



Communicating HTE Across Populations: Challenges and Opportunities


“Variability is the law of life, and as no two faces are the same, so no two bodies are alike, and no two individuals react alike and behave alike under the abnormal conditions which we know as disease.”

- Sir William Osler
(1849 – 1919)

Is there a right number?



FDASIA 2012: Section 907

- In the past years, stakeholders have been concerned about adequate and equal inclusion of women and minority groups in clinical trials.
- Congress directed FDA to take a closer look at and report on the inclusion and analysis of demographic subgroups in applications for drugs, biologics, and devices
- In August 2014, FDA delivered its *Action Plan to Enhance the Collection and Availability of Subgroup Data*
- The plan includes three overarching priorities for subgroups:
 1. Quality of Data
 2. Greater Participation
 3. Increased Transparency 

Snapshots Brief History

- 2014: Pilot Program
- January 1, 2015: Snapshot written for every New Molecular Entity (NME) and Original Biologic approved
- Goal to publish 30 days after approval
- Does not apply to previously approved drugs

Purpose of Drug Snapshots

- Provide Information to the public about who participated in the clinical trials for NMEs and original biologics
- Also includes information on study design, results of efficacy and safety studies, and whether there were observed differences in efficacy and side effects among sex, race, and age subgroups

Snapshots Audience

- Consumers
- Physicians, Statisticians, anyone who is interested in the data and analyses

“(MORE INFO)”

DRUG TRIALS SNAPSHOTS



U.S. Department of Health and Human Services

U.S. Food and Drug Administration Protecting and Promoting *Your* Health

[A to Z Index](#) | [Follow FDA](#) | [En Español](#)

Search FDA

n

[Home](#) | [Food](#) | [Drugs](#) | [Medical Devices](#) | [Radiation-Emitting Products](#) | [Vaccines, Blood & Biologics](#) | [Animal & Veterinary](#) | [Cosmetics](#) | [Tobacco Products](#)

Drugs

[Home](#) | [Drugs](#) | [Drug Approvals and Databases](#)

Drug Approvals and Databases

Approved Drug Products with
Therapeutic Equivalence
Evaluations (Orange Book)

Bioresearch Monitoring
Information System (BMIS)

Clinical Investigator Inspection
List (CLIL)

Dissolution Methods Database

Drug Establishments Current
Registration Site

☐ [Drug Trials Snapshots](#)

Drugs@FDA Database

FDA Adverse Event Reporting
System (FAERS)

National Drug Code Directory

Postmarket Requirements and
Commitments

[Approved Drugs](#)

☐

Resources for You

- [Inside Clinical Trials: Testing Medical Products in People](#)
- [The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)
- [CDER Conversations: Drug](#)

Drug Trials Snapshots

☐ [SHARE](#) | ☐ [TWEET](#) | ☐ [LINKEDIN](#) | ☐ [PIN IT](#) | ☐ [EMAIL](#) | ☐ [PRINT](#)

[Sign Up for Email Updates about Drug Trials Snapshots](#)

WHAT IS THE PURPOSE OF DRUG TRIALS SNAPSHOTS?

Drug Trials Snapshots provide consumers with information about who participated in clinical trials that supported the FDA approval of new drugs. The information provided in these Snapshots also highlights whether there were any differences in the benefits and side effects among sex, race and age groups. Drug Trials Snapshots is part of an overall FDA effort to make demographic data more available and transparent.

HOW TO USE SNAPSHOTS:

Each Snapshot includes contains information about the drug in a question and answer format. At the end of each section of the Snapshot, there is a shaded bar with the words "MORE INFO". Click the "MORE INFO" bar for more technical and detailed content. At the bottom of each Snapshot, there is a link to the drug's Package Insert as well as the medical review.

LIMITATIONS OF SNAPSHOTS:

The Snapshot is intended as one tool for consumers to use when discussing a drug's risks and benefits with their physician. Do not rely on Snapshots alone to make decisions regarding medical care. Do not use Snapshots to substitute for advice from your health care professional. Conclusions regarding how effective and safe a drug is among different sex, race, and age groups cannot always be made, often because the numbers of patients in some groups are too limited to allow for meaningful comparisons to other groups and to the overall results.

GLOSSARY

CLINICAL TRIAL: Voluntary research studies conducted in people and designed to answer specific questions about the safety or effectiveness of drugs, vaccines, other therapies, or new ways of using existing treatments.

COMPARATOR: A previously available treatment or placebo used in clinical trials that is compared to the actual drug being tested.

