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HIV TREATMENT BULLETIN

HTB is published in electronic format by HIV i-Base. As with all i-Base publications, subscriptions are free and can be ordered using the form on the back page or directly online:

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EDITORIAL

The third issue of HTB in 2018 features antiretroviral news, reviews of studies about drug pricing and HIV and pregnancy and two new guidelines online for comment.

We lead with approval in the US of the integrase inhibitor bicitegravir, in a fixed dose combination (FDC) with emtricitabine and TAF and of a generic FDC using a lower dose of efavirenz.

Regulatory decisions for the EU are expected later this year.

In the UK, pricing is likely to drive access – when the two largest HIV manufacturers will both have single-pill, once-daily, integrase-based FDCs.

A new review of drug pricing highlights again the difference between manufacturing cost and pricing, even for generic drugs.

We also report the launch of a large new study of ART in pregnancy, that includes dolutegravir, and, notably both TAF and TDF despite a recent (flawed) review in the BMJ calling for a return to AZT. Plus a new review about ART safety, where we also question some of the conclusions.

Two new UK guidelines from BHIVA are online for comment: UK standards of care and the HIV pregnancy guidelines. Both are updating previous versions from five years ago.

Finally, we highlight online resources that bring together a range of interviews, experiences and blogs from diverse activist involved in HIV care.

STOP PRESS: plus news that an NHS clinic in London will now prescribe generic PrEP...

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i-Base 2018 appeal

we still need your help...

Last year we launched a funding appeal to help i-Base continue to provide free publications and services.

Your help has been inspiring – and we hope this support will continue during 2018. If 1000 people support us with £5 a month we will be on course to meet our shortfall.

All help is appreciated.

<http://i-base.info/i-base-appeal-we-need-your-help>



ANTIRETROVIRALS

Bictegravir approved in the US in new integrase-inhibitor based FDC (Biktarvy)

Simon Collins, HIV i-Base

On 7 February 2018, the US FDA approved a new fixed dose combination (FDC) containing bictegravir, emtricitabine and tenofovir alafenamide (TAF). [1, 2]

Bictegravir is an integrase inhibitor with a 50 mg dose that does not need to be boosted or taken with food. It is coformulated with 200 mg emtricitabine and a 25 mg dose of TAF.

Bictegravir has a plasma half-life of 18 hours, which suggests some flexibility for adherence and a resistance profile that might retain sensitivity to resistance mutations associated with raltegravir and elvitegravir but that is similar to dolutegravir. [3]

Approval is based on results from four ongoing randomised phase 3 studies.

The FDC is manufactured by Gilead Sciences and will be marketed with the brand name Biktarvy.

For more details please see the full prescribing information. [4]

C O M M E N T

Faster US approval was due to a Priority Review designation, that enables companies to buy and submit vouchers for an FDA decision with six rather than ten months.

This FDC has already been submitted to the EMA for European approval, with a decision expected later in 2018.

Pricing information was not included in the press release but will play a key role in uptake of the bictegravir FDC, given that dolutegravir is coformulated with two off-patent NRTIs and ViiV Healthcare have ongoing studies using dolutegravir with only lamivudine.

Almost immediately after the bictegravir FDC approval, ViiV Healthcare announced plans for a study that is not yet even listed on the clinical trials registry. This will switch people who are stable on TAF-containing combinations to dolutegravir/lamivudine dual therapy. [5]

Also following the approval, ViiV filed a lawsuit alleging that Gilead was infringing dolutegravir patents. ViiV is seeking "financial redress". [6]

References

1. FDA HIV listserv. FDA approves BIKTARVY tablets (Fixed Dose Combination). (07 February 2018).
2. U.S. Food and Drug Administration approves Gilead's Biktarvy (bictegravir, emtricitabine, tenofovir alafenamide) for treatment of HIV-1 infection. (07 February 2018).
<http://www.gilead.com/news/press-releases>

3. Tsiang M et al. Antiviral activity of bictegravir (GS-9883), a novel potent HIV-1 integrase strand transfer inhibitor with an improved resistance profile. *Antimicrob Agents and Chem.* (September 2016). doi: 10.1128/AAC.01474-16.
<http://aac.asm.org/content/early/2016/09/13/AAC.01474-16.abstract>
4. Biktarvy prescribing information and patient leaflet.
<https://biktarvy.com>
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210251s000lbl.pdf (PDF)
5. ViiV press release. ViiV Healthcare launches eighth phase III study in two-drug regimen programme for HIV-1 treatment. (08 February 2018).
<https://www.gsk.com/en-gb/media/press-releases>
6. Beasley D. US FDA approves Gilead triple HIV drug, rival files lawsuit. *Reuters.* 7 February 2017.
<https://www.reuters.com/article/us-gilead-sciences-fda/u-s-fda-approves-gilead-triple-hiv-drug-rival-files-lawsuit-idUSKBN1FR3AJ>

