# Incorporating Health Literacy into the Development and Testing of Patient Labeling

Laurie Myers, Global Health Literacy Director
Merck & Co., Inc.

November 2, 2017

MERCK

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# Agenda

Define health literacy

Share process to build a health literate patient label

- Development
- Testing

Case study

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# What is health literacy?

US: The ability to obtain, process, and understand health information to make appropriate health decisions.[1]

**1.** US Department of Health and Human Services. *Healthy People 2010*. Washington, DC: US Government Printing Office; 2000

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# Health Literacy in the United States

**Only 12%** of adults have proficient health literacy.[1]

Risk factors for low health literacy include[2]:

- Age 65+
- Recent immigrants who do not speak English
- Racial/ethnic minorities
- Low income

1. US Dept Health & Human Services, Office of Disease Prevention & Health Promotion. http://www.health.gov/communication/literacy/issuebrief/. Accessed on 11/12/13
2. Weiss BD. *Health Literacy and Patient Safety: Help People Understand.* American Medical Association Foundation and American Medical Association. May 2007


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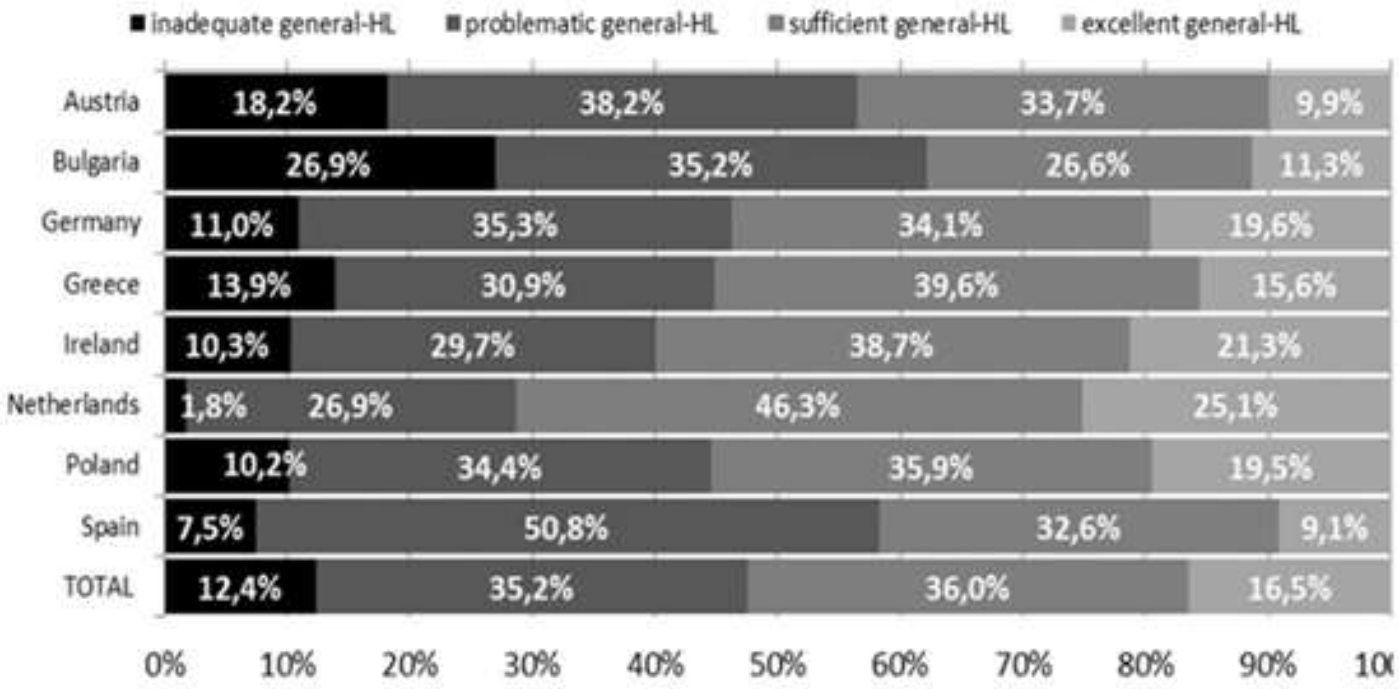
# Health Literacy in Europe

