AMCP Format v4.1: New Guidance on Evidence Requirements for Unapproved Products and Unapproved Uses

January 23, 2020
AMCP Webinar
Welcome

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Vice President, Policy & Government Relations
AMCP
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Type your question here
Faculty

Iris Tam, PharmD, FAMCP
Chair, AMCP Format Executive Committee and Senior Director, HEOR, Patient Access & Value Coeus Consulting Group

Jennifer S. Graff, PharmD
Member, AMCP Format Executive Committee and Vice President, Comparative Effectiveness Research National Pharmaceutical Council

Jeff White, PharmD, MS
Member, AMCP Format Executive Committee and Staff Vice President, Clinical Pharmacy Services IngenioRx
Update Process and Recommendations

Iris Tam, PharmD, FAMCP
Senior Director, HEOR, Patient Access & Value
Coeus Consulting Group
Format Executive Committee (FEC)

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Cynthia Reilly, MS, BS Pharm, AMCP Staff Liaison
Lisa Cashman, PharmD
Kevin Chang, PharmD
Cindy Giambrone, PharmD
Jennifer Graff, PharmD
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Ellen Whipple, BSPharm, PharmD
T. Jeffrey White, PharmD
Stephanie Yu, PharmD

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Kimberly Saverno, PhD, RPh
Iris Tam, PharmD, FAMCP, Chair
Patricia Thornewell, PharmD
John B. Watkins, BCPS
T. Jeffrey White, PharmD
Timeline for Version 4.1

- **2016**
  - Release of AMCP Format v4.0 April 2016

- **2018**
  - FEC considered how Guidance impact Format
  - FDA Final Guidance June 2018

- **2019**
  - Initiation of Format v4.1 draft
  - Call for public comments
  - AMCP Board approval
  - Unveiling at AMCP Nexus October 31, 2019
  - Release of AMCP Format v4.1 December 23, 2019
FDA Final Guidance (June 2018)

Sections A and B

• Firms’ communication of health care economic information (HCEI) to payors regarding approved drugs and approved/cleared devices. This pertains to and clarifies the statute found in the Food and Drug Administration Modernization Act [FDAMA] of 1997, Section 114.

Section C

• Firms’ communication to payors, formulary committees, and other similar entities about unapproved products and unapproved uses of approved/cleared products.
FDA Final Guidance (June 2018)

Sections A and B

• Firms’ communication of health care economic information (HCEI) to payors regarding approved drugs and approved/cleared devices.¹ This pertains to and clarifies the statute found in the Food and Drug Administration Modernization Act [FDAMA] of 1997, Section 114.²

Section C

• Firms’ communication to payors, formulary committees, and other similar entities about unapproved products and unapproved uses of approved/cleared products.¹

AMCP Format for Formulary Submissions, Version 4.1

December 23, 2019
# Key Terms Used in the AMCP Format

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product</td>
<td>Medical products such as pharmaceuticals, biologics, diagnostics, or medical devices</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Any company that develops, manufacturers, or markets drugs, tests, or medical devices</td>
</tr>
<tr>
<td>Health Care Decision Maker (HCDM)</td>
<td>Any health care personnel, committee, or organization that uses an evidence-based process for making health care coverage and reimbursement decisions for patient populations</td>
</tr>
<tr>
<td>Dossier</td>
<td>Comprehensive and concise report containing clinical and economic evidence and information about a medical product that is developed and communicated by the manufacturer to HCDMs for the purpose of formulary coverage, policy and reimbursement decision-making</td>
</tr>
<tr>
<td>Approval</td>
<td>General term to reflect the appropriate FDA regulatory decision-making process needed before a medical product may be commercialized</td>
</tr>
</tbody>
</table>

In General…

- The *Format* is a guidance, not a mandate
- Development of dossiers is at the discretion of the manufacturer
- Updates to dossiers should occur when new information becomes available; at the discretion of manufacturer
- Recipients of dossiers include HCDMs, payers, and entities that make or influence formulary, coverage, policy, and reimbursement decisions

PHASE 1

PHASE 2

PHASE 3

NDA SUBMISSION

Product Dossier

FDA APPROVAL of PRODUCT

NDA = New Drug Application

For illustrative purpose only. Timeline is not to scale. Milestone events shown may vary and may not be all inclusive of product’s life cycle. Manufacturer has discretion on the development of dossiers at all stages of life cycle.
**Format Version 4.0 (2016 – 2019):** New – Information Before FDA Approval

NDA = New Drug Application

*For illustrative purpose only. Timeline is not to scale. Milestone events shown may vary and may not be all inclusive of product’s life cycle. Manufacturer has discretion on the development of dossiers at all stages of life cycle.*
**Format Version 4.1 (2019 – present):**
New – Unapproved Product & Unapproved Use Dossiers

**Consider Dossiers Relative to Product Life Cycle**

- **Unapproved Product Dossier**
  - Product Dossier is a living document that evolves over time

- **Approved Product Dossier**

- **Unapproved Use Dossier**
  - Unapproved Use Dossier is a separate document that may coexist with Approved Product Dossier while FDA approval is being sought

**NDA = New Drug Application**
**sNDA = Supplemental New Drug Application**
For illustrative purpose only. Timeline is not to scale.
Milestone events shown may vary and may not be all inclusive of product’s life cycle
Manufacturer has discretion on the development of dossiers at all stages of life cycle.