US approve a lower dose efavirenz (400 mg) based generic FDC (Simfi Lo)

Simon Collins, HIV i-Base

On 7 February 2018, the US FDA approved a new generic fixed dose combination (FDC) that uses a lower dose of efavirenz (400 mg rather than 600 mg) together with lamivudine and tenofovir DF. [1]

Approval is primarily based on results from the randomised double-blind ENCORE1 study in 630 treatment-naive individuals that reported results three years ago. ENCORE1 reported similar efficacy with slightly fewer side effects in the 400 mg vs 600 mg efavirenz group. [2]

The most common psychiatric side effects were: abnormal dreams (8.7% vs 11.3%), insomnia (6.2% vs 6.5%), somnolence (3.1% vs 3.9%), depression (3.1% vs 1.6%), nightmare (1.9% vs 2.6%), sleep disorder (2.2% vs 1.3%), and anxiety (1.2% vs 1.3%), in the 400 mg vs 600 mg groups respectively.

Central nervous system (CNS) symptoms were reported by 40% vs 48% with dizziness (27% vs 35%) and headache (11% vs 11%) in the 400 mg vs 600 mg groups respectively. Different types of rash occurred in 32% vs 26%, with grade 3-4 rash reported in 3% vs 1% (all 600 mg vs 400 mg).

Approval is for adults and children weighing >35 kg.

The FDC is manufactured by Mylan and will be marketed with the brand name Simfi Lo.

For full details see the produced information for the FDC and for the individual drug components. [3]

C O M M E N T

The option to use this new reduced dose efavirenz-based FDC is welcome – and reducing the dose of a drug that was still under patent protection is an achievement – but results from ENCORE1 were first presented almost five years ago. [4]

Although this new formulation might improve quality of life for some people, the reduction in side effects with the 400 mg dose was modest. For this reason, efavirenz is no-longer recommended as a preferred first-line combination in UK guidelines.

Earlier this month Mylan also announced approval in the US and EU of their generic 600 mg efavirenz, that comes with 180 days marketing exclusivity. [5]

The Mylan low dose efavirenz FDC was granted FDA tentative approval (for use outside the US, in association with PEPFAR, even where there is still patent or exclusivity market protection for the product in the US) in March 2017. [6]

References

1. FDA HIV listserv. FDA approves SYMFI LO Tablets (Fixed Dose Combination). (07 February 2018)
2. ENCORE1 study group. Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial. *Lancet*. 2014 Apr 26;383(9927):1474-1482. doi: 10.1016/S0140-6736(13)62187-X. Epub 2014 Feb 10. [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(13\)62187-X/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)62187-X/fulltext)
3. Simfi Lo. Highlights of prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208255s000lbl.pdf (PDF)
4. Puls R et al. A daily dose of 400mg efavirenz (EFV) is non-inferior to the standard 600mg dose: week 48 data from the ENCORE1 study, a randomised, double-blind, placebo controlled, non-inferiority trial. 7th IAS Conference on HIV Pathogenesis, Treatment and Prevention, 30 June – 3 July 2013, Kuala Lumpur. Oral late breaker abstract WELBB01. <http://pag.ias2013.org/Abstracts.aspx?SID=74&AID=3137>
5. Mylan PR. Mylan expands access to HIV/AIDS medicines with launch of first generic Sustiva tablets. (01 February 2018). <http://newsroom.mylan.com/2018-02-01-Mylan-Expands-Access-to-HIV-AIDS-Medicines-with-Launch-of-First-Generics-Sustiva-R-Tablets>
6. US FDA. FDA antiretrovirals approved and tentatively approved in association with the President's Emergency Plan Expedited Review Process. 193. Tentative approval 10 March 2017. <https://www.fda.gov/InternationalPrograms/PEPFAR/ucm119231.htm>

ViV announces phase 3 study switching to dolutegravir/3TC dual therapy from TAF-containing ART

Simon Collins, HIV i-Base

On 8 February 2018, ViV Healthcare announced plans for a new phase 3 switch study using dual therapy of dolutegravir/3TC. [1]

The new study, called TANGO, plans to randomise 550 HIV positive people on stable ART containing tenofovir alafenamide (TAF) to either continue current treatment or switch to dual therapy using dolutegravir/3TC. The study will have sites in the US, Europe, Australia and Japan.

