Pharmacovigilance Is Critical for All Products

- Pharmacovigilance is the process of identifying and assessing adverse events (possible side effects) associated with a product.
- All biologics raise unique pharmacovigilance challenges:
  - Rare, but potentially serious side effects
  - Sensitivity to manufacturing process
  - Limited ability to predict clinical effect of manufacturing changes
- Effective pharmacovigilance requires the ability to link specific adverse events or adverse event trends with the responsible product.
Widespread Misattribution of Adverse Events in U.S.

• Analysis of adverse event reporting trends for eight small-molecule drug products, before and after generic entry

• The rate of adverse events reported for the brand product remained roughly the same after generic entry (for 6 of 8 drugs)

• Adverse events were being attributed to the brand name product when the patient was actually taking the generic
Zocor Example

Result: Pooling of adverse events for products that share the same non-proprietary name
Limited Product-Identifying Information in AE Reports

• Research also revealed that product name is often the only product identifying information included in adverse event reports
  • 90% of all reports in FDA’s adverse event database (FAERS) do not have lot numbers
  • There is no data field provided in the FAERS database for a national drug code (NDC) number, but NDC number is included in fewer than 1 in 10,000 FAERS reports
FDA: Need for Distinct Names to Facilitate Pharmacovigilance and Prevent Medication Errors

**tbo-filgrastim**: “unique nonproprietary names will facilitate postmarketing safety monitoring by providing a clear means of determining which ‘filgrastim’ product is dispensed to patients”

**ziv-afilbercept**: “unique nonproprietary names will facilitate postmarketing safety monitoring by providing a clear means of determining which ‘afilbercept’ product is dispensed to patients”

**ado-trastuzumab emtansine**: “FDA identified a potential for error between the currently marketed Herceptin (trastuzumab) and the proposed Kadcyla (“trastuzumab emtansine”) due to the similarity of the nonproprietary names as well as overlapping product characteristics”
Limitations of Using Distinct Brand Names

• Distinct brand names will help facilitate pharmacovigilance

• But, there are some limitations:
  • Lack of explicit statutory authority for FDA
  • Adverse event reports often do not include brand names or other meaningful product-identifying information beyond a product’s non-proprietary name
  • Prescribing can occur by non-proprietary name
    • “Due to the fact that healthcare providers may use nonproprietary names instead of proprietary names when prescribing and ordering products . . . FDA has determined the use of distinct proprietary names is insufficient to adequately address these concerns.” – FDA Proprietary Name Review for tbo-filgrastim
Global Perspective

• Some jurisdictions prohibit or discourage prescribing by brand name
  • China effectively prohibits prescribing biotherapeutics by proprietary name (with an exception for a patented biotherapeutic with a new active ingredient)
  • Colombia prohibits prescribing government-reimbursed biotherapeutics by proprietary name

• Clinicians and patients outside the United States report adverse events to FDA
Identical Names May Cause Confusion

• In a recent survey, 76% of physicians said having an identical nonproprietary name implies that two products have identical structures

• Biosimilars are highly similar, but not identical in structure

• FDA has recognized that identical names may cause confusion:
  • Using a distinct non-proprietary name for ziv-aflibercept would help reduce medication errors by “reducing confusion among healthcare providers who may consider use of the same nonproprietary name to mean that the biological products are indistinguishable from a clinical standpoint”
Distinct, But Related Non-Proprietary Names Protect Patients

- Approach taken by Australia and Japan
- Related “core” non-proprietary name will help to assess adverse events across a class of products, but distinguishing prefix or suffix allows for differentiation
- Distinct names will not present barrier to patient access
All patients deserve to have access to these life-changing biologic therapies.

Every adverse event matters, and patients deserve and expect to have every adverse event counted.