EFFICACY: How well the drug achieves the desired response when it is taken as described in a controlled clinical setting, such as during a clinical trial.

PLACEBO: An inactive substance or "sugar pill" that looks the same as, and is given the same way as, an active

DTS vs Package Insert



Drugs

Home > Drugs > Drug Approvals and Databases

Drug Approvals and Databases

Approved Drugs



Entresto



HOW TO USE THIS SNAPSHOT

The information provided in Snapshots highlights who participated in the clinical trials that supported the FDA approval of this drug, and whether there were differences among sex, race, and age groups. The "MORE INFO" bar shows more detailed, technical content for each section. Refer to the [ENTRESTO Prescribing Information](#) for complete information.

ENTRESTO (secubitril/valsartan)
(en-TRESS-toh)
Novartis Pharmaceuticals Corporation
Approval date: July 7, 2015

DRUG TRIALS SNAPSHOT SUMMARY:

What is the drug for?

ENTRESTO is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker, indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.

How is this drug used?

ENTRESTO is usually administered in conjunction with other heart failure therapies. In place of an ACE inhibitor or other ARB. The recommended starting dose of ENTRESTO is 49/51 mg (sacubitril/valsartan) twice-daily.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ENTRESTO safely and effectively. See full prescribing information for ENTRESTO.

ENTRESTO™ (sacubitril and valsartan) tablets, for oral use
Initial U.S. Approval: 2015

WARNING: FETAL TOXICITY

- See full prescribing information for complete boxed warning.
- When pregnancy is detected, discontinue ENTRESTO as soon as possible. (5.1)
- Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus. (5.1)

INDICATIONS AND USAGE

ENTRESTO is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker, indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction. (1.1)

ENTRESTO is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB. (1.1)

—DOSAGE AND ADMINISTRATION—

- The recommended starting dose of ENTRESTO is 49/51 mg (sacubitril/valsartan) twice-daily. Double the dose of ENTRESTO after 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient. (2.1)
 - Reduce the starting dose to 24/26 mg (sacubitril/valsartan) twice-daily for:
 - patients not currently taking an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents (2.2)
 - patients with severe renal impairment (2.3)
 - patients with moderate hepatic impairment (2.4)
- Double the dose of ENTRESTO every 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient. (2.2, 2.3, 2.4)

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: FETAL TOXICITY

- INDICATIONS AND USAGE
- DOSAGE AND ADMINISTRATION
 - Dosing
 - Dose Adjustment for Patients Not Taking an ACE Inhibitor or ARB or Previously Taking Low Doses of These Agents
 - Dose Adjustment for Severe Renal Impairment
 - Dose Adjustment for Hepatic Impairment
- DOSAGE FORMS AND STRENGTHS
- CONTRAINDICATIONS
- WARNINGS AND PRECAUTIONS
 - Fetal Toxicity
 - Angioedema
 - Hypotension
 - Impaired Renal Function
 - Hypokalemia
- ADVERSE REACTIONS
 - Clinical Trials Experience
- DRUG INTERACTIONS
 - Dual Blockade of the Renin-Angiotensin-Aldosterone System
 - Potassium-Sparing Diuretics

—DOSAGE FORMS AND STRENGTHS—

- Film-coated tablets (sacubitril/valsartan): 24/26 mg, 49/51 mg, 97/103 mg (3)

CONTRAINDICATIONS

- Hypersensitivity to any component. (4)
- History of angioedema related to previous ACE inhibitor or ARB therapy. (4)
- Concomitant use with ACE inhibitors. (4, 7.1)
- Concomitant use with aldiskins in patients with diabetes. (4, 7.1)

—WARNINGS AND PRECAUTIONS—

- Observe for signs and symptoms of angioedema and hypotension. (5.1, 5.3)
- Monitor renal function and potassium in susceptible patients. (2.4, 5.2)

ADVERSE REACTIONS

- Adverse reactions occurring ≥5% are hypotension, hypokalemia, cough, dizziness, and renal failure. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Dual blockade of the renin-angiotensin system: Do not use with an ACEi, do not use with aldiskins in patients with diabetes, and avoid use with an ARB. (4, 7.1)
- Potassium-sparing diuretics: May lead to increased serum potassium. (7.2)
- NSAIDs: May lead to increased risk of renal impairment. (7.3)
- Lithium: Increased risk of lithium toxicity. (7.4)

—USE IN SPECIFIC POPULATIONS—

- Lactation: Breastfeeding or drug should be discontinued. (8.2)
- Severe Hepatic Impairment: Use not recommended. (2.4, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 7/2015

7.3 Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors)

7.4 Lithium

9 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Hepatic Impairment

8.7 Renal Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacokinetics

12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.