This will become the eighth phase 3 study using dolutegravir/3TC dual therapy. It will be a non-inferiority study with a primary endpoint of viral suppression (<50 copies/mL) at week 48.

A footnote in the press release notes that the TANGO study is not yet registered on clinicaltrials.gov.

C O M M E N T

While the research question is important, the timing of this announcement seems rushed coming only a few hours after US approval for bicitegravir/emtricitabine/TAF in the FDC Biktarvy. [2]

TAF is integrated into all new Gilead FDCs and currently is used to justify a higher price compared to tenofovir DF which recently came off patent.

References

1. ViV press release. ViV Healthcare launches eighth phase III study in two-drug regimen programme for HIV-1 treatment. (08 February 2018). <https://www.gsk.com/en-gb/media/press-releases>
2. U.S. Food and Drug Administration approves Gilead's Biktarvy (bicitegravir, emtricitabine, tenofovir alafenamide) for treatment of HIV-1 infection. (07 February 2018). <http://www.gilead.com/news/press-releases>

US darunavir label updated: drug interactions and pregnancy

Simon Collins, HIV i-Base

Recent updates to the full prescribing information for darunavir includes changes linked to drug interactions and use in pregnancy. [1, 2]

Table 11 includes new information about anticonvulsants, antifungals, antipsychotics, narcotic analgesics metabolized by CYP3A, and platelet aggregation inhibitor as follows:

- Clonazepam. Clinical monitoring of anticonvulsants that are metabolised by CYP3A is recommended
- Perphenazine. A decrease in the dose of antipsychotics that are metabolised by CYP3A or CYP2D6 may be needed when co-administered with darunavir/ritonavir.
- Narcotic analgesics metabolised by CYP3A: e.g. fentanyl, oxycodone. Careful monitoring of therapeutic effects and adverse reactions associated with CYP3A-metabolised narcotic analgesics (including potentially fatal respiratory depression) is recommended with co-administration.
- Tramadol. A dose decrease may be needed for tramadol with concomitant use.
- Platelet aggregation inhibitor ticagrelor. Co administration of darunavir/ritonavir and ticagrelor is not recommended.

The section on use in pregnancy includes a pharmacology study in 35 HIV positive pregnant women comparing once-daily and twice-daily dosing. Results included lower drug exposure during the third trimester, especially in the once-daily arm. All 29 infants with available results were HIV negative at delivery or 16 weeks postpartum.

Please see full prescribing information for full details.

References

1. US FDA HIV email update. Darunavir (Prezista) label revised. (30 January 2018).
2. US FDA HIV email update. Darunavir/cobicistat (Prezcobix) label revised. (30 January 2018).

TREATMENT ACCESS

75% of WHO essential medicines could be cheaper: UK and South Africa both overpay

Polly Clayden, HIV i-Base

Most medicines in The WHO Model List of Essential Medicines (EML) can be manufactured and sold profitably at very low cost in all countries – according to an analysis published in BMJ Global Health, 29 January 2018.

The EML, created in 1977, includes medicines judged to be necessary for functional health systems. But many are unaffordable in nearly all low-income countries and some middle-income countries.

Andrew Hill and colleagues conducted an analysis to estimate generic prices for all medicines in solid oral dosage forms included in the EML. This group have previously used similar methods to analyse production costs for viral hepatitis, tuberculosis (TB) and cancer drugs.

The authors developed a generic price estimation formula by reviewing published analyses of cost of production for medicines and assuming manufacture in India – including costs of formulation, packaging, tax and a 10% profit margin.

They retrieved data on per-kilogram prices of active pharmaceutical ingredient (API) exported from India from an online database (infodriveindia.com). They then compared these estimates with the lowest available prices for HIV, TB and malaria drugs worldwide, and current prices in the UK, South Africa and India.

They were able to calculate production costs and estimated generic prices for 148/197 (75%) of medicines on the EML, showing that most essential medicines can be manufactured at low cost. Although most medicines on the EML are off-patent, they found 214/277 comparable prices in the UK, 142/212 in South Africa and 118/298 in India to be greater than the price expected based on production costs and a 10% profit margin.

