University Hospitals Sussex
NHS Foundation Trust

MP009 Guidelines for the Management of HIV in Pregnancy and Neonatal period

Maternity Protocol: MP009

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BSUH Guidelines for the management of HIV in pregnancy and postpartum

Multi-disciplinary team contact details

24-hour emergency HIV advice available on bleep 8075 (9-5pm) or via switchboard (5pm–9am)

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Please refer all women diagnosed during antenatal screening to the Specialist Health Advisor for Reproductive Health and Wellbeing (SHA) ASAP. While most women with a known diagnosis of HIV will have informed the Lawson Unit themselves, please contact the SHA if this has not yet happened. When a woman attends in labour or for an ELCS and the birth is following the individualised birth plans (in the brown folder on the maternity ward, in the woman's hand held notes and in the HIV T drive accessible by the HIV team) with no additional concerns, please notify the HIV team via bleep 8075/switchboard between 8am – 10pm.

The following situations are emergencies. Please notify the HIV team via bleep 8075/switchboard when a woman presents with:

- In labour or with SROM and the HIV VL is detectable >40 copies/ml
- Premature onset of labour/SROM before or within 4 weeks of starting ART
- Presentation after 28 weeks gestation with untreated HIV

- Diagnosis of maternal HIV after delivery, where the infant is less than 72 hours old
- Poor maternal adherence to ART with risk of resistance as well as lack of viral suppression

If a woman attends in labour or with SROM and her HIV status is unknown please discuss with the on-call Microbiology/ Infectious Disease consultant with regards to a point of care test being done by the laboratory. If the on-call microbiology/Infectious diseases consultant agrees that immediate testing would impact on patient management they will then contact the Biomedical Scientist (BMS) to arrange for the specimen to be processed.

For specimens originating from RSCH and RACH

After obtaining the specimen contact the BMS on call via switchboard at RSCH. The specimen must then be sent urgently to Pathology Reception.

This arrangement has been agreed with the virology consultant, Dr Mohammed Hassanibrahim.

Introduction

The prevalence of HIV amongst women giving birth in the UK is increasing year on year (1). Overall 2.2 per 1000 women giving birth in the UK are living with HIV, 3.5 per 1000 in London (2). The proportion of women who are aware of their HIV diagnosis prior to delivery has increased due to the Department of Health opt-out policy of routine antenatal HIV testing at the booking appointment, which commenced in Brighton in June 2000 (3,4). Vertical transmission of HIV without any intervention is as high as 25-30% (5). Interventions such as antiretroviral therapy (ART), birth planning, infant post-exposure prophylaxis (PEP) and avoidance of breastfeeding dramatically reduce vertical transmission of HIV. In 2016 the rate of vertical transmission in the UK in women with a viral load <40 copies/ml (VL) was 0.14% (6).
At BSUH all women living with HIV who are pregnant should be managed by the HIV in pregnancy specialist MDT at the Sunflower Clinic (contact details on page 1). Communication between team members is essential and each delivery (by whatever mode) should be planned. The mother will have a personal HIV birth plan which will be available in her HIV, obstetric and antenatal hospital held notes.

These guidelines are based on the British HIV Association guidelines for the management of HIV in pregnancy and postpartum 2018 (2020 third interim update). The full guideline is available here:

https://www.bhiva.org/file/5f1aab1ab9aba/BHIVA-Pregnancy-guidelines-2020-3rd-interim-update.pdf

Preconception management

All women living with HIV who are planning a pregnancy should be given advice regarding smoking, alcohol, diet and exercise as per NICE recommendations (7).

Vitamin supplementation

All women should take folic acid supplementation of 400 micrograms when trying to conceive or from the point they find out they are pregnant until the 13th week of pregnancy. In women planning pregnancy or who conceive while taking co-trimoxazole or dolutegravir, the dose of folic acid should be increased to 5mg (7,8). All pregnant and breastfeeding women (see neonatal feeding page 15) are advised to take vitamin D supplementation of 10 micrograms per day (400 units), increased to 1000 units in women with increased skin pigmentation, reduced exposure to sunlight or obesity (7).

Antiretroviral therapy

In line with national guidelines, all people living with HIV are now advised to start and continue ART indefinitely regardless of CD4 count. This follows the findings of the START study which found a 57% increased relative risk in AIDS events, serious non-AIDS events and death in those starting ART once their CD4 fell to <350 cells/mm3 compared to those

starting ART immediately (9). Treatment interruption is also associated with an increase in all-cause mortality so women should be advised that ART should be lifelong (10).

Women planning a pregnancy should be advised to start ART prior to conception and where possible aim for an undetectable viral load before trying to conceive. Zidovudine monotherapy and Short Term Anti-Retroviral Therapy (START) for the prevention of vertical transmission are no longer recommended due to the maternal benefits of lifelong ART.

The fertility needs of all women living with HIV should be taken into consideration when starting ART and appropriate drugs with good safety data in pregnancy, selected (see page 8).

Conception in serodifferent couples

If a woman is HIV negative but has a partner living with HIV who is undetectable and fully adherent to HIV treatment there is no indication for her to be repeatedly tested for HIV. This is because there is zero risk of HIV transmission during unprotected sex from anyone who is taking effective HIV treatment. This is based on the PARTNER study of HIV discordant couples, one of many such studies all of which have shown zero transmission. Undetectable equals untransmissable in the context of unprotected sex.

Screening and monitoring of pregnant women living with HIV

Psychosocial care

HIV is associated with an increased risk of poor mental health and all pregnant women living with HIV should be assessed for antenatal/postnatal depression at booking, 4-6 weeks post-partum and 3-6 months post-partum. The HIV team will also offer to link the woman in with local HIV woman's groups and peer-support.

Multiple Pregnancy

There is no increased risk of vertical transmission with multiple pregnancy.

Sexual health screening

All pregnant women living with HIV should be offered screening for sexually transmitted infections and bacterial vaginosis (BV). This screening will be arranged by the HIV team at a routine appointment. Treatment for any infection will follow BASHH guidelines (12). Women found to have BV should be treated even if asymptomatic due to the association between BV causing bacterial chorioamnionitis and vertical transmission.

Women with a history of genital HSV should be started on aciclovir 400mg TDS from 32 weeks gestation with the dual aims of reducing the risk of HIV transmission and reducing the risk of HSV recurrence or shedding at time of delivery. Women who present with a first episode of genital HSV in labour should be managed as per BASHH guidelines (13).

