A New Era in HIV Treatment: Generics and Quasi-Generics

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Chair, Fair Pricing Coalition
Learning Objectives

Upon completion of this presentation, learners should be better able to:

• Describe the burden of HIV prescription drug pricing and the potential value of cost containment, including lower-cost brand ("quasi-generic") and generic antiretrovirals in HIV treatment

• Assess complexities of drug pricing across payor systems and variability of potential cost savings

• Discuss cost as an increasingly important HIV treatment consideration and the potential for heightened payor regulation
Faculty and Planning Committee Disclosures
Please consult your program book.

- Treatment Action Group receives support from ViiV Healthcare, Gilead Sciences, Janssen Pharmaceuticals, and Merck
- Tim Horn does not receive any direct support or honoraria from any pharma

Off-Label Disclosure
The following off-label/investigational uses will be discussed in this presentation:

- There will be no off-label/investigational uses discussed in this presentation
Pharma Spending: % of Health Spending (2015)

Organisation for Economic Cooperation and Development.
https://data.oecd.org/healthres/pharmaceutical-spending.htm


Per-Person Spending (2017)

ACA Marketplace Plans

![Graph showing per-person spending for ACA Marketplace Plans](http://lab.express-scripts.com/lab/drug-trend-report/~media/2b56ec26c9a04ec2bcca0e9bf1ea8ff1.ashx)

Medicaid

![Graph showing per-person spending for Medicaid](http://lab.express-scripts.com/lab/drug-trend-report/~media/2b56ec26c9a04ec2bcca0e9bf1ea8ff1.ashx)

Express Scripts. 2017 drug trend report. http://lab.express-scripts.com/lab/drug-trend-report/~media/2b56ec26c9a04ec2bcca0e9bf1ea8ff1.ashx
The HIV (Treatment) Payor Patchwork

- Employer-based plans
- ACA Marketplace Plans
- Medicaid/Medicare
- Veterans Administration
- Ryan White/ADAPs
- Patient assistance programs & copay/coinsurance assistance
Why Drug Pricing Matters

1. CDC. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data United States and 6 dependent areas, 2015. 22(2).

HIV CARE CONTINUUM (2014)¹

- Need to do better with finite resources
- Evidence of payor resistance
  - Preference for older STRs; MTRs
    - 20% of plans only covering EFV/TDF/FTC; 15% of plans not covering any new (>2013) ARVs²
  - Highest coverage tiers/coinsurance amounts
- Growing recognition of cost as structural barrier to HIV prevention care and PrEP
Forecasting the Need for Cost Containment

• Ongoing efforts to repeal the ACA
• No Medicaid expansion where it is needed most
• Medicaid block grants, work requirements
• Increasing dependence on ADAP prescription drug coverage?
• Political paradox
  – bipartisan aversion to high drug prices *and* doing something bold about them
ENTER GENERICS (AND QUASI GENERICS)
### Three Pathways for Off-Patent Drugs

<table>
<thead>
<tr>
<th>Single-Source Brand (Innovator) Products</th>
<th>“Quasi-Generic” Brand (Innovator) Products</th>
<th>Multi-Source Generic (Non-Innovator) Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Doravirine/TDF/3TC</td>
<td>• EFV 400 mg/TDF/3TC</td>
<td>• Nevirapine (2012)</td>
</tr>
<tr>
<td></td>
<td>• EFV 600 mg/TDF/3TC</td>
<td>• ABC/3TC (2016)</td>
</tr>
<tr>
<td></td>
<td>• TDF/3TC</td>
<td>• Atazanavir (2018)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ritonavir (2018)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Darunavir (expected: 2020?)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• TDF/FTC (expected: 2021?)</td>
</tr>
<tr>
<td>• Cheaper (?)</td>
<td>• Cheaper still</td>
<td>• Cheapest</td>
</tr>
<tr>
<td>• Patent (20+ years) and exclusivity (5 years)</td>
<td>• Potential competition</td>
<td>• 6 months exclusivity possible</td>
</tr>
<tr>
<td>• Monopoly products</td>
<td>• Not interchangeable with any single-source products</td>
<td>• Competition based on demand</td>
</tr>
<tr>
<td>• Copay assist: likely</td>
<td>• Copay assist: yes (for now)</td>
<td>• Interchangeable with brand</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cheapest</td>
</tr>
</tbody>
</table>

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**Innovator:** New drug (chemical entities not previously approved by FDA) or new formulation manufacturer

