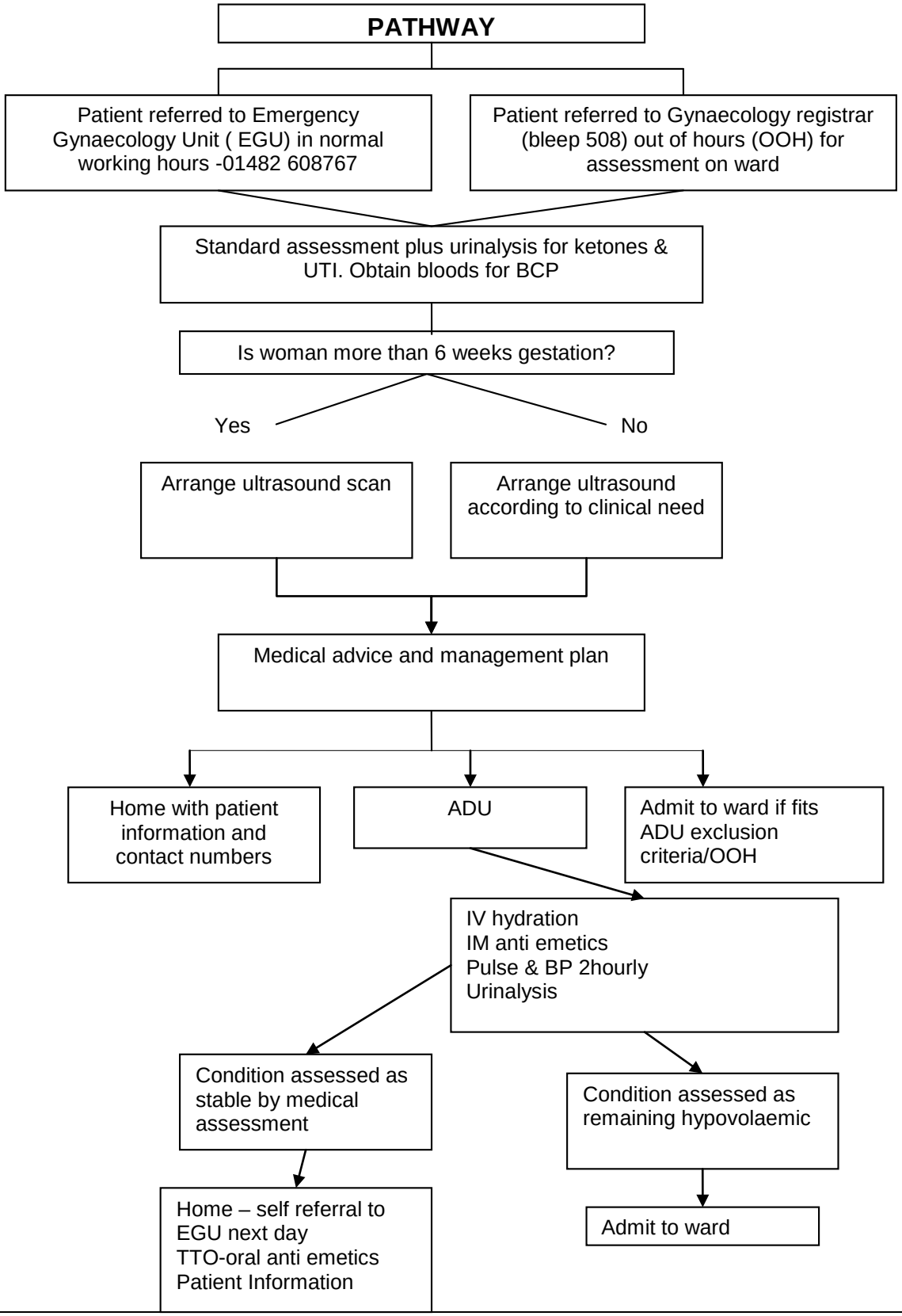
Hull University Teaching Hospitals NHS Trust

248 - Management Of Severe Nausea And Vomiting And Hyperemesis Gravidarum In Pregnancy Guideline