Full guidelines from the British Association for Sexual Health and HIV can be found here:

https://www.bashh.org/guidelines

Laboratory monitoring of pregnant women living with HIV

All pregnant women, including those living with HIV should be offered syphilis and hepatitis B screening. Women living with HIV do not routinely require any additional laboratory monitoring at their antenatal appointments. The HIV team will arrange monitoring of the CD4 count, HIV viral load, FBC, U&E's and LFTs as per the schedule below.

Maternal HIV viral load is the key determinant of the risk of transmission (14,15) with a higher viral load increasing the risk, although transmission can occur even when HIV VL<40 copies/ml.

In women starting ART in pregnancy HIV viral load should be measured:

- At 2-4 weeks after initiation of ART (a 2-week VL may be useful for a rapid assessment of adherence, particularly in late-presenters)
- Then every 4 weeks until undetectable
- Once every trimester once undetectable
- At 36 weeks to inform the birth plan
- At delivery

In women starting ART in pregnancy CD4 count should be measured:

- As per routine HIV care
- At delivery

In women established on ART prior to pregnancy HIV viral load should be measured:

- At 2-4 weeks following any changes to HIV treatment
- At least once every trimester
- At 36 weeks to inform the birth plan
- At delivery

A second assay using a different type of viral load test should be used where there are discrepancies between viral load, CD4 count and clinical status. The majority of HIV vertical transmission occurs perinatally but a small percentage of transmission may occur in utero especially if the woman is seroconverting for HIV or has another infection such as chorioamnionitis or syphilis. Other risk factors for transmission may be maternal or obstetric.

Antenatal screening and diagnostic testing

Women should be offered routine ultrasound scanning and antenatal screening tests. If the combined screening for trisomies returns a high-risk result, non-invasive prenatal testing (NIPT) should be considered where possible to avoid invasive testing.

Invasive prenatal diagnostic testing (e.g., amniocentesis) should not be performed until the HIV status is known and where positive, testing should be deferred until the HIV viral load is

undetectable. When it is not possible to delay testing the woman should be given her standard ART with the addition of Raltegravir 400mg BD and a stat dose of Nevirapine 200mg 2-4 hours pre-procedure.

Antiretroviral therapy in pregnancy, intrapartum and postpartum

Some women may be aware of their HIV status prior to pregnancy and may conceive on ART. Other women will be newly diagnosed via antenatal testing.

Conceiving on ART

Most women who conceive on ART should be advised to continue their current regimen. Women should have their ART modified or switched if:

- They are on D4T/DDI due to a risk of lactic acidosis
- They are on a non-standard regimen:
  - PI monotherapy
- Pharmacokinetic data does not support use in pregnancy:
  - Atazanavir/Cobicistat
  - Darunavir/Cobicistat
  - Elvitegravir/Cobicistat
- There is an absence of pharmacokinetic data in pregnancy:
  - Raltegravir 1200mg OD (should be switched to 400mg BD)
  - Modified release Nevirapine (should be switched to 200mg BD)
- Safety data does not support use of:
  - Tenofovir Alfenamide (TAF) in the first trimester of pregnancy
  - Dolutegravir at conception and the first 8 weeks post conception
  - Doravirine (contained in Delstrigo)
  - Bictegravir (contained in Biktarvy)

If women conceive on ART, they should continue on their current combination until they are seen by or discussed with the HIV Consultant for pregnancy (Dr Yvonne Gilleece) with the exception of D4T/DDI which should be switched to other ARVs immediately (contact the HIV team to arrange this).

Women not on treatment

All pregnant women including elite controllers should start combination ART and be advised to continue lifelong (9).

Treatment should be started:

- Within the first trimester if the baseline VL >100,000 copies/mL or CD4<200 cells/mm3
- At the start of the second trimester if the baseline VL is between 30,000 and 100,000 copies/mL
- ASAP in the second trimester if the baseline VL ≤30,000 copies/mL
- All women should start by 20-24 weeks gestation

Before starting treatment, it is important to test for
genotypic HIV resistance so that an effective antiretroviral regimen can be selected for the patient. A resistance test should be performed and the results available before starting ART unless the woman presents after 28 weeks gestation. A resistance test should be considered if a woman fails to suppress and should be performed if a woman discontinues her ART.

Choice of ART when initiating therapy in pregnancy

Choice of antiretroviral therapy in pregnancy		
	Recommended	Alternative
NRTI backbone	ABC/3TC TDF/FTC	AZT/3TC TAF/FTC after first trimester
Third agent	EFV ATZ/r	RPV DAR/r RAL BD DTG if after 8 weeks
If VL >100,000 or failing to suppress	RAL 400mg BD (as part of/in addition to a 3-drug containing regimen)	
Avoid TDF/FTC with LPV/r (16) Avoid bictegravir (biktarvy), cobicistat, doravirine (delstrigo), elvitegravir/c, modified release nevirapine or OD raltegravir due to pharmacokinetic data/absence of data **ABC: Abacavir; AZT: Zidovudine; ATZ/r: Atazanavir/ritonavir; DAR/r: Darunavir/ritonavir; DTG: Dolutgeravir; EFV: Efavirenz; FTC: Emtricitabine; LPV/r: Lopinavir/ritonavir; RAL: Raltegravir; RPV: Rilpivirine; TAF: Tenofovir alafenamide; 3TC: Lamivudine; TDF: Tenofovir disoproxil fumarate**		

Zidovudine monotherapy and Short Term Anti-Retroviral Therapy (START) for the prevention of vertical transmission are no longer recommended. This is consistent with national and international guidelines that recommend that all people living with HIV should be started on ART regardless of CD4 count.

ART when presenting in labour

This is an emergency and the HIV team should be contacted immediately (see page 1). The woman should be started on ART as follows:

- Nevirapine 200mg STAT
- Start Zidovidine 300mg BD + lamivudine 150mg BD (Combivir)
- Start Raltegravir 400mg BD
- IV Zidovudine 2mg/kg for 1 hour and then 1mg/kg/hour continuous infusion until placental cord clamped
- If preterm and infant unlikely to absorb enteral PEP give mother 2 doses of TDF: Tenofovir disoproxil fumarate
- Infant should receive high-risk PEP (see below)
- If vaginal delivery not imminent proceed to caesarean section

Intrapartum IV zidovudine

Intrapartum IV zidovudine is recommended if the VL is known to be >1000 copies/mL or if the VL is unknown in a woman not on HIV treatment. It should be started if the above criteria are met in women who present in labour, present with spontaneous rupture of membranes or those admitted for ELCS. There is no evidence of any additional benefit from

IV intrapartum zidovudine where a woman is on HIV treatment and the viral load is <1000 copies/mL. The dose of maternal IV ZDV is 2mg/kg for the first hour, followed by 1mg/kg/hour continuous infusion thereafter until the cord is clamped. When used at elective CS the infusion should be started 4 hours before the procedure.

