

currently licensed DAA therapies sofosbuvir, sofosbuvir/ledipasvir fixed-dose combination (FDC), daclatasvir, dasabuvir, grazoprevir/elbasvir FDC and sofosbuvir/velpatasvir FDC have not shown teratogenicity in small-animal studies, but have variable ability to cross the placenta and into breast milk [56-58].

Paritaprevir/ribavirin/ombitasvir FDC and daclatasvir have both shown risk of malformations in small animals at supranormal dose exposures [59,60].

There is no evidence that HCV can be transmitted vertically in the absence of HCV viraemia, therefore only viraemic patients would be considered for therapy. The current standard of care in HCV therapy is DAA-based IFN-free therapy with or without ribavirin [61]. There are no definitive studies on the safety of HCV antiviral therapy during pregnancy.

Finally, it is recognised that a small number of individuals with both HCV and HIV are HCV antibody negative but HCV viraemic. Where there is evidence of liver inflammation or fibrosis, profound immune deficiency or risk factors, an HCV viral load assay should be performed.

7.2.3	Pregnant women with both HCV and HIV should not be treated for HCV with ribavirin-based directly acting antiviral (DAA) therapies, and all women who discover they are pregnant while receiving treatment should discontinue HCV therapy immediately.	1B
7.2.4	Women with both HCV and HIV of child-bearing age wishing to become pregnant should be prioritised for DAA-based HCV therapy.	2D

Given the issues with treatment during pregnancy and the postnatal period, it is the writing group's view that HCV-infected women of child-bearing age wishing to become pregnant should be prioritised for DAA-based anti-HCV therapy regardless of fibrosis stage, and should delay pregnancy until after treatment is completed or longer if ribavirin based as noted above. See section 9 for guidance on subsequent screening of the infant.

7.2.5	Vaccination against HBV is recommended for all women with both HCV and HIV after the first trimester, unless already immune.	1C
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Immunisation for HBV uses an inactivated vaccine. Limited data are available on the use of HBV vaccination in pregnancy and none in pregnant women living with HIV. Moreover, no randomised trial has been performed to determine the optimum dosing schedule for use in pregnancy [62]. Nevertheless, several guidelines indicate that pregnancy is not a contraindication for HBV immunisation, including in pregnant women with both HCV and HIV [25].

In single-arm open studies in HIV-negative persons, seroconversion rates for HBV are no different in the pregnant and non-pregnant woman and no fetal risks have been reported. In a prospective clinical trial in pregnant women, an accelerated schedule at 0, 1 and 4 months was found to be effective and well tolerated, and had the advantage of potential completion prior to delivery [63]. Patients with higher CD4 cell counts and on cART generally show improved responses to vaccination. Regardless of CD4 cell count, anti-HBs level should be measured 6–8 weeks after completion of vaccination. In a systematic review and meta-analysis of five studies, an increased-dose HBV vaccination schedule improved anti-HBs response rates compared to standard-dose HBV vaccination (OR 1.96; 95% CI 1.47–2.61) with separate randomised trial data demonstrating improved serological response with four-dose regimens [64].

7.2.6	In all HAV non-immune women with both HCV and HIV, HAV vaccination is recommended, after the first trimester as per the normal schedule (0 and 6 months);	1A
	unless the CD4 cell count is <300 cells/mm ³ , when an additional dose (0, 1 and 6 months) may be indicated.	1D

Immunisation for HAV also uses an inactivated vaccine and data for HAV vaccination in this setting are similarly limited. Individuals living with HIV with CD4 cell counts <300 cells/mm³ should receive three instead of the

standard two doses of HAV vaccine over 6–12 months [25].

7.2.7	In the absence of obstetric complications, normal vaginal delivery can be recommended if the woman is receiving effective cART for HIV, irrespective of HCV viral load.	2C
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As HCV antiviral therapy is contraindicated in pregnant women due to possible teratogenicity, mode of delivery remains the only possible risk factor amenable to intervention. No randomised studies of CS compared to normal vaginal delivery to prevent vertical transmission of HCV have been performed. In HCV mono-infection, two meta-analyses failed to show a significant decrease in HCV vertical transmission among women who underwent CS compared with women who gave birth vaginally (OR 1.10–1.19) [48]. In the first European Paediatric Hepatitis Network (EPHN) cohort, a subgroup analysis of women with both HCV and HIV ($n=503$; 35.4%) demonstrated a reduced risk of vertical transmission of HCV with CS (OR 0.43; 95% CI 0.23–0.80) [65]. However, in a later analysis also from the EPHN ($n=208$; 15.0%) no such association was found (OR 0.76; 95% CI 0.23–2.53) [40]. In this later analysis, the rate of vertical transmission of HCV was reduced (8.7% vs 13.9%) and more women probably received cART (41%), which was associated with a significant HCV viral load reduction compared to those who received HIV monotherapy or no therapy (OR 0.26; 95% CI 0.07–1.01). There was also a trend towards lower HCV viral load in this group, which may in part explain the findings. In addition, in a small French cohort of women with both HCV and HIV (29% on cART), rates of vertical transmission did not differ significantly between infants born by vaginal delivery or CS [66]. A recent systematic review concluded that no intervention, in terms of mode of delivery, obstetric intervention or avoidance of breastfeeding, reduces the risk of HCV transmission [67]. cART should be given to all pregnant women with both HCV and HIV, regardless of CD4 cell count or HIV viral load because of the evidence of increased HIV vertical transmission in this group.

7.2.8	cART should be continued postpartum in all women with both HIV and HCV regardless of HCV viraemia, fibrosis stage or CD4 cell count.	1A
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Recommendations for lifelong ART are in line with current BHIVA guidelines [68] and section 6 in these guidelines. Furthermore, effective HIV suppression improves liver histology even in the absence of effective HCV treatment [69,70].

7.3 References

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