Broad Recommendations / Summary

The objective of this guideline is to facilitate appropriate assessment and outpatient /inpatient management of women with severe nausea and vomiting (hyperemesis gravidarum) on the Emergency Gynaecology Unit (EGU), Antenatal Day Unit (ADU) and inpatient wards



248 MANAGEMENT OF SEVERE NAUSEA AND VOMITING ANDHYPEREMESIS GRAVIDARUM IN PREGNANCY

1 PURPOSE / LEGAL REQUIREMENTS / BACKGROUND

The aim of this guideline is to provide best clinical practice information regarding the diagnosis and subsequent management of nausea and vomiting of pregnancy (NVP) and hyperemesis gravidarum HG for the Emergency Gynaecology Unit (EGU), Antenatal Day Unit (ADU) and inpatient wards.

It gives advice for multidisciplinary professionals involved in the care of women with these conditions, including how to counsel and support women before, during and after their pregnancies.

2 GUIDELINE DETAILS

Nausea and vomiting in Pregnancy (NVP) should only be diagnosed when onset is in the first trimester of pregnancy and other causes of nausea and vomiting have been excluded.

HG can be diagnosed when there is protracted NVP with the triad of more than 5% prepregnancy weight loss, dehydration and electrolyte imbalance

An objective and validated index of nausea and vomiting such as the Pregnancy-Unique Quantification of Emesis (PUQE) score can be used to classify the severity of NVP. (Appendix 1)

How should the woman be managed?

1.Women with mild NVP should be managed in the community with antiemetics.

2. Ambulatory daycare management should be used for suitable patients when community/primary care measures have failed and where the PUQE score is less than 13.

3.Inpatient management should be considered if there is at least one of the following:
-continued nausea and vomiting and inability to keep down oral antiemetics
-continued nausea and vomiting associated with ketonuria and/or weight loss (greater than 5% of body weight), despite oral antiemetics
-confirmed or suspected comorbidity (such as urinary tract infection and inability to tolerate oral antibiotics).

NVP affects up to 80% of pregnant women and is one of the most common indications for hospital admission among pregnant women. HG is the severe form of NVP, which affects about 0.3–3.6% of pregnant women.

Symptoms include:-

- Prolonged and severe nausea and vomiting
- Dehydration
- Ketosis
- Hypotension
- Increased risk of Deep Vein Thrombosis (DVT) (NHS Choices 2012)

Re-hydration is the first line treatment for hyperemesis gravidarum

On preliminary diagnosis of hyperemesis gravidarum in primary care;-
GP, ED or Midwife to refer woman to Emergency Gynaecology Unit (EGU) / Gynaecology service

Community management patients with nausea and vomiting

Community management of patients should be encouraged in patients with nausea and vomiting with mild ketonuria (1-2 +), they would benefit with a trial of oral antiemetic's.

OUTPATIENT MANAGEMENT

Inclusion Criteria for outpatient management

Inability to maintain adequate hydration/history of vomiting > 5 times a day
Moderate ketonuria (3 - 4 +)
Patient who continue to have Nausea and Vomiting despite oral antiemetics or are unable to tolerate oral antiemetics commenced by their GP.
Clinical signs of dehydration

Exclusion Criteria for outpatient management

- Medical co morbidity i.e. diabetes, thyrotoxicosis, cardiac disease, epilepsy,
- Molar pregnancy
- Urinary tract infection
- Patient requiring potassium chloride replacement

Outpatient Management

Initial Assessment/treatment

Baseline observations to be taken and recorded by nursing staff

Patient's history, examination and investigations results are recorded on emergency care pathway.