Management of common symptoms in pregnancy

Nausea and vomiting

Antiretrovirals may also increase the incidence of nausea and vomiting in pregnancy. To avoid increasing pill burden, anti-emetics should only be used when other interventions have failed to control nausea and vomiting. The following advice may aid adherence with antiretrovirals if a pregnant woman is struggling with morning sickness:

- Adjust timings of antiretrovirals, to avoid the times when morning sickness is worst.
- Eat smaller meals and snack more frequently rather than eating just a few larger meals.
- Try to eat more bland foods. Avoid foods that are spicy, greasy or strong smelling.
- Leave some dry crackers by your bed. Eat one or two before you get up in the morning.
- Ginger is very helpful. It can be used in capsule or as ginger root powder. Fresh root ginger peeled and steeped in hot water can help.
- Acupressure and acupuncture may help. Anti-nausea acupressure bands are available from most chemists.
- Try not to drink with your meal or straight after. It is better to wait an hour and then sip drinks. It is important for pregnant women not to become dehydrated though so do remember to drink outside mealtimes.
- Peppermint is also useful. It can be taken in tea or in chewing gum.

If the risk of ART interruption is exceeded by the risk of failure due to intermittent ART exposure as a consequence of vomiting, ARV should be temporarily withheld for the minimum amount of time required. If on an NNRTI or Raltegravir a resistance test should be considered.

Anti-emetics in pregnancy

1st line: Cyclizine 50mg tds orally or IM

2nd line: Promethazine 25mg nocte orally and up to 25mg qds

or

Prochlorperazine 5mg orally up to three times each day or 25mg rectally twice each day. QT caution with ATZ/r, DAR/r and Rilpivirine.

Try first line anti-emetic for 3-4 days before prescribing second line anti-emetic. For patients with persistent/severe nausea and vomiting, see RCOG green top guidance for Nausea and Vomiting in Pregnancy: https://www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg69-hyperemesis.pdf
Domperidone should not be co-administered with a boosted PI. Concerns about drug interactions can be discussed with our pharmacy team (see contact details page 1).

Managing diarrhoea as a side-effect of antiretrovirals

The following dietary interventions may help reduce the incidence of diarrhoea:

- Soluble fibre is particularly helpful when watery stools are a problem as they help to absorb the excess water and bulk the stool. Soluble fibre can be found in white rice, pasta.
- Replace lost fluids and electrolytes with dioralyte.
- Loperamide is not for routine use in pregnancy.

Dyspepsia and reflux in pregnancy

There are a number of important drug-drug interactions between gastric acid modifying drugs and antiretrovirals. If in any doubt please contact the HIV pharmacy team or on-call SpR (see page 1 for contact details).

Use of antacids e.g., calcium carbonate (Rennies) or alginates e.g., sodium alginate and potassium bicarbonate (Gavison Advance) are recommended for use due to low side effect profiles. Where symptoms persist or worsen, treatment escalation will reviewed on an individual case basis and will depend on ART regimen. See table below for summary of interactions between ART and gastric acid modifying drugs.

Summary of major drug-drug interactions between acid modifying agents and ART

	PPIs	H2 antagonists	Antacids
Atazanavir	**Contraindicated**	**Caution:** Low dose H2A dosed once daily 4-12 hours after atazanavir may be considered on an individual basis (consider risk/benefit/availability)	Can be used 1 hour before or 2 hours after atazanavir
Rilpivirine	**Contraindicated**	**Caution:** Low dose H2A dosed once daily 4-12 hours after rilpivirine may be considered on an individual basis (consider risk/benefit/availability)	Can be used 2 hours before or 4 hours after Rilpivirine
Raltegravir BD	No interaction	No interaction	Aluminium and magnesium antacids contraindicated. Calcium carbonate antacids can be used with BD raltegravir. Separate if by 4 hours if possible.
Dolutegravir	No interaction	No interaction	Can be used 6 hours before or 2 hours after dolutegravir

Pain Management in Pregnancy and labour

Summary of co-administration of ART with commonly used analgesia and potential interactions:

ART	ANALGESIA			
	BUPIVACAINE	**FENTANYL**	**MORPHINE / DIAPMORPHINE**	**PETHIDINE**
bPI: **AZT/r** **DAR/r**	Potentially increased levels of bupivacaine. Monitor and dose adjust accordingly.	Increased fentanyl levels, prolonged adverse effects including respiratory depression. Consider dose reduction and monitor carefully.	Monitor for efficacy and toxicity (potentiated CNS effects). Adjust dose if required.	Consider alternative, decreased pethidine levels, increased levels of neurotoxic metabolite.
INSTI: **DTG** **RAL**	No interaction	No interaction	No interaction	No interaction
NNRTI: **EFV** **RPV**	**EFV:** Potentially decreased levels of bupivacaine. Monitor for efficacy.	**EFV:** Potentially decreased levels of fentanyl. Monitor for efficacy.	**EFV:** Increased levels of diamorphine/morphine. Consider dose reduction and monitor.	**EFV:** Consider alternative to pethidine; increased risk of seizures due to increased levels of neurotoxic metabolite.
NRTI: **AZT** **FTC** **3TC** **TAF** **TDF**	No interaction	No interaction	No interaction	No interaction

Codeine / dihydrocodeine, diclofenac can be used orally for short courses following appropriate dosing regimens.