The estimated generic prices ranged from US\$0.01 per tablet (glyceryl trinitrate 500 µg) to US\$1.45 per tablet (darunavir 800 mg), and were strongly skewed towards lower prices in the range.

The authors found a strong correlation between the estimated generic prices with current global lowest prices for HIV, TB and malaria drugs. Lowest available prices were higher than estimated generic prices for 214/277 (77%) of comparable products in the UK, 142/212 (67%) in South Africa and 118/298 (40%) in India. Lowest available prices were over three times the estimated generic price for 47% of products compared in the UK and 22% in South Africa.

Overall the authors concluded that most items in the WHO EML are sold in the UK and South Africa at significantly higher prices than those calculated from production costs. “Generic price estimation and international price comparisons can be expanded to empower government price negotiations, and to support cost-effectiveness calculations at international and national levels. Assuming an absence of barriers to market entry, a wide range of the drugs on the EML can be profitably sold at very low prices in all countries” they wrote.

C O M M E N T

This analysis is excellent, contains a wealth of supplementary information and is worth reading in full. Generic competition (and huge demand) led to massive price reductions for antiretrovirals in the early 2000s.

Similar price reductions for more medicines would enable wider treatment of other diseases in low- and middle-income countries.

Reference

Hill AM et al. Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Global Health*. DOI: 10.1136/bmjgh-2017-000571. 29 January 2018.
<http://gh.bmj.com/content/3/1/e000571>

PREGNANCY & PMTCT

New HIV pregnancy study uses latest ART: IMPAACT 2010 study (VESTED) study includes dolutegravir and tenofovir alafenamide (TAF)

Polly Clayden, HIV i-Base

The US National Institutes of Health recently launched VESTED: a large international study comparing the safety and efficacy of three ART regimens for HIV positive pregnant women and their infants. [1]

VESTED or IMPAACT 2010 is a phase 3 study that aims to enrol 639 ART naive HIV positive women at 14–28 weeks gestation. [2]

The women will be randomised to one of three treatment arms.

- Efavirenz (EFV)/emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF).
- Dolutegravir (DTG)/FTC/ tenofovir alafenamide (TAF).
- DTG/FTC/TDF.

Their infants will also be enrolled and will receive local standard of care for HIV prophylaxis and infant feeding options, which might be breast or formula feeding.

Primary endpoints include the proportion of mothers with viral load less than 200 copies/mL at delivery. The study will also compare rates of adverse pregnancy outcomes, plus maternal and infant adverse events, between arms.

Both mothers and infants will be monitored for 50 weeks after delivery. The study is expected to last for approximately three years.

The first mothers have begun receiving treatment at clinical trial sites in Zimbabwe. Sites in the US, Botswana, Brazil, Haiti, India, Malawi, South Africa, Tanzania, Thailand, Uganda, are open for enrolment or expected to open in the next few months.

C O M M E N T

VESTED is a key ART optimisation study, so it is excellent news that it has started. It is also one of very few studies looking at TAF in pregnancy.

The randomised DolPHIN-2 study, comparing DTG-based to EFV-based ART in late-presenting women, with sites in South Africa and Uganda, has also recently begun. [3]

Almost 60 low- and middle-income countries have adopted or have plans to transition to DTG-based ART and PEPFAR is supporting rapid uptake in the countries where it operates. [4, 5]

Early adoption of DTG has led to reassuring pregnancy data from Botswana, which, combined with those from high-income countries will make countries more comfortable with adopting DTG for pregnant women. [6] But clinical trial data on DTG are still needed and any data on TAF in pregnancy are woefully lacking.

It is also notable that two arms of the NIH funded VESTED study include TDF/FTC, despite the much-rejected recent recommendation from the British Medical Journal (BMJ) against using these drugs in pregnancy. [7]

The ADVANCE study, ongoing in South Africa, is evaluating the same three ART regimens as VESTED in non-pregnant adults but any women that become pregnant during the study can remain on their randomised treatment. [8]

The i-Base Fit for Purpose report tracks and reviews ongoing or planned ART optimisation initiatives for adults and children. [9] Our next edition will be published in March 2018 to coincide with CROI.