## About half of respondents have limited health literacy[1]




[1]Sorensen K et al. (2015), Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU); Eur J Public Health 25;6:1053-1058)

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# Patient Labeling for New Molecules

Goal: Maximize comprehension for all audiences, including those with limited health literacy

Past: Comprehension testing across education levels

- Few presented with limited health literacy
- Directionally lower comprehension scores

Cross-divisional team at Merck, including legal

Partnership with academia

- Dr. Ruth Parker (Emory)
- Dr. Michael Wolf (Northwestern)

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# Development

Merck develops initial draft of patient label

Northwestern/Emory apply evidence-based best practices

Merck reviews, with few changes

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# Testing

Focus groups in Chicago and Atlanta

- Draft label refined
- Merck reviews, with few changes

Comprehension testing

- Qualitative research (usually 60 people)
  - Aim for 25% low health literacy
  - Includes respondents who match demographics of disease, those with the condition, and caregivers (if appropriate)
- Labeling revised with input from Northwestern/Emory

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# Updated Approach to Testing

- Inclusion of health literacy assessment
  - Recruiter database, phone screen, and comprehension testing
- Significant efforts to find people with low health literacy
  - May include recruitment at literacy and senior centers
  - No requirement for desktop computer
  - In-person research targeted for respondents with limited health literacy
- Combination of open and closed book assessment

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# High Comprehension

| Average Comprehension Scores Across Literacy Levels (n=777)* | | | | |
|---|---|---|---|---|
| | Patients (n=380) | Caregivers (n=160) | Gen Pop (n=237) | Overall (n=777) |
| Limited Health Literacy (n=219) | 89% | 88% | 90% | 89% |
| Adequate Health Literacy (n=558) | 94% | 94% | 93% | 93% |
| Overall | 93% | 93% | 91% | 92% |

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# Positive Patient Feedback

Respondents stated they would be more likely to:

- Read the information
- Keep the information as a reference
- Understand how to correctly use the medication
- Have a clear understanding of risks
- Ask questions

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# FDA-approved ZINPLAVA PPI

**Patient Information**
**ZINPLAVA™ (zin-PLAH-va)**
**(bezlotoxumab)**
**Injection, for intravenous use**

**What you need to know about ZINPLAVA**

- Before you receive ZINPLAVA, be sure you understand what it is for and how it is given.
- ZINPLAVA helps decrease the risk of C-diff (*Clostridium difficile* infection) from coming back by working with the antibiotic that you are taking to treat your C-diff. ZINPLAVA does not replace the antibiotic. ZINPLAVA is not an antibiotic.
- Keep taking your antibiotic for your C-diff as directed by your doctor.
- If you have questions about ZINPLAVA, ask your doctor or pharmacist.
- Keep this Patient Information for ZINPLAVA so you can read it again.

## What is ZINPLAVA?

ZINPLAVA is a prescription medicine used to help decrease the risk of C-diff from coming back in people 18 years of age or older who are taking an antibiotic for C-diff and who have a high risk of C-diff coming back.

C-diff is a bacterial infection that can damage your colon and cause stomach pain and severe diarrhea. When people get C-diff, they often take an antibiotic to get rid of the infection. Even when treated by an antibiotic, C-diff can come back within weeks to months. ZINPLAVA helps to decrease the risk of the infection from coming back. It works when given along with the antibiotic that you are taking to treat C-diff.

## How will I receive ZINPLAVA?

- You will receive ZINPLAVA into your vein through an IV (intravenously).
- You do not need to do anything to prepare for receiving ZINPLAVA.
- You will receive ZINPLAVA in 1 dose and it will take about 1 hour.
- If you miss your appointment, call your doctor right away to reschedule it.

## Is ZINPLAVA right for me?

**Children**

- It is not known if ZINPLAVA is safe and effective in children under 18 years old.

**Pregnancy**

- If you are pregnant or trying to get pregnant, tell your doctor before you receive ZINPLAVA.
- It is not known if ZINPLAVA will harm your baby while you are pregnant.
- You and your doctor should decide together if you will receive ZINPLAVA.