History

- Previous history of NVP/HG
- Quantify severity using PUQE score: nausea, vomiting, hypersalivation, spitting, loss of weight, inability to tolerate food and fluids, effect on quality of life
- History to exclude other causes:
  - – abdominal pain
  - – urinary symptoms
  - – infection
  - – drug history
  - – chronic *Helicobacter pylori* infection

Examination

- Temperature
- Pulse
- Blood pressure
- Oxygen saturations
- Respiratory rate
- Abdominal examination
- Weight
- Signs of dehydration
- Signs of muscle wasting
- Other examination as guided by history

Investigation

- Urine dipstick: quantify ketonuria as 1+ ketones or more
- MSU
- Urea and electrolytes:
  - -hypokalaemia/hyperkalaemia
  - -hyponatraemia
  - -Dehydration
  - -renal disease
- Full blood count:
  - -infection
  - -anaemia
  - -haematocrit
- Blood glucose monitoring:
  - exclude diabetic ketoacidosis if diabetic
- Ultrasound scan:
  - -confirm viable intrauterine pregnancy
  - -exclude multiple pregnancy and trophoblastic disease
- G&S only if bleeding

Management

IV access and treatment to be prescribed on EGU
Transfer to ADU with handover of care from nursing staff to midwives
Assess pulse & BP 2 hourly, document on standard observation chart
Infusion of 1 litre of 0.9% sodium chloride over 2 hours followed by 1 litre of 0.9% sodium chloride over 2-4 hours, prescribed on IV chart.
Promethazine hydrochloride 25mg IM QDS

Discharge Criteria

Re-check ketones after 2 L of IV fluid replacement. If 2+ or less and reasonably well clinically with no tachycardiac >100 or temp >37.5 could be discharged.
Prescribe Promethazine 25mg BD or alternative if this already had and not worked
Ensure direct line for EGU given
Provide a discharge letter for the woman with contact numbers
Provide patient information on management of nausea and vomiting

Exclusion Criteria for Discharge

Remains hypovolaemic (pulse > 100, systolic BP < 80mmHg) following 2 litres of fluid
Pyrexia over 37.5
BCP result outside normal range;-

Sodium	135 -145
Potassium	3.5- 5.5
Creatinine	51-107

<u>Complementary therapies</u>

Ginger

Ginger may be used by women wishing to avoid antiemetic therapies in mild to moderate Nausea and Vomiting in Pregnancy(NVP)

Acustimulations – acupressure and acupuncture

Women may be reassured that acustimulations are safe in pregnancy. Acupressure may improve NVP.

Hypnosis
Hypnotic therapies should not be recommended to manage NVP and HG.

INPATIENT MANAGEMENT

If patient does not fit inclusion criteria for outpatient management or patient failing to respond to outpatient management then patient should be admitted for inpatient management.

Women require treatment in a psychologically supportive environment by appropriate staff.

Differential diagnosis to be considered

Hyperemesis is a diagnosis of exclusion. Onset is always in the first trimester and other causes of vomiting should be excluded. These include:

Infection	UTI, hepatitis
Drug induced	Iron supplementation, antibiotics, opiates
Metabolic	Thyrotoxicosis, hyperparathyroidism/hypercalcaemia, diabetic ketoacidosis, uraemia, Addison disease
Gastrointestinal	Gastroenteritis, reflux oesophagitis, appendicitis, cholecystitis, small bowel obstruction, pancreatitis

Complications

Mallory-Weiss tears of the oesophagus and haematemesis

Weight loss, muscle wasting and weakness

Inadequate nutrition leading to thiamine (vitamin B1) deficiency with risk of Wernicke's encephalopathy

The symptoms of Wernicke's encephalopathy include diplopia, abnormal ocular movements, ataxia and confusion. It can be precipitated in states of thiamine deficiency by IV dextrose so is avoided particularly in the first 24-48hrs of treatment.

Wernicke's encephalopathy is associated with 40% fetal loss.

Hyponatraemia

Plasma sodium of <125 mmol/l can cause lethargy, seizures and respiratory arrest. Rapid reversal and severe hyponatraemia itself can cause central pontine myelinolysis.

Venous thromboembolism due to the combination of pregnancy, dehydration and immobility.

Other vitamin deficiencies include B12 and B6 which can cause anaemia and peripheral neuropathy.

Abnormal biochemistry and recurrent severe hyperemesis is associated with lower birth rates and IUGR.

