BUJAK, Magdalena, RULEWSKA, Natalia, GRABOWSKI, Filip, SIEMKO, Jakub, NESKA, Dagmara, PRYSTACKA-SZAR, Dominika, STADLER-SZAJDA, Justyna, CZYŻNIKIEWICZ, Adrianna, STOŁOWSKI, Wenancjusz and WAŚNIOWSKA, Magdalena. Treatment of Fibromyalgia - duloxetine or pregabalin? Journal of Education, Health and Sport. 2025;80:57856. eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.80.57856
https://apcz.umk.pl/JEHS/article/view/57856

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 16.01.2025. Revised: 02.03.2025. Accepted: 02.04.2025. Published: 05.04.2025.

Treatment of Fibromyalgia- duloxetine or pregabalin?

Magdalena Bujak
Krakow University Hospital
https://orcid.org/0009-0008-9274-3595
Natalia Rulewska
Provincial Specialist Hospital in Ciechanów
https://orcid.org/0009-0008-4515-7403
Filip Grabowski
Provincial Specialist Hospital in Ciechanów
https://orcid.org/0009-0007-0466-2764
Jakub Siemko
Ludwika Błażka Provincial Multi-Specialist Hospital in Inowrocław
https://orcid.org/0009-0009-9318-9458
Dagmara Neska
Ludwika Błażka Provincial Multi-Specialist Hospital in Inowrocław
https://orcid.org/0009-0003-1900-954X

Dominika Prystacka-Szar
Ludwik Rydygier Memorial Specialized Hospital in Krakow
https://orcid.org/0009-0003-6533-4247
Justyna Stadler-Szajda
Ludwika Błażka Provincial Multi-Specialist Hospital in Inowrocław
https://orcid.org/0000-0002-1742-1835
Adrianna Czyżnikiewicz
Ludwika Błażka Provincial Multi-Specialist Hospital in Inowrocław
https://orcid.org/0009-0007-4541-7175
Wenancjusz Stołowski
Ludwika Błażka Provincial Multi-Specialist Hospital in Inowrocław
https://orcid.org/0009-0009-0317-1212
Magdalena Waśniowska
Stefana Żeromskiego Specialist Hospital in Kraków
https://orcid.org/0009-0006-0614-8307

Abstract

Introduction: Fibromyalgia (FM) is a complex and chronic condition characterized by widespread pain, fatigue, and disrupted sleep, often accompanied by mood disturbances and cognitive difficulties. The pathophysiology of FM involves heightened pain sensitivity, altered neurotransmitter levels, and neurochemical imbalances, including elevated substance P and glutamate. Duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), has demonstrated efficacy in managing FM symptoms, particularly pain, functional impairment, and quality of life. Pregabalin, another widely used FM medication, reduces pain by modulating calcium channels and neurotransmitter release, improving sleep and reducing fatigue. Comparative studies indicate that duloxetine may offer broader benefits, including reduced healthcare utilization, due to its dual role in pain relief and mood stabilization. While pregabalin may be preferred in patients with specific comorbidities like functional dyspepsia, duloxetine's antidepressant effects make it a compelling option for individuals with depression-related FM symptoms.

Aim of the study: The study aimed to analyze the current treatment of Fibromyalgia and compare two main treatment methods, duloxetine and pregabalin.

Review method: The following keywords, such as fibromyalgia treatment, duloxetine, and pregabalin, have been included in the search phrases used to thoroughly examine research publications available on Pubmed.

Conclusion: This review highlights the importance of personalized treatment strategies for FM, integrating pharmacological and non-pharmacological approaches within a biopsychosocial framework. By tailoring therapies to individual needs, clinicians can optimize outcomes and improve patient quality of life.

Keywords: Fibromyalgia; treatment; duloxetine; pregabalin

Introduction

Chronic and pervasive musculoskeletal pain is the hallmark of fibromyalgia, an illness that frequently manifests with additional symptoms like exhaustion, digestive issues, and changes in mood and sleep patterns [1]. FM is a diverse illness that is frequently linked to certain conditions such as infections, neurological or mental conditions, diabetes, and rheumatic diseases [2]. When the symptoms fit established criteria and a somatic disease that adequately explains the symptoms is ruled out, a general practitioner can typically make the diagnosis [3]. A hyperactive pain detection and processing system may be present in fibromyalgia patients, as evidenced by several brain imaging studies that show enhanced activation of the pain processing network in response to nociceptive stimuli (relative to healthy controls). Additional research indicates that FM patients exhibit decreased pain inhibitory network connection or activation [4]. Patients diagnosed with fibromyalgia have been found to have higher plasma norepinephrine levels. Dopamine and serotonin levels, on the other hand, were lower than in the healthy group, which may highlight the discomfort and dispersed pain perception. However, glutamate increases the sensitivity of FM pain. Neuropeptide substance P is an important player in the pathophysiology of fibromyalgia. Compared to healthy