**Patent:** PTO designation; 20-plus years of protection, but frequently challenged by generic manufacturers

**Exclusivity:** FDA designation, often concurrent with patent; no generic patent challenges during this period
Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

- **INSTI + 2 NRTIs**: DTG/ABC/3TC\(^a\) (AI)—if HLA-B*5701 negative
- **DTG + tenofovir\(^{d}/\)FTC\(^{a}\)** (AI for both TAF/FTC and TDF/FTC)
- **EVG/c/tenofovir\(^{d}/\)FTC** (AI for both TAF/FTC and TDF/FTC)
- **RAL\(^{c}\) + tenofovir\(^{d}/\)FTC\(^{a}\)** (AI for TDF/FTC, AII for TAF/FTC)

Whereas TDF and TAF are comparable and 3TC and FTC are interchangeable.

Recommended Initial Regimens in Certain Clinical Situations

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

- **Boosted PI + 2 NRTIs**: (In general, boosted DRV is preferred over boosted ATV) (DRV/c or DRV/r) + tenofovir\(^{d}/\)FTC\(^{a}\) (AI for DRV/r and AII for DRV/c)
- **(ATV/c or ATV/r) + tenofovir\(^{d}/\)FTC\(^{a}\)** (BI)
- **(DRV/c or DRV/r) + ABC/3TC\(^a\)** —if HLA-B*5701–negative (BII)
- **(ATV/c or ATV/r) + ABC/3TC\(^a\)** —if HLA-B*5701–negative and HIV RNA <100,000 copies/mL (CI for ATV/r and CII for ATV/c)

- **NNRTI + 2 NRTIs**: EFV + tenofovir\(^{d}/\)FTC\(^{a}\) (BI for EFV/TDF/FTC and BII for EFV + TAF/FTC)
- **RPV/tenofovir\(^{d}/\)FTC\(^{a}\)** (BI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm\(^3\)

- **INSTI + 2 NRTIs**: RAL\(^{c}\) + ABC/3TC\(^a\) (CII)—if HLA-B*5701–negative and HIV RNA < 100,000 copies/mL

Regimens to Consider when ABC, TAF, and TDF Cannot be Used:\(^{d}\) DRV/r + RAL (BID) (CI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm\(^3\)
- **LPV/r + 3TC\(^a\)** (BID)\(^{e}\) (CI)

HHS-Recommended Coformulated NRTIs

- **TDF/3TC (2018)**
  - Quasi-generic/branded
  - No direct competition (yet)
  - Bioequivalent to stand-alone TDF and stand-alone 3TC
  - Comparators: TDF/FTC, TAF/FTC(?)
    - ~$1,000 vs. $1,650/month
  - Copay assistance expected
  - *NOT APPROVED FOR PrEP!!!*

- **ABC/3TC (2016)**
  - Generic/unbranded
  - Several competitors
  - Bioequivalent to brand-name coformulated ABC/3TC
  - Comparator: branded ABC/3TC
    - ~$115 vs. $1,250/month
  - No copay assistance

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**ACTHIV 2018: A State-of-the-Science Conference for Frontline Health Professionals**
Low(er)-dose EFV, TDF, and 3TC

- Contains 400 mg EFV and 3TC (vs. 600 mg EFV and FTC in standard STR)
- Int’l ENCORE1 trial (n = 630)
  - Non-inferior to standard STR
  - No difference in frequency of A/Es, d/c rates, QoL, etc.
  - A/Es related to study drug more frequent in stand. arm (p=0.008)
- U.S. WAC 40% < EFV/TDF/FTC
  - ~$19,000 vs. ~$32,000; copay assist.

Approval ≠ Availability

• Generic approval often precedes commercial availability

• Availability largely determined by patent challenge rulings and confidential agreements

• Best guess for launch of generic TDF/FTC: 2021
YES, BUT WILL THEY REDUCE COSTS?
Savings from Generics: $253 Billion in 2016

Generics Cost Savings: HIV

Economic Savings Versus Health Losses: The Cost-Effectiveness of Generic Antiretroviral Therapy in the United States


Drug Pricing: The Simple Version

- Average Wholesale Price (AWP)
- Wholesale Acquisition Cost (WAC)
- Nonfederal Average Manufacturer Price (Non-FAMP)

**Generics**
- Federal Upper Limit
- State Maximum Allowable Cost
- Federal Ceiling; “Big 4” Price
- Supplemental discounts negotiated (VA and DoD)