In refractory cases or history of previous admissions, check:
– TFTs: hypothyroid/hyperthyroid
– LFTs: exclude other liver disease such as hepatitis or gallstones, monitor malnutrition
– calcium and phosphate
– amylase: exclude pancreatitis
– ABG: exclude metabolic disturbances to monitor severity

Temporarily discontinue any drugs that may cause nausea and vomiting e.g. iron supplements

1 Litre 0.9% sodium chloride with 20 mmol KCl or Compound Sodium Lactate solution (Hartmann's solution) over 2-4 hours. If Na is <125 seek consultant advice.

IV fluids may cause osmotic demyelination syndrome, never use double strength saline. Fluid replacement with glucose should be avoided particularly in the first 24-48 hours to avoid the risk of Wernicke's encephalopathy

Monitor fluid balance carefully with strict input / output recordings

Regular antiemetics – see treatment regimens in appendix A. It is acceptable to prescribe the first line antiemetic on a regular basis and the second line prn. If there is no or limited response to therapy after 48 hours of this regime move onto to consider regular 2nd/3rd/4th line therapy giving a minimum of 48hrs to assess effect

Consider the addition of ranitidine or omeprazole

Consider thromboprophylaxis with LMWH and can discontinue thromboprophylaxis when the hyperemesis resolves. [RCOG, 2015]. Therefore every admitted woman with hyperemesis should receive LMWH.

Ongoing management

IV fluid replacement with KCL added, as required, depending on biochemical profile results until tolerating oral fluids and diet. Infusions rates for fluid replacement should run at a minimum of 1 litre fluid over 4-6 hours in first 24 hours. Fluid and electrolyte regimes should be adapted daily according to daily measurements of serum sodium and potassium if further IV rehydration is required.

Urea and serum electrolyte levels should be checked daily in women requiring intravenous fluids.

Histamine H2 receptor antagonists or proton pump inhibitors may be used for women developing gastro-oesophageal reflux disease, oesophagitis or gastritis.

Thiamine supplementation (either oral or intravenous) should be given to all women admitted with prolonged vomiting, especially before administration of dextrose or parenteral nutrition.

Women admitted with HG should be offered thromboprophylaxis with low-molecular-weight heparin unless there are specific contraindications such as active bleeding. Thromboprophylaxis can be discontinued upon discharge.
Women with previous or current NVP or HG should consider avoiding iron-containing preparations if these exacerbate the symptoms.

- Daily weight and urine dipstick
- Encourage fluid and food intake in small frequent amounts
- Folic acid 400mcg daily if first trimester

Thiamine therapy

Routine thiamine supplementation is recommended for women admitted with hyperemeis gravidarum to prevent Wernicke's Encephalopathy.

If able to tolerate oral tablets thiamine hydrochloride tablets should be prescribed 25-50mg TDS

If IV treatment required Pabrinex® (which contains 250mg thiamine per pair of ampoules) can be given once a week. One pair of ampoules should be given diluted in 100ml of Sodium Chloride 0.9% infused over 30 to 60 minutes. Potentially serious allergic reactions may rarely occur during or shortly after parenteral administration. Therefore intravenous administration should be infusion over a minimum of 30 minutes and facilities for treating anaphylaxis (including resuscitation facilities) should be available when parenteral thiamine is administered.

Severe Hyperemesis

The majority of women will improve following rehydration and antiemetics. If no improvement, management needs to be discussed with the consultant. Severe refractory hyperemesis is associated with multiple admissions, psychological morbidity and is a physically a disabling condition impacting on work, time at home and psychological wellbeing. It can be difficult to treat and women may request a termination of pregnancy.

The following may need to be considered:

-Dietician input

Ondansetron (Zofran), a 5-HT3 receptor antagonist, is authorized for the management of nausea and vomiting . Recent epidemiological studies report a small increased risk of orofacial malformations in babies born to women who used ondansetron in early pregnancy. Key evidence was an observational study of 1.8 million pregnancies in the USA of which 88,467 (4.9%) were exposed to oral ondansetron during the first trimester of pregnancy. The study reported that ondansetron use was associated with an additional 3 oral clefts per 10,000 births (14 cases per 10,000 births versus 11 cases per 10,000 births in the unexposed population). Clinical Judgment must be made using the available evidence and the risks for mother and baby of malnutrition in early pregnancy, that a licensed treatment (for example doxylamine/pyridoxine(Xonvea) is not suitable or not sufficient alone to control severe nausea and vomiting in pregnancy, and there is a special clinical need to use ondansetron, then this decision should be made in consultation with the patient after she has been fully informed of the potential benefits and risks of the different treatment options.