Paracetamol and nitrous oxide (Entonox®) do not interact with ARVs and can be used

Other commonly used medications in labour/complications:

Antihypertensives:

	Labetalol	**Nifedipine**	**Methyldopa**
bPI: **AZT/r** **DAR/r**	Potentially decreased levels labetalol, titrate to effect	Increased nifedipine levels, adjust dose/monitor for toxicity, consider ECG monitoring	No interaction
INSTI: **DTG** **RAL**	No interaction	No interaction	No interaction
NNRTI: **EFV** **RPV**	EFV: Potentially decreased levels labetalol, titrate to effect	EFV: Potentially decreased levels nifedipine, titrate to effect	No interaction
NRTI: **AZT** **FTC** **3TC** **TAF** **TDF**	No interaction	No interaction	No interaction

Tocolysis:
Nifedipine (see under antihypertensives above)

Preterm labour or pre-eclampsia:
Magnesium sulphate: no interaction with IV formulation, separate times from raltegravir/dolutegravir if oral.

Obstetric haemorrhage:
Ergometrine, do not coadminister with bPI or EFV
Oxytocin QT caution with boosted PIs (bPI) ATV/r DAR/r and rilpivirine
Carboprost, misoprostol no interaction

Antibiotics in labour:
bPI may increase clindamycin, EFV may decrease clindamycin: consider dose adjustment, monitor for toxicity/efficacy
No interaction with benzylpenicillin, cefuroxime, metronidazole

Interaction information taken from Liverpool HIV Drug Interaction website: https://.hiv-druginteractions.org and Summary of Product Characteristics.

Mode of delivery

A plan for mode of delivery should be made between with the result of the 36-week viral load taking the wishes of the woman and any obstetric factors into consideration. An individualised birth plan will be written by Dr Yvonne Gilleece and copies placed in the handheld antenatal notes and HIV T drive and HIV notes (filed in patient objects on Millcare).

In the absence of an obstetric indication the 36-week viral load should guide decision making regarding mode of delivery as follows:

- If VL <40 copies/mL: plan for vaginal delivery (VBAC can be offered)
- If VL 40 – 399 copies/mL: elective CS should be considered (see below)
- If VL ≥400 copies/mL: elective CS at 38 weeks

Data from the National Surveillance for HIV in Pregnancy and Childhood has shown that when the VL is undetectable there is no difference in the rate of vertical transmission between normal vaginal delivery and elective caesarean section. In women with an HIV VL between 50–399 copies/mL the transmission rate is 0.26% following CS vs 1.1% following vaginal delivery, representing a 4-fold increase in risk (6). It is therefore essential to make a birth plan for those that fall in this bracket that considers the actual VL, trajectory of VL, time on ARVs, adherence, obstetric issues and maternal wishes.

ECV and vaginal birth after CS (VBAC) can be offered to women with a documented viral load <50 copies/mL.

Elective vaginal delivery

This may be considered for all women with an undetectable viral load. The cord should be clamped early with no physiological 3rd stage of labour [38]. Labour should be managed as for HIV negative women, apart from the following considerations based on the BHIVA HIV in Pregnancy guidelines (updated 2019):

- Data from the pre-ART era has shown little or no risk of increased vertical transmission with the use of amniotomy, fetal scalp electrodes and blood sampling, instrumental delivery and episiotomy. These procedures should not be avoided when there is an obstetric indication.
- In a woman with a VL<50 copies/mL it is unlikely that the type of instrument used in an instrumental delivery will affect transmission and the instrument the operator feels is most appropriate should be used as in the non-HIV population.
- There is scant safety evidence to support water births in women living with HIV; however, women who choose a water birth should be supported to achieve this where the viral load is<50 HIV RNA copies/mL

Elective pre-labour Caesarean section

If an elective CS is undertaken to reduce the risk of vertical transmission it should be booked at 38 weeks gestation. If an elective CS is undertaken for an obstetric reason then the timing should be decided by the obstetric team (usually at 39 weeks gestation).

Where the VL is >1000 copies/mL, maternal IV intrapartum zidovudine should be started four hours before the procedure and continued until the cord is clamped.
Appropriate peri-operative antibiotics should be prescribed for all CS. Fundal pressure at CS is no concern.

Management of spontaneous rupture of membranes (SROM)

In the pre-ART era, a number of studies suggested that prolonged rupture of membranes (>4 hours) resulted in an increase in vertical transmission. This data was based on women with either untreated HIV or women on zidovudine monotherapy, neither of which are consistent with the standard of care today. A review by the National Surveillance of HIV in Pregnancy and Childhood showed a vertical transmission rate of 0.12% (1/809) women with SROM <4 hours and 0.15% (1/655) in women with SROM ≥4 hours in women on ART with an undetectable viral load (17). Following the publication of this data BHIVA no longer recommend delivery within 4 hours but instead recommend that in all cases of term pre-labour SROM in women with an undetectable viral load, delivery within 24 hours should be the aim.

Acute and chronic chorioamnionitis are associated with perinatal as well as in utero transmission of HIV. Routine antibiotics are no longer recommended for women following SROM but there should be a low threshold to start antibiotics and expedite labour in women with intrapartum pyrexia.

SROM at term (>37 weeks' gestation)

- In all cases of term pre-labour SROM delivery should be within 24 hours.
- ART should be optimised where required
- If VL<40 copies/mL: immediate induction/augmentation of labour
- If VL 50 – 399 copies/mL: immediate CS (taking birth plan and the actual VL, trajectory of VL, time on ART, adherence, obstetric issues and maternal wishes into account after contacting HIV team via switchboard)
- If VL >400 copies/mL: immediate CS (category 2)

ART should be reviewed by the HIV team in all cases where the presenting woman is known or suspected to have a detectable viral load and optimised where appropriate. Intrapartum IV Zidovudine is recommended in untreated women and in those with known VL>1000 copies/mL. It can be considered on a case-by-case basis in women with a VL <1000 copies/mL but there is no evidence of additional benefit, especially if intensive neonatal PEP is given.

