COMING SOON:
GENERIC ARVs

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PATENTS AND EXCLUSIVITY 101
Myriad Policies

- Patents issued >1996 have term of 20 years
- Only certain patents are eligible for extensions:
  - Delays caused by USPTO processes
  - Some 17-year patents issued before June 1995
  - Patent term restoration to account for time lost satisfying regulatory requirements
      - Cannot exceed 5 years; cannot extend patent life beyond 14 years post approval
  - Pediatric exclusivity (additional six months)
Patent and Exclusivity Timeline: The Simple Version

- Original Patent Term: 20 years
- Hatch-Waxman Extension: ~24 months
- Pediatric Exclusivity: 6 months

ANDA can be filed with FDA at start of extension period, with tentative approval during period, and marketing started at end of extension and exclusivity period.
Patent and Exclusivity Timeline: A Bit More Detail

- Original Patent Term: 20 years
- 30 mo. stay
- 5 mo. stay for NCE

- If no infringement:
  - Hatch-Waxman Amendment permits 6-month Exclusivity to generic challenger/manufacturer
THE GENERIC ARV “PIPELINE”
# Best Guess Patent Expirations: HHS-Recommended ARVs

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Combination patents: TDF/emtricitabine (2021), abacavir/lamivudine (2016), elvitegravir/cobicistat/tenofovir/emtricitabine, and *TAF-inclusive formulations*. 
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Generic Regimens of the Near Future

Darunavir
Atazanavir
Efavirenz

+ 

Abacavir + Lamivudine
Tenofovir + Lamivudine
The Big Questions

- Will these agents remain recommended by HHS guidelines?
- Single-tablet regimens (STRs) vs. multi-tablet regimens (MTRs)
  - Virtually no datasets indicating MTRs inferior to STRs
  - However... STRs preferred among PLWHIH and providers
  - All-generic STRs likely to be produced in time
Generic Regimens of the Near Future

Merck STR:
Doravirine (MK-1439) plus
generic tenofovir and lamivudine

Tobira FDC:
Cenicriviroc and generic lamivudine
For use with third agent

OTHERS???
REGULATORY REQUIREMENTS
## Regulatory Requirements

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<th>Originator/Innovator Drugs -- NDA*</th>
<th>Generic Drugs – ANDA**</th>
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<td>Animal Studies</td>
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* New drug application
** Abbreviated new drug application
Generic Equivalence

- Must contain the same active pharmaceutical ingredient (API)
- Must involve the same route of administration, formulation, and dosing
- Must also meet stringent criteria for bioequivalence
  - Extent (and, often, the rate) of absorption must not differ significantly from that of the originator drug
- *Generic drug that meets these standards should not behave any differently, either in terms of efficacy or safety outcomes*
Establishing Bioequivalence

Bioequivalence at a Glance

- **Originator**: Red line
- **Generic**: Black line

- **$T_{max}$**: time required to achieve the maximum concentration.
- **MTC**: minimum toxic concentration.
- **MEC**: minimum effective concentration.
- **Shaded area**: the therapeutic window for which efficacy and safety have been established.
Bioequivalent, Not Identical

• Despite API bioequivalence:
  – Generic may be different size, shape or color
  – May contain different inactive ingredients/exipients:
    • Binding materials
    • Flavoring agents
    • Dyes
    • Preservatives
  – Rarely a source of serious problems
Therapeutic Windows

- Narrow windows: warfarin, levothyroxine, digoxin
  - Care required when generics are used
- Wide windows: modern-day ARVs
  - Even with variation, Cmax is below max. tolerated dose (MTC)
  - Problem with older drugs (e.g., stavudine, first-generation PIs)
YES... BUT WILL THEY SAVE MONEY?
Mathematical Modeling

Quality-adjusted life expectancy, costs, and incremental cost-effectiveness ratio comparisons:

- Efavirenz (generic) + Lamvudine (generic) + Viread®
- Efavirenz (generic) + Truvada®
- Atripla®

$1 Billion in Savings! ... ?

- Assuming 75% price drop for generics:
  - 40% reduction in the total regimen cost ($15,300 > $9,200; $6,100 saved per year)
  - $42,500 in healthcare system savings in lifetime costs per person
  - If all U.S. patients start/switch to efavirenz/lamivudine/Viread: $920 million saved in first year alone
  - Efavirenz + Truvada®: $560 million saved

Assumptions

• Efavirenz/lamivudine/Viread 7% less virologically effective vs. Atripla
  – Overly pessimistic?

• 75% price reduction
  – Similar to that seen when generic competition ensued for other diseases:
    • simvastatin for hypercholesteroleemia (↓66%)
    • methylphenidate for ADHD (↓72%)
    • warfarin (↓85%)

Will there be sufficient competition?

- HIV technically a rare disease
- Will ARVs remain HHS recommended?
- Will patients or providers help increase demand, despite tradeoffs?
  - Efficacy concerns (e.g., 3TC vs. FTC)
  - STR vs. MTR (even if QD)
  - Loss of pharma co-pay assistance programs
What Will Insurers Do?

• ADAP
  – Brand-name ARVs already deeply discounted (~50%). Will generics be able to compete?
  – Will scale-back of RW appropriations require greater cost mgmt. by ADAPs?
  – However, major shift to Medicaid and Qualified Health Plans

• Medicaid
  – Medicaid drug rebate program: 23% for brand-name drugs; 13% for generics – is this enough?
  – Given important differences, will generic ARVs be mandatory?
What Will Insurers Do?

- Private Plans
  - Most likely to benefit from lower-cost generics
  - Interpretations of cost-effectiveness data
    - Formulary practices vs. HHS recommendations
    - STRs vs MTRs
  - Risk pushback from patients, providers, and activists?
The (Even Bigger) Questions

- Will generics create a two-class HIV care system in U.S.?
  - The haves and have-nots
  - Can we afford another structural barrier?
- Will cost savings actually be reinvested into cash-strapped programs needed to improve prevention, care, and treatment outcomes?
Talking Points

• Competition is good
  – Key to price reductions
• Beware of anti-generics rhetoric
• Leverage generic prices in new brand-name drug pricing advocacy
• Push for brand-name/generic FDCs, STRs
Talking Points

• Be cognizant (and critical) of policy landscape
  – Generic Drug User Fee Amendment (GDUFA)
• Work to ensure cost savings are reinvested in HIV care and prevention programs
• Be mindful of formulary changes based solely on cost
  – Evidence-based prescribing practices a must