RECALLED BY US FDA?

USFDA have detected NDMA levels above the acceptable intake limit in some extended release metformin: Metformin Hydrochloride Extended-Release Tablets USP 500mg and Metformin Hydrochloride Extended-Release Tablets USP 750mg. (immediate release metformin not affected)

⇒ ARE METFORMIN IN MALAYSIA AFFECTED ?

As of 15th Oct press statement, 68 registered Metformin in the market have undergone testing. It was found NOT to contain NDMA and therefore do not exceed the impurity limit.

⇒ What is NDMA ?

Common sources of Nitrosamines are from water and foods like cured and grilled meats, dairy products and vegetables. Exposure is common. FDA has set daily acceptable intake limits for nitrosamines and recommends regular testing of drugs for impurities. Recalls will be warranted if exceeded daily acceptable intake limits.

⇒ GENERALLY HOW IS IT FORMED?

FDA found that it could be due to drug's manufacturing process or its chemical structure or even the conditions in which they are stored or packaged. For now, the agency believes that it is not found in the metformin active pharmaceutical ingredient but could be due to other processes.

⇒ WHAT IS THE LONG TERM EFFECT OF NDMA?

If exposed above acceptable levels over long periods of time, it may increase risk of cancer. A person taking a drug that contains nitrosamines at-or-below the acceptable daily intake limits every day for 70 years is not expected to have an increased risk of cancer.

Preparations in HCTM are NOT affected.

REFERENCE :

1) FDA.GOV/DRUGS/DRUG-SAFETY-AND-AVAILABILITY/QUESTIONS-AND-ANSWERS-NDMA-IMPURITIES-METFORMIN-PRODUCTS

2) THESUNDAILY.MY/LOCAL/RECALLED-METFORMIN-PRODUCTS-NOT-REGISTERED-IN-MALAYSIA-GX4617239

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