Preterm SROM (<37 weeks' gestation)

- SROM >34 weeks should be managed as above (following consultation with obstetrics and neonatology) with the addition of prophylaxis group B strep prophylaxis
- IM corticosteroids should be administered as per national guidelines.
- SROM <34 weeks requires discussion between obstetrics, neonatology and HIV to plan for timing and mode of delivery

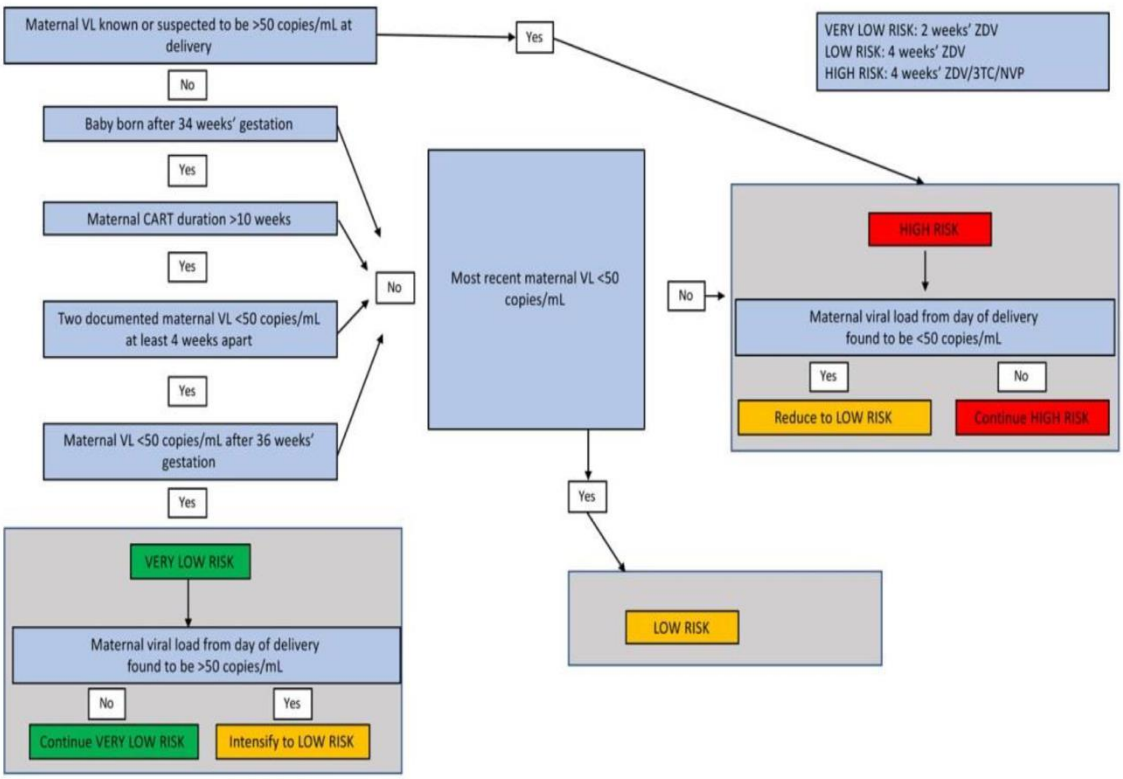
- ART should be optimised in all cases with consideration of transplacental fetal loading where an infant is unlikely to absorb PEP enterally

Neonatal management

Neonatal post-exposure prophylaxis (PEP)

All infants born to women living with HIV should receive PEP. The midwife responsible for the woman should check that the neonatal drugs required are available prior to delivery. The HIV pharmacist and paediatric pharmacists can help with this. In all cases neonatal PEP should be started within four hours of delivery. The duration and drug regimen used in neonatal PEP is determined by the maternal HIV viral load and duration of maternal ART. The anticipated plan for neonatal PEP will be documented on the individualised birth plan and confirmed by the HIV team. Neonatal PEP will be reviewed with the maternal HIV viral load which should be available ASAP and definitely within 72 hours. The HIV team will arrange for this sample to be taken as soon as possible after birth and will liaise with the paediatric team to ensure that paired samples are sent from the infant.

Choice of neonatal PEP should follow the algorithm below:



Very low risk PEP – zidovudine monotherapy for 14 days

Two weeks of neonatal zidovudine monotherapy (see below for dosing) is recommended if ALL of the following criteria are met:

- The woman has been on ART for over 10 weeks
- There are two documented maternal HIV VL < 50 copies/mL during pregnancy at least 4 weeks apart
- Maternal HIV VL <50 copies/mL at or after 36 weeks

If the maternal VL from the day of delivery is found to be >50 copies/mL, the zidovudine should intensified to three drug PEP and the regimen extended to 4 weeks.

Low risk PEP – zidovudine monotherapy for 28 days

Neonatal zidovudine monotherapy should be extended to four weeks if:

- The criteria for very low risk PEP are not met but the maternal HIV VL is <50 copies/mL at 36 weeks or later
- If the infant is born prematurely (<34 weeks) but the most recent maternal HIV VL is < 50 copies/mL

High risk PEP – Triple therapy for 28 days

In cases where the risk of vertical transmission is high, the infant should receive combination PEP including zidovudine, lamivudine and nevirapine. Stop nevirapine after 2 weeks, in view of long half-life, continue other PEP agents for full 4 weeks.
Combination PEP is indicated if:

- Maternal birth HIV VL is known to be or likely to be > 50 copies/mL on the day of birth
- If there is uncertainty about recent maternal adherence
- If the maternal VL is not known

Drugs used in neonatal PEP

Most infants will receive 2-4 weeks of zidovudine monotherapy. This can be given orally by syringe and the mother should be shown how to measure and administer this prior to discharge. If there is a concern about the oral route, IV zidovudine can be given.

Where combination PEP is indicated the infant should receive nevirapine and lamivudine in addition to zidovudine. Occasionally alternative combinations can be used but this should only be on advice from the HIV team.

Pneumoncystis pneumonia (PCP) prophylaxis

Co-trimoxazole should not be prescribed routinely for HIV-exposed infants, even when the maternal VL >50 copies/mL. Co-trimoxazole should be prescribed from 4 weeks of age to any infant with a positive PCR screening test for HIV before 4 weeks of age.

For all drug dosing in infants please see appendix 1.

Neonatal feeding

Breastfeeding is a route for HIV transmission with a risk of between 10-25% when the mother has untreated HIV. Even with an undetectable HIV VL there is a small risk of transmission. The PROMISE trial which looked at transmission as a consequence of breastfeeding while women were on ART found a transmission rate of 0.3% at 6 months and 0.6% at 12 months. In the UK and other high-income countries formula feeding is recommended as this carries no risk of HIV transmission. This is different to World health Organisation guidelines which recommend exclusive breast feeding as in many parts of the world women are unable to afford infant formula or do not have access to clean water to

mix formula, and the risk of malnutrition and diarrhoeal disease outweighs the risk of vertical transmission of HIV. The rationale for the conflicting guidelines should be explained to women who may have had a previous child in a different setting.