-Domperidone

-TPN

-Investigate social situation but do not assume psychological factors are responsible, particularly in cases of severe hyperemesis, which carries a higher rate of morbidity

Multidisciplinary team
In women with severe NVP or HG, input may be required from other professionals, such as midwives**,** nurses, dieticians, pharmacists, endocrinologists**,** nutritionists and gastroenterologists, and a mental health team, including a psychiatrist.

Suggested corticosteroid therapy
Corticosteroids: hydrocortisone 100 mg twice daily IV and once clinical improvement occurs, convert to prednisolone 40–50 mg daily PO, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached
Women with NVP and HG should have an individualised management plan in place when they are discharged from hospital.

Severe NVP or HG
Women with severe NVP or HG who have continued symptoms into the late second or the third trimester should be offered serial scans to monitor fetal growth.

Discharge
Make sure the woman is drinking and maintaining hydration. ketones 2 or less and pulse rate of <100.

If LFTs or TFTs were abnormal ensure follow up is arranged in their consultant led clinic.

Women requesting a termination of pregnancy
Woman with hyperemesis wishing a termination can be referred to the Pregnancy Advisory Service. Professional counselling can be arranged by the Pregnancy Advisory

Future pregnancies
Women with previous HG should be advised that there is a risk of recurrence in future pregnancies.

Early use of lifestyle/dietary modifications and antiemetics that were found to be useful in the last pregnancy is advisable to reduce the risk of NVP and HG in their next pregnancy.

3 PROCESS FOR MONITORING COMPLIANCE

How often should monitoring take place?	Every three years
Who is responsible for monitoring?	The Gynaecology unit
How will you record your findings	Through audit
Where will you report the findings?	Audit meetings
Who is responsible for developing an action plan?	Health professional undertaking the audit
Who is responsible for implementing these actions?	All consultant gynaecologists
How will you follow up on these actions?	Re-audit
How will lessons be shared locally and if necessary externally?	Audit meeting and conferences

4 REFERENCES

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5 APPENDICES

APPENDIX 1 : Pregnancy-Unique Quantification of Emesis (PUQE) index

APPENDIX 2 : Treatment Regimens

Document Control			
Reference No:	248	**First published:**	August 2009
Version:	4	**Current Version Published:**	June 2020
Lead Director:	Mr Vize	**Review Date:**	May 2023
Document Managed by Name:	E Morris	**Ratification Committee:**	Health Group Governance
Document Managed by Title:	PDN Gynaecology	**Date EIA Completed:**	
Consultation Process			
The guideline was reviewed by Dr Stevenson Elizabeth Morris and Mr Boakye and sent to gynaecology and obstetrics guideline groups, clinical areas /consultants /Mr.Boakye and Mr. Vize			
Key words (to aid intranet searching)			
Hyperemesis, vomiting, pregnancy			
Target Audience			
All staff	**Clinical Staff Only**	Non-Clinical Staff Only	
Managers	Nursing Staff Only	Medical Staff Only	

Version Control			
Date	**Version**	**Author**	**Revision description**
October 2009	V1	Janet Cairns	New guideline
May 2012	V2	Sarah Mableson, Caroline Harrison, Julie Lazenby	Review and update
May 2014	V2.1	Obstetric Guidelines Group	Amendment to monitoring form – frequency of audit
February 2016	V3	E Morris	Update
May 2017	V3.1	E Morris Mr Boakye	New guidance
June 2020	V3.2	Jayne Gregory	Renewal and updated to reflect drug safety alert in regards to Ondansetron

APPENDIX 1: Pregnancy-Unique Quantification of Emesis (PUQE) index

Total score is sum of replies to each of the three questions. PUQE-24 score: Mild ≤ 6; Moderate = 7–12; Severe = 13–15.