References

1. US National Institutes of Health press release. NIH begins large HIV treatment study in pregnant women. 24 January 2018. <https://www.nih.gov/news-events/news-releases/nih-begins-large-hiv-treatment-study-pregnant-women>
2. US National Institutes of Health. Evaluating the efficacy and safety of dolutegravir-containing versus efavirenz-containing antiretroviral therapy regimens in HIV-1-infected pregnant women and their infants (VESTED). ClinicalTrials.gov Identifier: NCT03048422. <https://clinicaltrials.gov/ct2/show/NCT03048422>
3. US National Institutes of Health. Dolutegravir in pregnant HIV mothers and their neonates (DolPHIN-2). ClinicalTrials.gov Identifier: NCT03249181. <https://clinicaltrials.gov/ct2/show/NCT03249181>
4. World Health Organisation. Transition to new antiretrovirals in HIV programmes. July 2017. <http://apps.who.int/iris/bitstream/10665/255888/1/WHO-HIV-2017.20-eng.pdf> (PDF)
5. Sibery G. PEPFAR support for transition to tenofovir disoproxil fumarate/lamivudine/dolutegravir (TLD). ICASA Conference, Abidjan, Cote d'Ivoire. 4–9 December 2017.
6. Clayden P. Preliminary results on dolutegravir use in pregnancy are reassuring. HTB. 10 August 2017. <http://i-base.info/htb/32182>
7. Clayden P. Experts disagree with controversial BMJ support for older HIV drugs in pregnancy. HTB. 1 October 2017. <http://i-base.info/htb/32705>
8. US National Institutes of Health. ADVANCE Study of DTG + TAF + FTC vs DTG + TDF + FTC and EFV + TDF+FTC in First-line Antiretroviral Therapy (ADVANCE). ClinicalTrials.gov Identifier: NCT03122262. <https://clinicaltrials.gov/ct2/show/NCT03122262>
9. Clayden P. Antiretroviral treatment optimisation for adults and children. 20 July 2017. <http://i-base.info/htb/32022>

Association between timing of maternal ART and risk of infants born small for gestational age in Dutch ATHENA cohort

Polly Clayden, HIV i-Base

HIV positive women receiving ART before conception had an increased risk of infants being born small for gestational age in the Netherlands, according to data published in 19 January 2018 in PLOS ONE. However, the link is only related to protease inhibitors and the study makes no adjustment for changes in standards of care.

The study included singleton uninfected infants born to mothers registered in the ATHENA cohort 1997–2015. The investigators used multivariate logistic regression analysis for single and multiple pregnancies to evaluate predictors of small for gestational age (SGA), preterm delivery and low birth weight.

In total, 1392 singleton births – born to 1022 mothers – were included in the analysis. Of the mothers, 550 received ART before or at the time of conception for a median of 3.48 years (IQR 2.08–5.35).

Women who started ART before conception were older (32.7 vs 28.8), on an NNRTI-based regimen (47.8% vs 20.8%) and with a lower nadir CD4 count (55.6% vs 22.0% were of <200 cells/mm³) compared to women who started ART after conception, all $p < 0.001$. They were also more often multiparous (70.2% vs 62.8%), $p < 0.01$. Median baseline CD4 count at the start of pregnancy were similar between the two groups.

Of the total births, 331/1392 (23.8%) children were SGA (birth weight less than 10th percentile for gestational age): 27.3% vs 21.5% in women who started ART before and after conception respectively, $p = 0.01$.

In multivariate analysis, adjusting for ART regimen, region of origin and parity (variables with $p \leq 0.1$ in the univariate analysis) the risk for SGA was significantly higher among women who started ART before vs after conception: OR 1.35 (95% CI 1.03 to 1.77), $p = 0.028$.

Multivariate analysis also suggested a significantly increased risk of SGA for mothers who received a PI-based regimen before conception vs those who received this regimen after conception: OR 1.49 (95% CI 1.08 to 2.10), $p = 0.016$.

The investigators noted that they did not see this increased risk of SGA for infants of mothers who started a NNRTI-based regimen before vs after conception: OR 0.97 (95% CI 0.62 to 1.52), $p = 0.91$.

Preterm delivery (<37 weeks) occurred in 14.7% of infants. When the investigators looked at the association between preterm delivery and preconception ART, this was significant in univariate analysis, but it did not remain so in multivariate analysis: OR 1.39 (95% CI 0.94 to 1.92), $p = 0.06$. Nor did the risk for very preterm delivery (<32 weeks): OR 1.25 (95% CI 0.86 to 1.86), $p = 0.22$.

Low birth weight (<2.5 kg) was seen in 12.4% of infants.