A plan for infant feeding will be made prior to delivery at an HIV clinic appointment after discussion with the woman. Women who choose to formula feed will be offered cabergoline 1mg stat within 24 hours of delivery to remove the discomfort of lactation without breastfeeding. Abstaining from breastfeeding can have financial and psychological repercussions and will require support from the MDT. The Sussex Beacon and SHA/RJ can help women to access additional peer support and financial aid to assist with formula feeding.

If a woman has an undetectable HIV viral load with good adherence to ART and chooses to breastfeed they should be supported to do so. The risk of transmission should be discussed and the woman informed of the need for additional monthly maternal and infant blood monitoring. Maternal ART must be continued throughout and women advised to feed for as short a time as possible, exclusively, for a maximum of 6 months. Solids must not be introduced whilst breastfeeding as this increases the transmission risk. Women should be advised to stop feeding if there is any suggestion of mastitis or infant gastrointestinal symptoms as per "The Safer Triangle".

Written information should be provided and is available here:
BSUH 'HIV and breastfeeding your baby' Leaflet (Appendix 2)
https://www.bhiva.org/file/5bfd3080d2027/BF-Leaflet-1.pdf

If a woman elects to breastfeed her baby with a detectable viral load it is essential that the case is discussed with the MDT and a referral to social services considered.

If breastfeeding assess compatibility of any medication (https://www.sps.nhs.uk/) and check ARV interactions with HIV pharmacy team

Diagnosis of infant HIV status

All infants should have a blood sample taken for an HIV DNA PCR as soon as is practical after birth (within 48 hours maximum). This should be sent to the laboratory paired with a maternal sample. The HIV team will liaise with the paediatric team to co-ordinate these samples.

Non-breastfed infants should be tested:

- Within 48 hours of birth
- If high risk (see neonatal PEP) at 2 weeks
- At 6 weeks (or at least 2 weeks after cessation of neonatal PEP)
- At 12 weeks (or at least 8 weeks after cessation of neonatal PEP)
- On other occasions if additional risk
- HIV antibody testing for seroreversion should be checked at 22-24 months

Breastfed infants should be tested:

- Within 48 hours of birth
- Prior to discharge
- At 2 weeks
- Monthly during breastfeeding
- At 4 weeks after cessation of breastfeeding
- At 8 weeks following cessation of breastfeeding
- HIV antibody testing for seroreversion should be checked at 22-24 months

HIV/Hepatitis B (HBV) co-infection

Due to overlapping epidemiological risk factors, hepatitis B infection is more common in people living with HIV. Despite HIV co-infection being associated with increased HBV DNA levels, there is no evidence that co-infection with HIV increases the risk of HBV vertical transmission.

The majority of women co-infected with HIV and HBV will experience no worsening of their liver function during pregnancy. However, hepatic exacerbations and cases of fulminant hepatic failure have been reported.

ART which also treat HBV should be used as per national guidelines. Tenofovir, emtricitabine and lamivudine are safe in pregnancy. TAF may used after the first trimester (REF IMPACT). Entecavir is contraindicated in pregnancy due to the risk of teratogenicity. Nevirapine and zidovudine should be avoided where possible due to hepatotoxicity. Vaginal delivery can be considered.

All infants born to HBV infected mothers should receive neonatal HBV post-exposure prophylaxis:

- Hepatitis B vaccination within 24 hours of birth followed by the national vaccination schedule
- + HBIg if:
    - Maternal HBV DNA >10^6 IU/mL
    - Mother is HBeAg positive or anti-HBeAb negative or "e" status unknown

HBV vertical transmission rates:

- HBeAg positive: 70-90%
- HBeAg negative: 10-40%
- With neonatal HBV PEP: 0-14%

HIV/Hepatitis C (HCV) co-infection

In HCV monoinfection vertical transmission is seen in 5% of cases. This is increased by up to 2.82-fold in HIV/HCV co-infection but only in women where the HIV VL is detectable and she is not receiving ART. Consequently, control of HIV viraemia is the priority in reducing vertical transmission of both HIV and hepatitis C.

While data is variable, there is no clear effect of mode of delivery on vertical transmission in HCV mono-infection. Vaginal delivery can be considered in women with HIV/HCV co-infection. Breastfeeding does not transmit HCV in monoinfection.

At present HCV treatment is not recommended in pregnancy. Those wishing to conceive should be prioritised for treatment prior to conception. Please refer to Dr Yvonne Gilleece.

Postpartum management of women

All women are recommended to continue ART postpartum. Adherence can decline in the post-partum period for wide range of factors and women should be reviewed within 4-6 weeks by the HIV team. This appointment will be made by the HIV team prior to discharge from hospital. All those providing care to the woman should be alert to the risk of post-natal depression and access support where needed.

A plan for future contraception should be made antenatally and if required ART can be changed to support a woman's choice. This will be followed up in the Lawson Unit at the 6 week post-partum check and condom use advised in the interim.

Women living with HIV should be offered an annual cervical screen.

Where a woman has been newly diagnosed with HIV in pregnancy, testing of her partner and other children should be completed if not already done. This will be arranged by the Specialist Health Advisor for Reproductive Health and Wellbeing.

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Appendix 1: Drug dosing for infants (BHIVA)

<table>
<tr><th>DRUG</th><th>DOSE</th><th>COMMENTS/SIDE EFFECTS</th></tr>
<tr><td colspan="3">NRTIs: nucleoside reverse transcriptase inhibitors</td></tr>
<tr><td>Zidovudine
(ZDV) (Retrovir®)
Also known as azidothymidine (AZT)