**Private sector prices**
- Rebates to PBMs
- Copay assistance
- Other price concessions

**340B Price**
- Medicaid Price
- Supplemental rebates and discounts negotiated (including ADAPs)

**Average Manufacturer Price (AMP)**
- Best Price
- Unit rebate: 23.1% / 13% of AMP or AMP – Best Price plus CPI penalties

- Federal Supply Schedule (FSS) Price
- Federal Ceiling Price

**Nonfederal Average Manufacturer Price (Non-FAMP)**
- 76% of non-FAMP minus additional discounts
<table>
<thead>
<tr>
<th>ARV Regimen</th>
<th>Retail Pharmacy Acquisition Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand Name</strong></td>
<td></td>
</tr>
<tr>
<td>DTG + TDF/FTC or TAF/FTC</td>
<td>$3,226/month</td>
</tr>
<tr>
<td>ELV/CABO/TAF/FTC</td>
<td>$2,944/month</td>
</tr>
<tr>
<td>DTG/ABC/3TC</td>
<td>$2,718/month</td>
</tr>
<tr>
<td><strong>Mixed (Brand and Quasi-generic or Generic)</strong></td>
<td></td>
</tr>
<tr>
<td>DTG + TDF/3TC</td>
<td>$2,603/month*</td>
</tr>
<tr>
<td>DTG + ABC/3TC</td>
<td>$1,730/month</td>
</tr>
<tr>
<td><strong>All Generic</strong></td>
<td></td>
</tr>
<tr>
<td>NVP + ABC/3TC</td>
<td>$131 – $388/month</td>
</tr>
</tbody>
</table>


*NADAC data for TDF/3TC not available; based on WAC price.*
Market Forces Rule

- Unique to HIV care: limited demand among patients and providers
- Payors and the power of “NO”
- Utilization management: step therapy
  - Example: DTG plus TDF/3TC or ABC/3TC, switch to BIC/TAF/FTC or DTG/ABC/3TC with renal/bone/adherence needs
  - Difficulty of implementing population-level cost-containment measures in the face of individualized treatment needs
  - The big risk: poor virologic suppression, resistance, risk of transmission should MTR factor in to adherence challenges
Who Benefits from Cost Savings?

- No clear pathway for reinvesting cost savings in HIV prevention and care
- Recognize indirect savings to purchases and payors, along with societal benefits
- Do PLWHIV benefit?
  - Low copays on generics vs. copay assistance for monopoly products?
  - Might safety and adherence risks outweigh cost savings potential?
PATIENT AND PROVIDER PREFERENCE
Patient & Provider Choice: The Big Questions

• Is TAF preferable to TDF for all PLWHIV?
  – TAF more favorable effects on renal markers and BMD, but TDF still a Guidelines-recommended component of initial regimens for most people with HIV based on well-established safety and efficacy

• Are QD STRs preferable to QD MTRs for all PLWHIV?
  – STRs are easier to use with fewer monthly copays, but data supporting or refuting superiority are limited; STRs and MTRs among Guidelines-recommended initial regimens for most people with HIV
STR to MTR Switches: Patient & Provider Attitudes

- Southern Alberta, Canada
- 13 providers, 607 DTG/ABC/3TC STR users
- Survey: Switch from STR to DTG plus generic ABC/3TC?
- All providers: de-simplifying could be done safely
- Patients: Mixed agreeability

Case Question

- A 26-year-old male who recently tested positive for HIV presents for care. His eGFR is 120 mL/min/1.73 and he is HLA-B*5701 negative. You prescribe BIC/TAF/FTC but his insurance rejects the claim on the grounds of a formulary preference for:
  - EFV/TDF/FTC or EFV/TDF/3TC, or
  - DTG plus quasi-generic TDF/3TC (coformulated), or
  - DTG plus generic ABC/3TC (coformulated)
Your next step is to:

1. Counsel patient and resubmit prescription for DTG plus TDF/3TC
2. Counsel patient and resubmit prescription for DTG plus ABC/3TC
3. Counsel patient and resubmit prescription for EFV-based STR
4. Appeal immediately, at risk of delaying therapy start
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https://api.cvent.com/polling/v1/api/polls/sp-fvqwm8

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Conclusion

• It’s here: era of ARV drug cost considerations
• Generics and quasi-generics can potentially increase competition and lead to lower prices for purchasers and payors
  – Some payors will likely benefit more than others
• Providers and patients should discuss pricing and access, along with efficacy, safety, and ease of administration
• Increased payor regulation of formularies possible
  – Need strong guidelines addressing when this is acceptable or unacceptable
  – Report overly restrictive/dangerous measures: speakup.hiv