In multivariate analysis, the risk of low birth weight was not statistically different between women who started ART before vs after conception: OR 1.34, (95% CI 0.94 to 1.92), $p = 0.11$. And there was no difference between the two groups in very low birth weight: OR 1.36 (95% CI 0.64 to 2.90), $p = 0.42$.

COMMENT

Perhaps more striking than the elevated risk of SGA among women who received ART before conception was the comparison that investigators made to the Dutch HIV negative Generation R population. In this group the overall risk of SGA was far lower (1.8%). And in this was similar the subset of HIV negative women of sub Saharan African origin (1.4%).

This suggests differences directly or indirectly associated with being HIV positive had a larger impact than the differences between timing of starting ART.

In the discussion, the investigators note that few data exist describing a potential link between SGA and HIV, ART and PI-based regimens. And the data are not consistent among the existing studies. One study found an increased risk of SGA in HIV positive women who were not receiving ART.

More information is needed about the mechanisms underlying foetal growth restriction in HIV positive pregnant women receiving ART. The investigators stressed that only when the potential impact of ART is fully understood can the optimal regimen for HIV positive women of childbearing age be determined.

This dataset compiled results from nearly 20 years during a period of very different approaches to HIV treatment. Despite mentioning this as a limitation – “This study covered several years of observation. Over time the guidelines for cART initiation changed and were based on different CD4-cell count levels.” – the authors did not stratify results by calendar year.

It is important that no association between timing of ART and SGA (or with low birth weight) was seen with NNRTI-based ART, which most women now use. PI use is already avoided in pregnancy and in the future access to integrase inhibitors will increasingly become standard of care.

References

Snijedewind IJM et al. Preconception use of cART by HIV-positive pregnant women increases the risk of infants being born small for gestational age. PLOS ONE (2018), 13(1):e0191389. DOI: 10.1371/journal.pone.0191389. (19 January 2018).

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0191389>

TRANSMISSION & PREVENTION

London clinic to prescribe generic PrEP privately at £55 for 30 tablets

Simon Collins, HIV i-Base

On 10 February 2018, the sexual health clinic at 56 Dean Street in Soho launched a new programme that will provide generic tenofovir DF/emtricitabine, the dual pill that protects against HIV.

This will use private prescriptions in a way that will still let people access free NHS monitoring. The initial price is slightly more than the cheapest online supplier – approximately £55 compared to £35 for 30 tablets. Although online suppliers provide discounts for buying in bulk, sometimes buying PrEP online includes additional import taxes. The Dean Street price might also be reduced in the future. The price for the patent version is approximately £400.

Buying generic PrEP online is safe and legal for individuals, but clinics in England have, until now, not been able to provide private prescriptions for the generic formulations. This challenges the situation that allows NHS clinics in Scotland to prescribe generic PrEP free to their patients. Until now, drug commissioning services in England have been waiting for a decision on patent rights currently waiting in the European courts.

People will still have to make routine appointments for HIV testing and other monitoring for PrEP, but they will be able to opt in to private prescription for generic PrEP.

This programme is also an attempt to manage the rapid enrolment in the ongoing PrEP IMPACT study. Launched in September 2017, the 56 Dean Street clinic was fully enrolled by November.

Even at sites where places are still available, the study has already recruited more than half of the original 10,000 allocation.

Although perhaps ten thousand people in London are believed to be buying generic PrEP online – mainly gay and bisexual men – exact figures are not available.

It is unclear whether Gilead Sciences will challenge the new clinic programme.

For more details see the PrEPshop website:

<http://dean.st/prepshop>

GUIDELINES

BHIVA standards of HIV care (2018): online for comment

BHIVA.org

A draft of the 2018 update to the BHIVA *Standards of Care for People Living with HIV* is now online for public comment.

The deadline for comments is 17.30 on Tuesday 20 February 2018.

<http://www.bhiva.org/standards-of-care-consultation.aspx>

This publication is an update to the 2013 edition.

The standards cover:

- Testing, diagnosis and prevention
- Person-centred care
- HIV outpatient care and treatment
- Complex HIV care
- Sexual and reproductive health
- Psychological care
- HIV across the life course
- Developing and maintaining excellent care.

UK HIV pregnancy guidelines (2018): online for comment

BHIVA.org

A draft of the 2018 update to the *Guidelines for the management of HIV infection in pregnant women (BHIVA)* is now online for public comment.

The deadline for comments is Tuesday 20 February 2018.