Liquid – 10 mg/mL</td><td><u>Oral:</u>
<table>
<tr><th>Gestation +/- weight</th><th>Dose</th></tr>
<tr><td><30/40 gestation at birth</td><td>2 mg/kg twice a day</td></tr>
<tr><td>30–34/40 gestation at birth</td><td>2 mg/kg twice a day for 2/52 then 2 mg/kg three times a day</td></tr>
<tr><td>≥34/40 gestation at birth and ≤2 kg</td><td>4 mg/kg twice a day – round dose up to the nearest 0.5 mg to assist administration</td></tr>
<tr><td>≥34/40 gestation at birth and >2 kg</td><td>See dose banding table</td></tr>
</table>
<u>Duration oral dosing:</u>
• Very low risk monotherapy – 2 weeks
• Low risk monotherapy – 4 weeks
• Combination therapy – 4 weeks
<u>Intravenous:</u>
• ≥34/40 gestation – 1.5 mg/kg four times a day
• <34/40 gestation – 1.5 mg/kg twice a day, change to four times a day at 34/40</td><td>Anaemia, neutropenia
<table>
<tr><th>Weight range (kg)</th><th>Oral dose (equivalent to 4 mg/kg) <u>TWICE A DAY</u></th><th>Volume to be given orally <u>TWICE A DAY</u></th></tr>
<tr><td>2.01–2.12</td><td>8.5 mg</td><td>0.85 mL</td></tr>
<tr><td>2.13–2.25</td><td>9 mg</td><td>0.9 mL</td></tr>
<tr><td>2.26–2.37</td><td>9.5 mg</td><td>0.95 mL</td></tr>
<tr><td>2.38–2.50</td><td>10 mg</td><td>1 mL</td></tr>
<tr><td>2.51–2.75</td><td>11 mg</td><td>1.1 mL</td></tr>
<tr><td>2.76–3.00</td><td>12 mg</td><td>1.2 mL</td></tr>
<tr><td>3.01–3.25</td><td>13 mg</td><td>1.3 mL</td></tr>
<tr><td>3.26–3.50</td><td>14 mg</td><td>1.4 mL</td></tr>
<tr><td>3.51–3.75</td><td>15 mg</td><td>1.5 mL</td></tr>
<tr><td>3.76–4.00</td><td>16 mg</td><td>1.6 mL</td></tr>
<tr><td>4.01–4.25</td><td>17 mg</td><td>1.7 mL</td></tr>
<tr><td>4.26–4.50</td><td>18 mg</td><td>1.8 mL</td></tr>
<tr><td>4.51–4.75</td><td>19 mg</td><td>1.9 mL</td></tr>
<tr><td>4.76–5.00</td><td>20 mg</td><td>2 mL</td></tr>
</table></td></tr>
<tr><td>Lamivudine (3TC) (Epivir®)
Liquid 10 mg/mL</td><td><u>Oral:</u> usually as part of combination therapy
2 mg/kg twice a day – round dose up to nearest 0.5 mg to assist administration</td><td>Anaemia, neutropenia
(much less common than with ZDV)</td></tr>
<tr><td>Abacavir (ABC) (Ziagen®)
Liquid 20 mg/mL</td><td><u>Oral:</u> usually as part of combination therapy
2 mg/kg twice a day– round dose up to nearest 1 mg to assist administration</td><td>Hypersensitivity reactions have not been noted in neonates</td></tr>
<tr><td>Tenofovir
(TDF) (Viread®)
245 mg tenofovir disoproxil = 300 mg TDF</td><td><u>Oral:</u> usually as part of combination therapy
All doses now based on tenofovir disoproxil salt (TD)
(*245 mg TD tablet dissolved in 24.5 mL water gives 10 mg/mL)
4.9 mg/kg (0.49 mL/kg*) once a day (round dose up to the nearest 0.5 mg (<10 mg) or 1 mg (≥10 mg) to assist administration)</td><td>Renal dysfunction: consider monitoring renal function weekly</td></tr>
<tr><td colspan="3">NNRTI: non-nucleoside reverse transcriptase inhibitor</td></tr>
</table>

Nevirapine (NVP) (Viramune®) Liquid 10 mg/mL	**Oral: usually as part of combination therapy** 2 mg/kg once a day for 1 week, then 4 mg/kg once a day – round doses *up* to the nearest 0.5 mg to assist administ *If mother has already received >3 days of nevirapine:* 4 mg/kg once a day – (round doses *up* to the nearest 0.5
INSTI: integrase strand transfer inhibitor	
Raltegravir (RAL) (Isentress®) 100 mg sachets for oral suspension (10 mg/mL)	**Oral: usually as part of combination therapy** 1.5 mg/kg once a day from birth to day 7, then 3 mg/kg t until 4 weeks of age. See dose banding:

Body weight (kg)	Dose
In full-term neonates >37 weeks	
Birth to 1 week – once a day dosing	
2 to <3 kg	4 mg once a day
3 to <4 kg	5 mg once a day
4 to <5 kg	7 mg once a day
1 to 4 weeks – twice a day dosing	
2 to <3 kg	8 mg twice a day
3 to <4 kg	10 mg twice a day
4 to <5 kg	15 mg twice a day

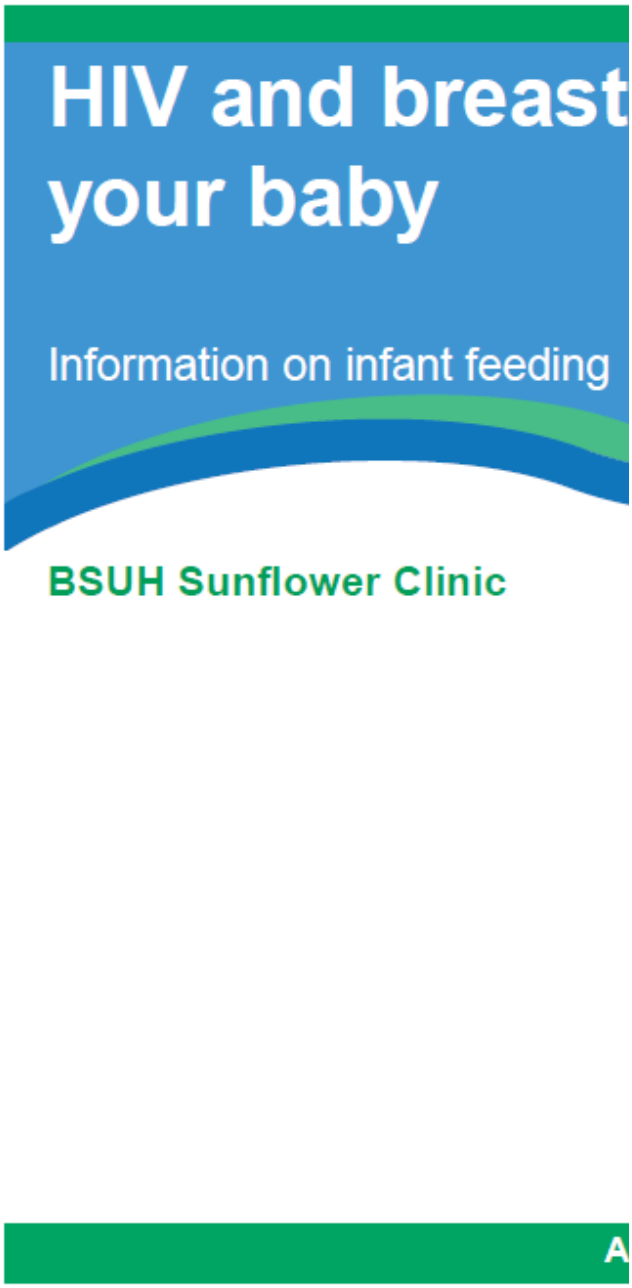
PI - protease inhibitor	
Lopinavir/ritonavir (Kaletra®) Liquid: 5 mL = (Lopinavir 400 mg + ritonavir 100 mg)	**Oral: usually as part of combination therapy** 300 mg/m² (of lopinavir) twice a day – use dose banding