**Breastfeeding**

- If you are breastfeeding or plan to breastfeed, tell your doctor before you receive ZINPLAVA.
- It is not known if ZINPLAVA gets in your breast milk and will be passed to your baby.
- You and your doctor should decide together if you will receive ZINPLAVA.

**Medical Conditions**

- Tell your doctor about any medical conditions you have now or have had before.
- Make sure to tell your doctor if you have or have had congestive heart failure (CHF).

**Other Medicines**

- **Tell your doctor about all of the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.



## What are the possible side effects of ZINPLAVA?

**ZINPLAVA may cause serious side effects, including:**

- **Heart failure.** Heart failure may happen in people who receive ZINPLAVA and can be serious. People with a history of congestive heart failure (CHF) who received ZINPLAVA had a higher rate of heart failure and death than those who did not receive ZINPLAVA.

**Common side effects of ZINPLAVA:**

The most common side effects that may happen on the day of or the day after receiving ZINPLAVA:

- nausea
- headache
- fever
- feeling tired
- shortness of breath
- feeling dizzy
- high blood pressure

The most common side effects that may happen up to four weeks after receiving ZINPLAVA:

- nausea
- fever
- headache

**If you have any side effect that bothers you or does not go away, tell your doctor.**
There may be other side effects to ZINPLAVA that are not listed. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

## General information about the safe and effective use of ZINPLAVA.

Medicines are sometimes prescribed for purposes other than those listed in the Patient Information. You can ask your pharmacist or doctor for information about ZINPLAVA that is written for doctors.

## What if I have questions?

- Call your doctor.
- Call Merck, the company that makes ZINPLAVA, at 1-800-444-2080.
- Go to the website – www.ZINPLAVA.com
  You can also find the full prescribing information written for doctors at www.ZINPLAVA.com

## What are the ingredients in ZINPLAVA?

The active ingredient is: bezlotoxumab
The inactive ingredients are: citric acid monohydrate, diethylenetriaminepentaacetic acid, polysorbate 80, sodium chloride, sodium citrate dihydrate, and water for injection, USP. ZINPLAVA may also contain sodium hydroxide.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Manufactured by: Merck Sharp & Dohme Corp., a subsidiary of
**MERCK & CO., INC.**, Whitehouse Station, NJ 08889, USA
U.S. License No. 0002

At:
MSD Ireland (Carlow)
County Carlow, Ireland

For patient information: www.merck.com/product/patient/home.html

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Issued: 10/2016
uspplmk6072-v-1610r000



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# ZINPLAVA: PI vs. PPI Comparison

| Attribute | USPI | USPPI |
|---|---|---|
| Length | 9 pages | 2 pages |
| Product Description | INDICATIONS AND USAGE (Section 1); DESCRIPTION (Section 11) | What you need to know about ZINPLAVA; What is ZINPLAVA? |
| Route of Administration | DOSAGE AND ADMINISTRATION (Section 2) | How will I receive ZINPLAVA? |
| Special Warnings | WARNINGS AND PRECAUTIONS (Section 5) | ZINPLAVA may cause serious side effects including: |
| Side Effects | ADVERSE REACTIONS (Section 6) | Common side effects of ZINPLAVA: |
| Special Populations | USE IN SPECIFIC POPULATIONS (Section 8) | Is ZINPLAVA right for me? |
| Clinical Information | CLINICAL PHARMACOLOGY (Section 12); CLINICAL STUDIES (Section 14) | *Not included in the PPI* |

**For full product labeling, see ZINPLAVA.COM**

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# ZINPLAVA: Product Description

**USPI: INDICATIONS AND USAGE**

- ZINPLAVA™ is indicated to reduce recurrence of *Clostridium difficile* infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence.

**USPPI: What is ZINPLAVA?**

- ZINPLAVA is a prescription medicine used to help decrease the risk of C-diff from coming back in people 18 years of age or older who are taking an antibiotic for C-diff and who have a high risk of C-diff coming back.

**USPI: Limitation of Use**

- ZINPLAVA is not indicated for the treatment of CDI. ZINPLAVA is not an antibacterial drug. ZINPLAVA should only be used in conjunction with antibacterial drug treatment of CDI. [See Dosage and Administration (2.1).]

