

Memorandum of Meeting
NCPDP
May 1, 2014
1:00pm to 2:00pm, CR 1211/White Oak Bldg. 51

SUBJECT: Meeting with National Council for Prescription Drug Programs (NCPDP) to listen to their comments and views regarding nonproprietary names of biological products

ATTENDEES:

NCPDP Representatives

Anne Johnston, Senior Director, Data Management, Express Scripts
John Klimek, Senior Vice President, Standards and Information Technology, NCPDP
Patrick Lupinetti, Senior Vice President and Editorial Director, Knowledge Base Services, First Databank
Gerry McEvoy, Asst. Vice President of Drug Information, American Society of Health-System Pharmacists (ASHP)
Shawn McKinney, Clinical Editor, Drug File, Wolters Kluwer Health
Patty Milazzo, Director, Drug File, Wolters Kluwer Health
Kay Morgan, Senior Vice President, Drug Products & Industry Standards, Elsevier
Gilliam Wootton, Senior Vice President, Avalere

FDA

Robert Ball, MD, MPH, Deputy Director, Office of Surveillance and Epidemiology, CDER
Leah Christl, PhD, Associate Director for Therapeutic Biologics, OND Therapeutic Biologics and Biosimilars Team (TBBT), OND, CDER
Steven Kozlowski, MD, Director, Office of Biotechnology Products, OPS, CDER
Yana R. Mille, RPh, Senior Science Policy Advisor, OPS, CDER
Peter Taschenberger, JD, MPH, Regulatory Counsel, Office of Medical Policy Initiatives, OMP, CDER
Maryll Toufanian, JD, Associate Chief Counsel for Drugs
Janice Weiner, JD, MPH, Senior Regulatory Counsel, Office of Regulatory Policy, CDER
Sandra Benton, Senior Policy Analyst, Office of Medical Policy, CDER

BACKGROUND:

NCPDP requested this meeting to “discuss how decisions made by the Agency on assigning nonproprietary names to biologics in a non-traditional manner can impact healthcare computerized systems and potentially lead to medication errors and other issues.” These issues relate to the citizen petitions related to biosimilar nomenclature, which are pending with FDA as of the date of the meeting. NCPDP submitted a copy of the letter requesting this meeting to two of the dockets established for these petitions. FDA stated that it was open to meeting with NCPDP, but it would be a “listening session” (i.e., FDA would be unable to answer questions or expand on any issues beyond what is in the public domain and what we have stated in the published draft guidance documents). FDA also stated that a summary of this meeting will be posted in the public dockets for the pending citizen petitions related to biosimilars nomenclature.¹

¹ See Docket Nos. FDA-2013-P-1153, FDA-2013-P-1398, and FDA-2014-P-0077.

DISCUSSION SUMMARY:

After providing an overview of NCPDP, NCPDP representatives presented their concerns regarding the nonproprietary naming of biological products in a “non-traditional manner,” referring to the nomenclature recently applied to ziv-aflibercept, ado-trastuzumab emtansine, and tbo-filgrastim (presentation attached). Points made by NCPDP included:

- integrated drug compendia² provide raw data to end users, and end users develop and provide the interface or application to access that data;
- although drug compendia data provide various product attributes and clinical information, the main attributes used to facilitate customer searches and reports from databases are the active ingredient, dosage form, route of administration and strength;
- products with different nonproprietary names but the “same” active ingredient could result in the products being placed in “different categories” (see slide 11);
- if there is a name change for a drug product or different naming practices put in place by FDA, each integrated drug compendia may implement different solutions in different systems;
- mapping can take place to ensure similar products can be seen in the various systems but that takes time and effort.

NCPDP noted that a legitimate reason for distinction between a biosimilar product’s nonproprietary name and the nonproprietary name of its reference product is that biosimilars can be licensed for fewer than all conditions of use of the reference product. NCPDP noted that indications can be linked by code. NCPDP explained that the core value is the active ingredient; indications are attached and are classified with the product.

With respect to use of nonproprietary names in spontaneous reporting systems, NCPDP responded that the name is not as accurate as other identifiers for a product, such as NDC codes and lot tracking.

NCPDP noted that with ado-trastuzumab emtansine,³ some compendia followed the standard procedure of using the USAN (i.e., trastuzumab emtansine) without the prefix.

NCPDP also stated that UNII codes, not names, are used to distinguish drug substances in databases. The organization stated that the database terminology is critical to allow computer systems to communicate drug related information efficiently and unambiguously. Thus, when different non-proprietary names are assigned to products that have the same UNII code, confusion is likely. The different non-proprietary name suggests that there is a difference that the prescriber should be aware of, yet the code indicates the products are the same. As NCPDP asserted earlier, there are ways to mitigate the confusion but early notification is essential to allow for sufficient time for appropriate mapping of the data to occur.