Weight range (kg)	SA range (m²)	Kaletra volume to be given orally TWICE A DAY
1–1.5	0.1–0.13	0.5 mL
1.51–2	0.14–0.16	0.6 mL
2.01–2.5	0.17–0.19	0.75 mL
2.51–3	0.20–0.21	0.8 mL
3.01–3.5	0.22–0.24	0.9 mL
3.51–4	0.25–0.26	1 mL
4.01–4.5	0.27–0.28	1.1 mL
4.51–5	0.29–0.30	1.2 mL

FI: fusion inhibitor	
Enfuvirtide (Fuzeon®) (T-20)	**Intravenous: usually as part of combination therapy** 2 mg/kg IV twice a day (as infusion over 30 minutes) **Method:** To reconstitute the 108 mg vial slowly add 1.1 m for injections from the vial of diluent provided to the vial enfuvirtide powder, do not shake or invert the vial. The p

	take up to 45 minutes to dissolve. The resulting solution 90 mg in 1 mL. Add 1 mL (90 mg) of the solution to 10 ml for injections, then further dilute to 45 mL with water fo do not shake or invert the syringe. The final solution cont in 45 mL (2 mg in 1 mL) from which to administer the req
PCP prophylaxis	
Co-trimoxazole (Septrin®) 240 mg in 5 mL liquid	**BW ≥2 kg** 120 mg = 2.5 mL **BW <2 kg** 60 mg = 1.25 mL ONCE a day on 3 days per week

Appendix 2: BSUH HIV and breastfeeding your baby


HIV and breast
your baby
Information on infant feeding
BSUH Sunflower Clinic
A

Information for mothers

The safest way for a mother living with
baby is to bottle feed using formula mil
an undetectable viral load and choose
can help you make it as safe as possib
be as safe as using formula. You will n
'The Safer Triangle'.

The Safer Triangle means

Healthy Breasts f

No Virus + Happy Tums + Healthy B
Only breastfeed if your HIV is undetect
baby are free from tummy problems A
are healthy with no signs of infection.

If HIV virus becomes detectable in y
Stop breastfeeding and start using forr
milk you have expressed and stored. F
only until you have spoken with your H

If your baby has diarrhoea or vomiti
Feed your baby with formula milk only.
formula milk even after their tummy is

2

If you have diarrhoea or vomiting, or or infection:

Stop breastfeeding and feed your baby breast milk that you expressed more tha tummy or breast problem began. If your you are ill, continue feeding your baby f did not receive formula milk you may re days (48hrs) after your breast problem i problems you must contact your HIV cli

Happy tums

Diarrhoea and vomiting show that a tum tummy is irritated it may be more likely t blood stream and infect your baby. If yo not absorb your HIV medication properl you have a 'happy tummy'.

No virus

If the HIV virus in your blood is detectab breast milk, and HIV will enter your baby should only breastfeed if your HIV is un

Healthy breasts for mums

There may be HIV in your breast milk if bleeding, have thrush or develop an infe

BHIVA guidelines on the management of pregn

These four golden rules will help to
while breastfeeding.

1 Taking your meds = Giving you

The HIV medicines you take protect yo
You need to be 'undetectable', with no
to breastfeed your baby. The only way
medications at the right time every day.

Every day you are already caring for yc
warm and comforted. Taking your HIV
possible is just another part of the love
to your child.

2 Short and sweet

The fewer breastfeeds your baby ever
your baby will have of becoming HIV p
your HIV medication, your baby has do
infected with HIV if you breastfeed for 1
before your baby is 6 months old. By 6
start first (weaning) foods. Good first fo
vegetables like potatoes or carrots, sof
with formula milk. Babies' tummies are
Using formula milk only while weaning
vitamins and calories he or she needs t
protected from any risk of HIV infection
bottle at first, try having someone else
bottle – what your baby won't accept fr
from someone else!

3 Breast milk only

If you choose to breastfeed you shoul
This is known as exclusive breastfeec
other foods may irritate the baby's tur
HIV infection. If you are 'exclusively b
baby is receiving no other food or drir
vitamins or prescribed medicines. You
your own expressed breast milk. We r
early on, so your baby gets used to a

4 Be prepared

Breastfeeding doesn't always go to pl
faces the same challenges during bre
Living with HIV means these situation
extra planning. Advice for a breastfee
HIV may not be correct for you and yc
tell your community midwife about you
are giving you the right advice for you
uncertain about something ask your sp
children's nurses, or your HIV doctor.

Get comfortable

Good feeding positions are better for
reduce the chance of injuries to your r
inflamed breast (known as mastitis) c
in your milk. Ask your specialist midwi
help with breastfeeding positions.

Expressing milk

'Expressing' milk means gently squeez
your breast into a sterile container to u
later. One of the most useful ways to p
difficulties is to express and freeze you
breasts and tummy are healthy and fre
load is undetectable. You can express
that has been boiled in water for 10 mi
cool. You can also use a breast pump.
one from places such as Boots or Argo
electric and cost from £10 to more thar

Your milk can be safely stored in a ster
pre-sterilised plastic breast milk bags (
date and the amount of milk on the cor

You can keep your expressed milk:

- In the fridge for up to five days at 4
  Using a fridge thermometer (about
  Curry's) is the best way to make su
  temperature.
- For two weeks in the ice compartme
- For up to six months frozen in a free

Ask your community midwife for more
and storing milk.

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Disclaimer
The information in this leaflet is for guidance purposes only and is in no way intended to replace professional clinical advice by a qualified practitioner.

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