**USPPI: What you need to know about ZINPLAVA (excerpt)**

- ZINPLAVA helps decrease the risk of C-diff (Clostridium difficile infection) from coming back by working with the antibiotic that you are taking to treat your C-diff. ZINPLAVA does not replace the antibiotic. ZINPLAVA is not an antibiotic.
- Keep taking your antibiotic for your C-diff as directed by your doctor.

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# ZINPLAVA: Warnings & Precautions

**USPI: WARNINGS AND PRECAUTIONS – Heart Failure**

- Heart failure was reported more commonly in the two Phase 3 clinical trials in ZINPLAVA-treated patients compared to placebo-treated patients. These adverse reactions occurred primarily in patients with underlying congestive heart failure (CHF). In patients with a history of CHF, 12.7% (15/118) of ZINPLAVA-treated patients and 4.8% (5/104) of placebo-treated patients had the serious adverse reaction of heart failure during the 12-week study period *[see Adverse Reactions (6.1)].* Additionally, in patients with a history of CHF, there were more deaths in ZINPLAVA-treated patients, 19.5% (23/118) than in placebo-treated patients, 12.5% (13/104) during the 12-week study period. The causes of death varied and included cardiac failure, infections, and respiratory failure.
- In patients with a history of CHF, ZINPLAVA should be reserved for use when the benefit outweighs the risk.

**USPPI: What are the possible side effects of ZINPLAVA?**

**ZINPLAVA may cause serious side effects, including:**

- **Heart failure.** Heart failure may happen in people who receive ZINPLAVA and can be serious. People with a history of congestive heart failure (CHF) who received ZINPLAVA had a higher rate of heart failure and death than those who did not receive ZINPLAVA.

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# ZINPLAVA: Adverse Reactions (1)

**USPI: ADVERSE REACTIONS – Clinical Trial Experience**

- The most common adverse reactions following treatment with ZINPLAVA (reported in ≥4% of patients within the first 4 weeks of infusion and with a frequency greater than placebo) were **nausea**, **pyrexia**, and **headache** (see Table 1).
- Serious adverse reactions occurring within 12 weeks following infusion were reported in 29% of ZINPLAVA-treated patients and 33% of placebo-treated patients. Heart failure was reported as a serious adverse reaction in 2.3% of the ZINPLAVA-treated patients and 1.0% of the placebo-treated patients *[see Warnings and Precautions (5.1)].*

Infusion Related Reactions

- Overall, 10% of ZINPLAVA-treated patients experienced one or more infusion specific adverse reactions on the day of, or the day after, the infusion compared to 8% of placebo-treated patients. Infusion specific adverse reactions reported in ≥0.5% of patients receiving ZINPLAVA and at a frequency greater than placebo were **nausea** (3%), **fatigue** (1%), **pyrexia** (1%), **dizziness** (1%), **headache** (2%), **dyspnea** (1%) and **hypertension** (1%). Of these patients, 78% and 20% of patients experienced mild and moderate adverse reactions, respectively. These reactions resolved within 24 hours following onset.

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# ZINPLAVA: Adverse Reactions (2)

## USPPI: What are the possible side effects of ZINPLAVA?

**Common side effects of ZINPLAVA:**

The most common side effects that may happen on the day of or the day after receiving ZINPLAVA:

- nausea
- headache
- fever
- feeling tired
- shortness of breath
- feeling dizzy
- high blood pressure

The most common side effects that may happen up to four weeks after receiving ZINPLAVA:

- nausea
- fever
- headache

**If you have any side effect that bothers you or does not go away, tell your doctor.**

There may be other side effects to ZINPLAVA that are not listed. Call your doctor for medical advice about side effects.
You may report side effects to FDA at 1-800-FDA-1088.

| USPI Term | Patient-Friendly Term |
|---|---|
| Nausea | Nausea |
| Headache | Headache |
| Pyrexia | Fever |
| Fatigue | Feeling Tired |

| USPI Term | Patient-Friendly Term |
|---|---|
| Dyspnea | Shortness of breath |
| Dizziness | Feeling dizzy |
| Hypertension | High blood pressure |

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# Key Takeaways

It is possible to achieve information about medicines that is well understood by individuals of all health literacy levels

It requires a thoughtful approach, reflecting best practices from the field of health literacy

Feel free to contact me at: Laurie_Myers@Merck.com

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