Snapshots are not a drug label

Snapshots

Intended for public

Consumer-friendly language

Focus on subgroup data and analysis

Links to FDA reviews

30 days after drug approval

Prescribing Information

Intended for healthcare professionals

Technical language

Comprehensive resource for drug information

Not linked to FDA reviews

Published with drug approval

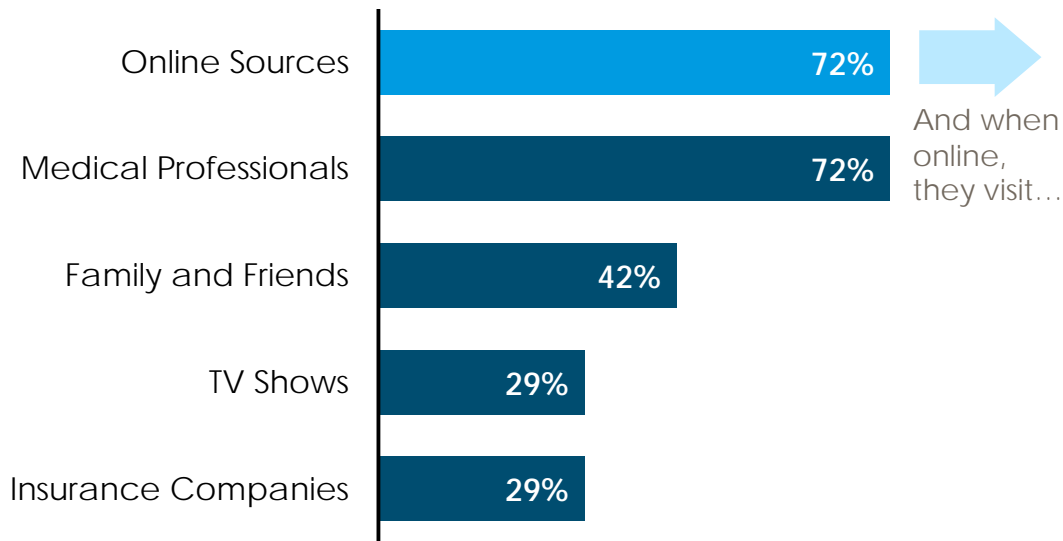
Important Questions

1. Is there enough data to make conclusions about efficacy and safety for all subgroups?
2. How many patients per subgroup are needed?
3. When is generalizability ok?
4. When differences among subgroups are seen, when are differences clinically meaningful?

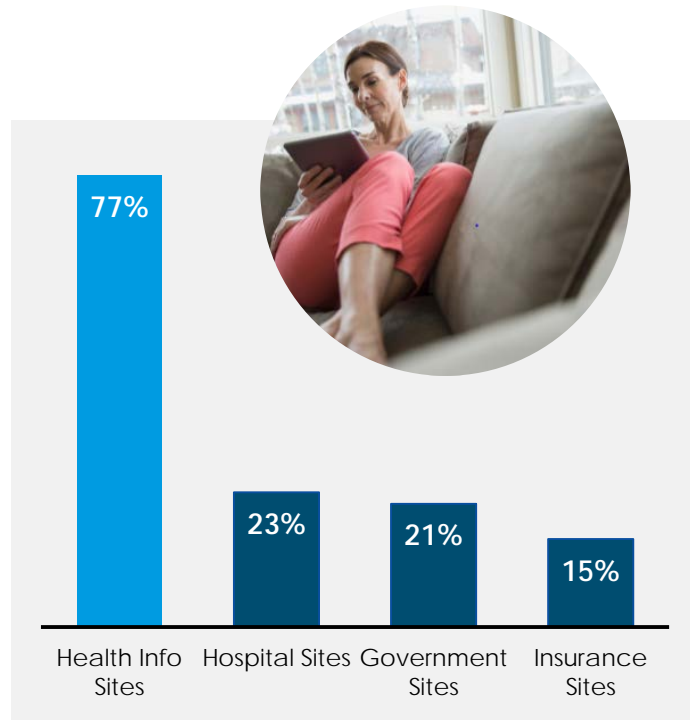


Today's connected healthcare consumer

Online health information sites help patients and caregivers stay better informed



And when online,
they visit...