Motherisk PUQE scoring system					
In the last 24 hours, for how long have you felt nauseated or sick to your stomach?	Not at all(1)	1 hour or less (2)	2–3 hours(3)	4–6 hours(4)	More than 6 hours (5)
In the last 24 hours have you vomited or thrown up?	7 or more times (5)	5–6 times(4)	3–4 times (3)	1–2 times(2)	I did not throw up (1)
In the last 24 hours how many times have you had retching or dry heaves without bringing anything up?	No time (1)	1–2 times(2)	3–4 times(3)	5–6 times(4)	7 or more times (5)
PUQE-24 score: Mild ≤ 6; Moderate = 7–12; Severe = 13–15.					
How many hours have you slept out of 24 hours? _____ Why?					
On a scale of 0 to 10, how would you rate your wellbeing? *0 (worst possible) ' 10 (the best you felt before pregnancy)*					
Can you tell me what causes you to feel that way?					

APPENDIX 2 : Treatment Regimens

First line	1.Promethazine 12.5–25 mg 4–8 hourly PO, IM, IV or PR **(After 24 hours switch to oral)** 2.Cyclizine 50 mg PO, IM or IV 8 hourly **(After 24 hours switch to oral)** 3.Prochlorperazine 5–10 mg 6–8 hourly PO; 12.5 mg 8 hourly IM/IV; 25 mg PR daily (Note: risk of extrapyramidal side effects) 4.Chlorpromazine 10–25 mg 4–6 hourly PO, IV or IM; or 50–100 mg 6–8 hourly PR ***If there is no response to therapy after 48 hours of regular antiemetics dosing move onto second line therapy***
Second line	Metoclopramide 5–10 mg 8 hourly PO, IV or IM (maximum 5 days' duration) **NOTE: Caution in patients under 20 yrs as extrapyramidal effects and oculogyric crises may occur. Such side effects subside within 24 hours of stopping the drug** Domperidone 10 mg 8 hourly PO; 30–60 mg 8 hourly PR Ondansetron 4–8 mg 6–8 hourly PO; 8 mg over 15 minutes 12 hourly IV
Third line **After discussion with Consultant**	***If there is no response to therapy after 48 hours of regular antiemetics dosing move onto third line therapy*** Corticosteroids: hydrocortisone 100 mg twice daily IV and once clinical improvement occurs, convert to prednisolone 40–50 mg daily PO, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached **40mg OD 3/7 Continue to decrease by 5mg increments until** **5mg OD 3/7 Then decrease by 1mg every 3 days until** **1mg OD for 3/7 Then STOP** ***TOTAL of 36 days steroid therapy*** ***The reduction of the steroid dose can be altered if the patient begins to feel nausea and vomiting recurring. (i.e. if the nausea and vomiting restarts at 5mg od then increase back to 10mg od for 3/7 and reduce slowly***

IM intramuscular; **IV** intravenous; **PO** by mouth; **PR** by rectum.

Ondansetron

Studies on the safety of ondansetron are mixed. A large retrospective analysis of data from the Danish birth registry of 608 385 pregnancies found no increased risk of major birth defect, stillbirth, preterm labour or small-for-gestational age. However, a case–control study42 with 4524 cases and 5859 controls found a two-fold increased risk of cleft palate (adjusted OR 2.37, 95% CI 1.18–4.76), although the authors suggest that this association may be due to chance due to the large number of variables investigated. Data from the Swedish Medical and Birth Register demonstrated a small increased risk of cardiovascular defects and cardiac septal defects (OR 1.62, 95% CI 1.04–2.14, and risk ratio 2.05, 95% CI 1.19–3.28, respectively). For these reasons, the use of ondansetron should be limited to patients who are not adequately managed on the aforementioned antiemetics and preferably used after the first trimester of pregnancy.

Three small randomised studies have shown ondansetron to be superior to doxylamine and pyridoxine in reducing nausea and vomiting,44 equally effective but with fewer adverse effects than metoclopramide45 and more effective at reducing severe vomiting than metoclopramide. (RCOG 2016)