<http://www.bhiva.org/pregnancy-guidelines-consultation.aspx>

The guidelines provide guidance on best clinical practice in the treatment and management of pregnant women living with HIV in the UK and their infants.

The scope includes guidance on the use of antiretroviral therapy (ART) both to prevent vertical transmission of HIV and for the welfare of the mother herself, guidance on mode of delivery and recommendations in specific patient populations where other factors need to be taken into consideration, such as co-infection with other agents.

The 2018 guidelines have identified significant developments that have either led to a change in recommendation or a change in the strength of recommendation. More detail has been added in areas of controversy, particularly breastfeeding. A new section on the postnatal management of women has been added and prevalence data from the UK have been updated. Other changes include:

- All women are now recommended to start on treatment and remain on it lifelong, including elite controllers.
- The length of infant PEP has been shortened where risk of vertical transmission is very low.
- New data on the safety of raltegravir, rilpivirine, dolutegravir and elvitegravir have been added.
- Discussion on choice of NRTIs - especially that BHIVA support the safety of tenofovir DF during pregnancy.
- Information has been added on tenofovir alafenamide for hepatitis B and direct acting agents for hepatitis C.
- Updated infant feeding advice to include new data on breastfeeding and the emotional impact not breastfeeding may have on women. We discuss the use of cabergoline in non-breastfeeding women.
- Expanded section on 'The psychosocial care of women living with HIV during and after pregnancy' and moved its position within the guidelines.
- A new section on the postnatal management of women living with HIV.

ON THE WEB

Online resources

HIV conversations in the UK

A growing online resource of interviews with people who have been involved with the response to HIV in the UK.

Each interview lasts about 30 minutes and follows an overlapping structure of about 12 questions.

The majority of interviews are with HIV positive community activists but include other support workers, volunteers, doctors and nurses.

The diversity of the group provides insight into some inspiring stories from a few of the people who have made a difference to the HIV response in the UK.

So far, interviewees include Jonathan Blake, Jane Bruton, Ben Collins, Paul Decle, Barry Drew, Brian Gazzard, Catarina, Jean Hunt, Dan Glass, Fernando Monteiro, Angelina Namiba, Greg Owen, Silvia Petretti and Marc Thompson.

For further information, please contact Patrick Cash.

<http://hiv-conversations.uk>

<https://gmg.org.uk/hiv-conversations-medicinema-chelsea-westminster-hospital>

Women in Science: IAS feature

As part of the growing collection of online interviews, the International AIDS Society this month featured five women to share their experiences and insights into being a female scientist.

They are at different stages of their career paths and from different countries and backgrounds.

These are their stories...

<http://www.iasociety.org/Membership/IASONEVOICE/Stories/Women-in-science?>

- Sharon Lewin (Australia)
- Tavitiya Sudjaritruk (Thailand)
- Glenda Gray (South Africa)
- Kristel Paola Ramirez Valdez (Guatemala)
- Judy Auerbach (United States)

Yale CRIT conference: blogs on the threats from changes to drug regulation in the US and Europe

Last year a US conference brought together a diverse group of healthcare activists concerned about changes to drug regulations.

One outcome is a series of blogs from participants.

<https://law.yale.edu/centers-workshops/collaboration-research-integrity-and-transparency-crit/critical-thinking-blog>

- **Seven thoughts on the history and present practices of the FDA and uses of prescription drugs** - Donald Light and Joel Lexchin
- **Transparency by sleight of hand?** - Matthew Herder
- **Regulating medical products in the interest of the public** - Alain Alsahlani
- **Regulators must act in the public interest when considering real world evidence: examples from TB and HIV treatments** - Marcus Low and Catherine Tomlinson
- **Supporting evidence-informed practice by improving clinical research** - Rita Banzi
- **Randomised clinical trials will be needed for the foreseeable future** - Susan Ellenberg
- **What does a pro-patient, pro-public health regulatory agency look like?** - Michael Carome
- **Federal "right to try" legislation - perpetuating a misguided skepticism towards the FDA** - Jeanie Kim
- **Patient advocacy must be rooted in evidence and science literacy to make a real difference** - Fran Visco
- **Are payers willing to engage in evidence-based coverage decisions?** - Dan Ollendorf
- **What is the state of the evidence base for medical products we use currently?** - Tom Jefferson
- **Why high quality evidence matters: lessons from HIV activism and drug development** - Simon Collins
- **Deregulatory pressures on the FDA** - Alison Bateman-House and Arthur Caplan

FUTURE MEETINGS

Conference listing 2018

The following listing covers some of the most important upcoming HIV-related meetings and workshops.