Dr. Mehmet Oz

@DrOz

Cardiac Surgeon and Host of The Dr. Oz Show

New York, NY doctoroz.com

Born on June 11

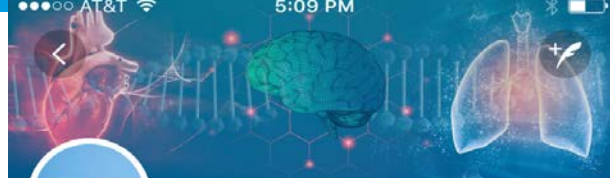
288 Following 4.1M Followers

Tweets Tweets & replies Media Likes

Pinned Tweet



Dr. Mehmet Oz @DrOz · 9/12/18
Mark your calendars - Season 10 of The Dr. Oz Show premieres on Mon. 9/17! Tune in all week for hard-hitting investigations and interviews. I can't wait for you to see what we have in store!



WebMD

@WebMD Follows you

WebMD and our medical team bring you the most trust-worthy and timely health news and information.

USA wb.md/2kilagk

402 Following 3M Followers

Tweets Tweets & replies Media Likes



WebMD @WebMD · 9m
"Back in 2009, it appeared that there might be less than 150 brands of supplements that contain drugs. Now it's clear that there are well over 1,000 brands of supplements that contain active drugs." wb.md/2IUeYnh



Mayo Clinic

@MayoClinic

An integrated clinical practice, education and research institution specializing in treating patients. Account maintained by @MayoClinic/MCCSM.

Minnesota, Florida, Arizona

mayocl.in/web

1,805 Following 1.8M Followers

Tweets Tweets & replies Media Likes



Mayo Clinic @MayoClinic · 1m
There are many benefits of eating a high-fiber diet. Here are some easy ideas for adding [#fiber](#) to your meals. mayocl.in/2QPfTs5





FDA



Following

U.S. FDA ✓

@US_FDA

Here you'll find the latest US Food and Drug Administration news and information. Privacy Policy - [fda.gov/privacy](https://www.fda.gov/privacy)

[fda.gov](https://www.fda.gov)

150 Following

218.2K Followers

Tweets

Tweets & replies

Media

Likes

U.S. FDA Retweeted



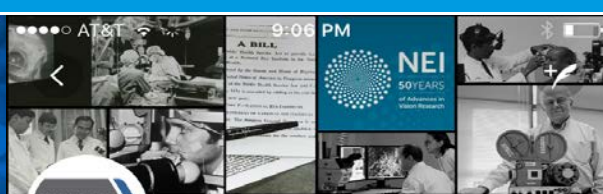
U.S. FDA ✓ @FDArecalls · 1d

The Quaker Oats Company Issues Voluntary Recall of a Small Quantity of Cap'n Crunch's Peanut Butter Crunch Cereal Distributed to Five Target Stores Due to Possible Health Risk [dlvr.it/qrS794](https://www.dlvr.it/qrS794)

3

36

15



NIH



Follow

NIH ✓

@NIH

Official Twitter account of the National Institutes of Health. NIH...Turning Discovery Into Health ®. Visit: [nih.gov](https://www.nih.gov) Privacy Policy: [go.usa.gov/x9svN](https://www.go.usa.gov/x9svN)

Bethesda, Maryland, USA [nei.nih.gov](https://www.nei.nih.gov)

274 Following

873K Followers

Tweets

Tweets & replies

Media

Likes

Pinned Tweet



NIH ✓ @NIH · 6d

Welcome! This week, the National Eye Institute (NEI) is taking over NIH's account. Follow along to learn more about NEI and the Nation's leading eye health and vision research! [#ThisIsNIH](https://twitter.com/ThisIsNIH) [#ThisIsNEI @NatEyeInstitute](https://twitter.com/NatEyeInstitute)



CDC



Follow

CDC ✓

@CDCgov

CDC's official Twitter source for daily credible health & safety updates from Centers for Disease Control & Prevention. Privacy policy: [bit.ly/2MhQ6Hp](https://www.bit.ly/2MhQ6Hp)

Atlanta, GA [cdc.gov](https://www.cdc.gov)

268 Following

1.1M Followers

Tweets

Tweets & replies

Media

Likes



CDC ✓ @CDCgov · 7h

Honey can contain bacteria that cause infant botulism, a serious illness that can lead to paralysis and death. Do not give honey or honey products, including honey pacifiers, to children younger than 12 months. Learn more: [go.usa.gov/xPGmf](https://www.go.usa.gov/xPGmf)



THANK YOU!

Any Questions?



DrJohnWhyte@gmail.com



[@DrJohnWhyte](https://twitter.com/DrJohnWhyte)