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Dossier Table of Contents

**Approved Product Dossier**
1. Executive Summary
2. Product Information & Disease Description
3. Clinical Evidence
4. Economic Value & Modeling Report
5. Additional Supporting Evidence
6. Dossier Appendices

**Unapproved Product Dossier & Unapproved Use Dossier**
1. Highlights & Overview
2. Product Information & Disease Description
3. Clinical Evidence
4. Economic Information

1: Highlights & Overview

1.1 Table Highlights for Unapproved Product (or Unapproved Use of an Approved Product)

- At-a-glance overview of key information
- No executive summary
- Some information may not be available
- Manufacturer should update accordingly

Shown here is Table 1.1 for Unapproved Product

2: Product Information & Disease Description

2.1 Product Information
• Clear statement that product (or use) is not FDA-approved
• Phase and status of product development
• Product information (generic/brand name, drug class, MOA, PK, dosing, etc)
• Indications being sought
• Timeline for commercialization
• Product pricing information (may be provided in Section 4)
• Patient utilization projections
• Product-related programs or services
• Factual information from studies (may be provided in Section 3)
• Other factual information per manufacturer’s discretion

2.2 Disease Description Some information may not be available
• Exact indication of unapproved product/use is not fully known until final FDA approval
• Epidemiology, risk factors, pathology, clinical presentation, burden of disease
3: Clinical Evidence

- 3.1 Study Summaries
- 3.2 Evidence Tables

- Factual presentation of studies (phase 1, 2, 3 studies; peer-reviewed publications; congress proceedings; ClinicalTrials.gov; data on file per manufacturer’s discretion)
- No characterizations or conclusions should be made regarding safety or effectiveness
- Provide study summaries or evidence tables or both

4: Economic Information

- Strongly recommended that manufacturers provide as much product pricing information as possible (for unapproved use, price of product is known but describe any potential changes)
- Budget impact and cost-effective models may not be feasible
- Possible ways in providing pricing information
  - Price ranges or corridors, rather than absolute dollar figure
  - Directional estimates relative to other treatment options
  - Rationale for pricing strategy

Key Challenges and Considerations

Jennifer Graff, PharmD
Vice President, Comparative Effectiveness Research
National Pharmaceutical Council
## What is an Unapproved Product Dossier? What is an Unapproved Use Dossier?

<table>
<thead>
<tr>
<th>Unapproved Product Dossier</th>
<th>Approved Product Dossier</th>
<th>Unapproved Use Dossier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document containing factual presentation of evidence supporting the development of an unapproved product</td>
<td>Comprehensive document containing clinical and economic evidence and information about an FDA-approved product, including off-label information supported by evidence</td>
<td>Document containing factual presentation of evidence supporting the development of an unapproved product</td>
</tr>
<tr>
<td>No characterizations/ conclusions should be made regarding the safety or effectiveness of the unapproved product</td>
<td>Used to convey the overall value proposition of the product</td>
<td>No characterizations/ conclusions should be made regarding the safety or effectiveness of the unapproved use</td>
</tr>
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</table>

## Why are new dossiers needed?

<table>
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<tr>
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<tbody>
<tr>
<td>HCDMs need to plan and budget for future coverage and reimbursement decisions about unapproved products before FDA approval</td>
<td>To evaluate an approved product for formulary, coverage, policy, or reimbursement decisions</td>
<td>HCDMs need to plan and budget for future coverage and reimbursement decisions about unapproved uses before FDA approval</td>
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Can product value proposition be communicated in a dossier?

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<th>Unapproved Use Dossier</th>
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</thead>
<tbody>
<tr>
<td>Factual evidence grounded in clinical and economic evidence and information may be provided.</td>
<td>Yes, value that is grounded in clinical and economic evidence and information may be described</td>
<td>Factual evidence grounded in clinical and economic evidence and information may be provided.</td>
</tr>
<tr>
<td>No characterizations or conclusions should be made regarding the safety or effectiveness of the unapproved product</td>
<td></td>
<td>No characterizations or conclusions should be made regarding the safety or effectiveness of the unapproved use</td>
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When should the dossier be available?

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<tbody>
<tr>
<td>Anytime before FDA approval</td>
<td>Anytime after FDA approval</td>
<td>Anytime before FDA approval</td>
</tr>
<tr>
<td>May be 6 to 12 months or up to 2+ years before FDA approval</td>
<td></td>
<td>May be 6 to 12 months or up to 2+ years before FDA approval</td>
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## What clinical content can be in the dossier?

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<tbody>
<tr>
<td>Factual presentation of clinical evidence for the unapproved product that is available at the time of communication</td>
<td>Clinical evidence and information regarding an approved product, including any off-label uses supported by evidence</td>
<td>Factual presentation of clinical evidence for the unapproved product that is available at the time of communication</td>
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What economic content, i.e., product pricing information can be in the dossier?

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<tr>
<td>Anticipated product price or reflected as a range</td>
<td>Product price; health economics and outcomes research; economic models on budget impact and cost-effectiveness</td>
<td>Anticipated product price or reflected as a range</td>
</tr>
<tr>
<td>The manufacturer has discretion on whether and how to provide economic information</td>
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# How are dossiers communicated?

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<tbody>
<tr>
<td>Used per manufacturer’s discretion to communicate information to HCDMs about an unapproved product</td>
<td>Used by the manufacturer to respond to unsolicited requests from HCDMs after FDA approval of the product (dossier contains on-label and any/all off-label information)</td>
<td>Used per manufacturer’s discretion to communicate information to HCDMs about an unapproved use</td>
</tr>
<tr>
<td>The manufacturer may provide the dossier based on their discretion and internal policies and procedures</td>
<td>Provided upon an unsolicited request only</td>
<td>The manufacturer may provide the dossier based on their discretion and internal policies and procedures</td>
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Who from the manufacturer can communicate or provide the dossier?

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>The FEC strongly recommends personnel with appropriate medical/clinical/scientific credentials, expertise, and responsibilities</td>
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Available at: http://bit.ly/AMCPFormat
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Type your question here
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To improve patient health by ensuring access to high-quality, cost-effective medications and other therapies.