² FDA Note: “drug compendia” is the term used by NCPDP and does not reflect any official compendia recognized by the FDA under regulation.

³ FDA Note: FDA determined that the use of a distinguishing prefix in the nonproprietary name for Genentech’s Kadcyla, an antibody-drug conjugate submitted in a 351(a) biologics license application (BLA), will be required to distinguish the product from Herceptin (trastuzumab), a previously licensed biological product submitted in a different 351(a) BLA by Genentech that contains the unconjugated monoclonal antibody to reduce the potential for medication errors.

The meeting ended with NCPDP offering to speak with FDA again about these issues and any other drug compendia issues.

Background

- NCPDP PowerPoint Presentation (attached)
- McCamish M, Gallagher A, Orloff J. Biosimilar by name and biosimilar by nature. *The RPM Report*. 2013. July/Aug:1-8.

NCPDP Meeting with FDA

1 May 14, 1:00-2:00pm

Naming Conventions and the Need for Consistency

Presenters:

Introduction - Gerald McEvoy (gmcevoy@ashp.org)

Gold Standard - Kay Morgan (morgan.k@goldstandard.com)

First Databank - Patrick Lupinetti (plupinetti@fdbhealth.com)



NCPDP

NCPDP is a not-for-profit ANSI-accredited Standards Development Organization.

Over 1,600 members representing drug manufacturers, chain and independent pharmacies, drug wholesalers, insurers, mail order prescription drug companies, claims processors, pharmacy benefit managers, physician services organizations, prescription drug providers, software vendors, telecommunication vendors, service organizations, government agencies and other parties.

All share an interest in electronic standardization within the pharmacy services sector of the health care industry.

NCPDP welcomes the opportunity to work with FDA to ensure our standards continue to serve their purposes in a world that includes biosimilars

Objectives

- Ensuring an accurate and consistent identification of drugs to meet the essential needs of US prescribers, dispensers and claims administrators
- Facilitating the paramount role and discretion of prescribers to determine proper medication for a patient
- Preserving the fundamental goal of patient safety
- Reinforcing other goals of the existing regulatory structure that promote transparency, efficiency and economy
- No system can compensate for the failure to enter complete and accurate records. Accuracy must be assured for the current system, and for any future systems, preemptively, if changes are needed.

How Drug Compendia Operate Today - What Happens When Changes Occur

Presenter:
Gold Standard - Kay Morgan
(morgan.k@goldstandard.com)

The Role of Drug Compendia

- **Integrated**
 - Used in Pharmacy Dispensing
 - Payer Decision to Reimburse
 - CMS
- **Reference**
 - Required by State Pharmacy Regulations
 - Drug and Product Information
 - CMS

Integrated Databases are the “Intel” Inside

- Only Provide Raw Data – Content
- End User Must Develop Interface/Application
- Just Data – Can and Will be Changed by End User
- Liability Always a Concern – so All is Reported



Reference Drug Compendia

- AHFS
- Micromedex (USP Information)
- Facts & Comparisons
- Multum
- Lexicomp
- Epocrates



Sources of Information

- Official Product Labeling
- FDA Web Site
- Primary Medical and Pharmacy Journals
- HDMA Product Form
- The Pharma Company



Drug Compendia Data Include:

Product Attributes

- NDC
- Product Description
- Packaging
- Pricing
- Image of Product
- Rx/OTC (Legend Status)
- DEA Status
- Approval – NDA,ANDA,BLA
- Therapeutic Equivalence

Clinical Information

- Indications
- Drug Interactions
- Adverse Events
- Contraindications/Precautions
- Dosing
- Mechanism of Action
- Pharmacokinetics
- Pregnancy/Breast Feeding Info

Drug Compendia Design

- Databases Organize Information
 - Active Ingredient
 - Dosage Form
 - Route of Administration
 - Strength
- Necessary to Facilitate Customer Searches and Reports

Design Example of New Classification

	Pristiq	Desvenlafaxine 505(b)(2)
Ingredient	Desvenlafaxine Succinate	Desvenlafaxine
Dosage Form	Extended Release Tablet	Extended Release Tablet
Route	Oral	Oral
Strength	100 and 50 mg	100 and 50 mg

Different Categories as ingredient is different

	Prozac	Prozac	Fluoxetine 505(b)(2)
Ingredient	Fluoxetine HCl	Fluoxetine HCl	Fluoxetine HCl
Dosage Form	Tablet	Capsule	Tablet
Route	Oral	Oral	Oral
Strength	10 mg	10, 20 and 40 mg	60 mg