8th International Workshop of HIV & Women

2 – 3 March 2018, Boston

www.virology-education.com

Conference on Retroviruses and Opportunistic Infections (CROI 2018)

4 – 7 March 2018, Boston

www.croiconference.org

BHIVA 'Best of CROI' Feedback Meetings 2018

Monday 19 March, London

Tuesday 20 March, Birmingham

Wednesday 21 March, Haydock

Tuesday 27 March, Cardiff

Wednesday 28 March, Wakefield

Thursday 29 March, Edinburgh

www.bhiva.org/BestofCROI2018.aspx

4th Joint BHIVA/BASHH Spring Conference

17 – 20 April 2018, Edinburgh

www.bhiva.org

12th INTEREST

29 May – 1 June 2018, Kigali

interestworkshop.org

Intl Workshop on Clinical Pharmacology 2018

Tbc May 2018, Washington

www.virology-education.com

22nd International AIDS Conference (AIDS 2018)

23 – 27 July 2018, Amsterdam

www.aids2018.org

International Workshop on HIV & Aging

13 –14 September 2018, New York, USA.

www.virology-education.com

Australasian HIV&AIDS Conference 2018

24 – 26 September 2018, Sidney

www.hivaidsconference.com.au

HIV Glasgow 2018

28 – 31 October 2018, Glasgow

www.hivglasgow.org

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

All i-Base publications are available online, including editions of the treatment guides.

<http://www.i-Base.info>

The site gives details about services including the UK Community Advisory Board (UK-CAB), our phone service and Q&A service, access to our archives and an extensive range of translated resources and links.

Publications and regular subscriptions can be ordered online.

The Q&A web pages enable people to ask questions about their own treatment:

<http://www.i-base.info/qa>

i-Base treatment guides

i-Base produces six booklets that comprehensively cover important aspects of treatment. Each guide is written in clear non-technical language. All guides are free to order individually or in bulk for use in clinics and are available online in web-page and PDF format.

<http://www.i-base.info/guides>

- Introduction to ART (September 2016)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (November 2016)
- HIV testing and risks of sexual transmission (June 2016)
- Guide to changing treatment and drug resistance (February 2015)
- Guide to HIV, pregnancy & women's health (December 2015)

New pocket guides

A new series of pocket-size concertina folding leaflets that is designed to be a very simple and direct introduction to HIV treatment.

The first five pocket leaflets are: Introduction to ART, HIV and pregnancy, ART and quality of life, UK guide to PrEP and HCV/ HIV coinfection.

We hope these are especially useful as low literacy resources.

The leaflets use simple statements and quotes about ART, with short URL links to web pages that have additional information in a similar easy format.

Order publications and subscribe online

All publications can be ordered online for individual or bulk copies. All publications are free. Unfortunately bulk orders are only available free in the UK.

<http://i-base.info/order>



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• **HIV Treatment Bulletin (HTB) every two months** **by e-mail**

• **Pocket leaflets** - *A7 small concertina-folded leaflets (2017)*

Pocket HCV coinfection **quantity** _____ **Pocket PrEP** **quantity** _____

Pocket ART **quantity** _____ **Pocket pregnancy** **quantity** _____

Pocket side effects **quantity** _____ **PrEP for women** **quantity** _____

• **Booklets about HIV treatment**

ART in pictures: HIV treatment explained (*June 2017*): 32-page A4 booklet **quantity** _____

Guide to hepatitis C coinfection (*April 2017*): 52-page A5 booklet **quantity** _____

UK Guide To PrEP (*November 2016*): 24-page A5 booklet **quantity** _____

Introduction to ART (*September 2016*): 48-page A5 booklet

HIV and quality of life: guide to side effects and long-term health (*Sept 2016*): 96-page A5 **quantity** _____

Guide to HIV testing and risks of sexual transmission (*July 2016*): 52-page A5 booklet **quantity** _____

Guide to HIV, pregnancy and women's health (*November 2015*): 52-page A5 booklet **quantity** _____

Guide to changing treatment: what if viral load rebounds (*Jan 2018*): 24-page A5 booklet **quantity** _____

• **Other resources**

HIV Treatment 'Passports' - Booklets for patients to record their own medical history **quantity** _____

Phoneline posters (A4) **quantity** _____

Please fax this form back, post to the above address, or email a request to HIV i-Base:

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