Different Categories as strength is different or dosage form is different

Compendia Groupings are Used as the Basis for a Variety of Outcomes

- Determining Equivalent Products
- Determining Candidates for Substitution
- Purchasing Decisions
- Auto Ship Programs
- Analytics
- ePrescribing Selection
- Electronic Health Records
- Prescription Fulfillment
- Claims Adjudication

**All will be disrupted if the naming conventions are changed.
Each process will have to be individually rebuilt to ensure patient safety and restore functionality to the system.**

Issues with Non-traditional Naming of Interchangeable Biologic Ingredients

Presenter:

First Databank - Patrick Lupinetti (plupinetti@fdbhealth.com)

The Case Against a Different Naming Practice for Biologicals

Applying different names for the same biological drug ingredients -

- Introduces confusion and unnecessary complexity
- Is contrary to historical FDA practice and policy
- Is opposed by virtually all pharmacy association stakeholders because it conflicts with normal pharmacy practice - employing an electronic database to recognize products by identifiers
- Is unnecessary for product recall or other patient safety considerations
- Undervalues the ability of existing systems (NDC- and Lot-based recalls) and new regulatory structures (track and trace) to provide adequate safeguards

Unnecessary Confusion and Complication is Inherently Dangerous

Changes to current practices are not trivial in effect and should only be made to address an identified problem after thorough risk analysis.

Multiplication of nonproprietary names would mean that:

- Products with shared ingredients will not be alphabetically adjacent
- Clinician decision-making and ability to identify therapeutic alternatives will be hampered
- The effort to map and identify alternatives will require additional expense, resources and time
- Patients' awareness of biosimilar availability will be limited
- State legislation efforts can hinder substitution even if FDA determines interchangeability

Contrary to Sound Economic Healthcare Policy and Congressional intent in BPCIA

- Concealing the existence of biosimilars will limit the availability of information and preclude consideration of lower cost options that increase access and affordability for patients
- Fostering a fundamentally anti-competitive practice that entrenches market position of innovator reference product
- Forecloses competition in the biologics market akin to the successful experience for small-molecule drugs
- Will undermine substitution even for those biosimilars that the FDA designates as interchangeable

I. Reversal of Traditional FDA Practice NPN Design traditionally left to USAN

“...established names (i.e., nonproprietary or generic name) do not undergo review by CDER. The United States Adopted Names Council (USAN) is responsible for selecting a United States Adopted Name (USAN) for drugs marketed in the U.S.”

FDA White Paper
How FDA Reviews Proposed Drug Names

“In the U.S. medication-use system, health care providers rely on the proprietary name as the critical identifier”

FDA Guidance on
Evaluation of Proprietary Names Feb 2010

II. International Naming Practice for Biologicals

“INNs should be based, as now, on considerations of molecular characteristics and pharmacological class. No specific process should be introduced for naming biosimilars. INNs for these products should be assigned according to the standard process for naming biologicals. **There should be no change in policy and no distinctive INN designation introduced to indicate a biosimilar product**...it should be explained that INN policy relates solely to nomenclature and that no distinctive INN designation is introduced to indicate a biosimilar product.”

2006 Recommendations

FDA To the WHO INN Expert Group

WHO Informal Consultation on International Nonproprietary Names (INN) Policy for Biosimilar Products

III. FDA Announced Position

“...to date, INNs have been granted on considerations of molecular characteristics and pharmacological class. However, the **US FDA is concerned about proposals to change this policy for biosimilars supposedly to allow for adequate pharmacovigilance and to prevent inappropriate substitution...**

...the INN is a useful tool but should not be the sole means of product identification for drug products including biologicals. All available tools should be employed, such as **lot number and national drug code...**

The US FDA believes that INNs should continue to be granted only on considerations of molecular characteristics and pharmacological class of the active ingredient.”

FDA to WHO Informal Consultation on International Nonproprietary Names (INN) Policy for Biosimilar Products

Available at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm375086.htm>

IV. ado-trastuzumab: Risks of Prefix-Based Differential Naming

[Posted 05/06/2013]



AUDIENCE: Risk Manager, Pharmacy, Oncology

ISSUE: The FDA notified health care professionals that the use of the incorrect nonproprietary name for the breast cancer drug Kadcyla (ado-trastuzumab emtansine) in some medication-related electronic systems poses a risk of mix-up with Herceptin (trastuzumab) and may result in medication errors.

The FDA-approved nonproprietary name for Kadcyla, ado-trastuzumab emtansine, should be used. However, some third-party publications, compendia references, health information systems (e.g., electronic health record systems and systems used for pharmacy prescription processing, wholesaler ordering, pharmacy ordering, etc.), and sites on the Internet are incorrectly using the United States Adopted Name (USAN), which is "trastuzumab emtansine," and omitting the "ado" prefix and hyphen.

- FDA application of different NPN created risk of confusion
- Until this instance, "incorrect use of USAN" was a contradiction

Conflict and Confusion



Search Results

Drug Name: Trastuzumab emtansine [USAN:INN]

Search Term: UNII-SE2KH7T06F

Description: Designed to deliver antimicrotubule age

Search Results

Preferred Substance Name:

ADO-TRASTUZUMAB EMTANSINE

UNII:

SE2KH7T06F

UNII: SE2KH7T06F

Substance Name: Trastuzumab emtansine [USAN:INN]

RN: 1018448-65-1



NCPDP

US Federal Medication Terminology UNII Codes

- Indistinguishable drug substance pairs
 - Filgrastim UNII: PVIM0M1GW
 - tbo-Filgrastim UNII: PVIM0M1GW
 - Aflibercept UNII: 15C2VL427D
 - ziv-Aflibercept UNII: 15C2VL427D
 - Codes not names are used to distinguish drug substances in databases
 - UNII purpose is to support initiatives by HIT



Consensus in Opposition to Arbitrarily Changing Current nonproprietary Naming System



To avoid a naming convention that may create confusion, **we recommend that biosimilar products maintain the same name as their reference biologic counterparts**...the use of unique individual nonproprietary names (INNs) could create the very public health issues that the FDA wishes to avoid: therapeutic duplication and general confusion relative to the appropriate use, safety and efficacy of biologic products.

Unique INNs for common active ingredients **may generally increase confusion, leading to increased safety concerns and possibly medication errors.**

May 25, 2012 Comments to Docket No. FDA-2011-D-0618
Draft Guidances Relating to the Development of Biosimilar Products;

American Society of Health-System Pharmacists (ASHP)

Grouping products by active ingredient that is conceptually equivalent provides a uniform, predictable, and effective way for healthcare professionals to identify drugs. For small molecule products, this grouping method has worked well for decades and this practice does not implicitly denote substitutability nor does this categorization inherently communicate bioequivalence or interchangeability. In addition, the current US standard nomenclature for naming clinical drug concepts, the National Library of Medicine's RxNorm, uses common root names among other things to normalize group products that conceptually are equivalent. **This terminology is critical in supporting semantic interoperability among drug terminologies and pharmacy knowledge base systems, allowing computer systems to communicate drug-related information efficiently and unambiguously.**

The American Society of Health-System Pharmacists (ASHP) comments to the Federal Trade Commission (FTC) on the topic of biosimilars as requested in the Federal Register on November 13, 2013.

National Association of Boards of Pharmacy (NABP)

The premise of using INNs as a naming convention is very different from, and could even be described as the opposite of, the current naming convention used for small molecule drugs where the innovator products and its generic counterparts have the same generic or non-branded name. The use of INNs as a naming convention is unfamiliar to health care providers and patients and could cause confusion, resulting in the incorrect drug being dispensed to patients or therapeutic duplication.

With these concerns in mind, **NABP respectfully requests that FDA require biosimilars products to have the same nonproprietary name as the reference biologics counterpart if the science so supports.**

NABP letter to Commissioner Hamburg, 17 April, 2013

Nonidentical INNs may:

- suggest to the prescriber that the active ingredient in products is different;
- create the (false) impression that interchangeable biosimilars have important, clinically relevant, distinguishable effects; and
- reduce uptake and substitution of interchangeable biosimilars

Any change in current nomenclature rules or standards should be informed by a better, and more complete, understanding of how such changes, including requiring a unique identifier for biologic INNs would impact prescriber attitudes and patient access, and affect postmarketing surveillance. Actions that solely enhance product identification during surveillance activities but act as barriers to clinical uptake are counterproductive.

Comments to FTC public comments 28th February 14, Available at <http://www.ftc.gov/news-events/events-calendar/2014/02/follow-biologics-workshop-impact-recent-legislative-regulatory>

Conclusions

A brand name unique to the product, and a nonproprietary name that describes the active pharmaceutical ingredient, are integral to current pharmacy data systems and the value of the records they provide on all medicines for all patients

- Prescribing in the US will likely be by brand name for the overwhelming majority of biologics
- Billing largely depends on the NDC#
- Current systems will adequately distinguish biosimilars

Changes to current systems risk compromising their value for all medicines, and impacting the safety for patients

NCPDP welcomes the opportunity to work with FDA to ensure our standards continue to serve their purposes in a world that includes biosimilars



Questions/Comments
Thank You