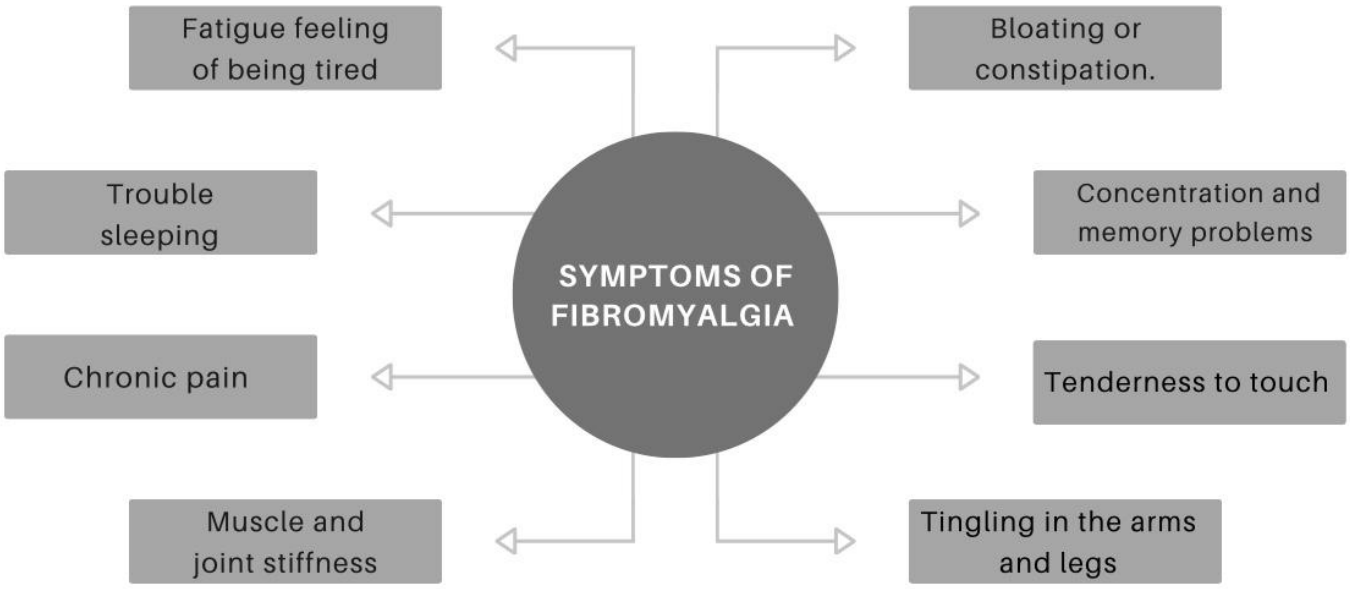
subjects, its content in the cerebrospinal fluid (CSF) is three times higher. Substance P plays a role in exaggerating the symptoms of fibromyalgia and moderating excessive pain [5]. The condition is totally unknown to the people who live around FM patients, which makes them doubt its existence. People with FM experience a lack of acceptance from those in their surroundings, including friends, family, coworkers, and themselves regarding the illness [6]. After a diagnosis, treatment can be difficult. Memantine, naltrexone, tapentadol, duloxetine, palmitoylethanolamide pills, and cannabinoids are among the potential therapy choices [7].

Treatment of Fibromyalgia

The FDA has only approved three medications for treating FMS: duloxetine, milnacipran, and pregabalin. However, there are several other medications used to treat chronic pain syndromes, including fibromyalgia. [8]. This group includes monoamine oxidase, inhibitors anti-inflammatory drugs (NSAIDs), and opioid analgesics [9]. Transcutaneous electrical nerve stimulation (TENS) has also been used in the treatment of FM. One of the studies proved that patients feel relief from pain by 30 % after TENS [10]. Non-pharmacological treatment includes physical activity in the form of exercises improving respiratory capacity/strengthening exercises, cognitive-behavioral therapies, multi-component therapies, acupuncture, hydrotherapy, and exercise meditation [11]. There is another treatment for FM called dietary intervention. Glutamate and other inflammatory substances are abundant in the majority of diets, which exacerbates FM symptoms. Conversely, people who eat a plant-based diet are more likely to have lower levels of cholesterol and saturated fat and more controlled blood glucose, which may help reduce some of the symptoms of FM [12].

Antidepressants, particularly the more recent generation, are without a doubt the most successful class of medications. These consist of drugs having noradrenergic and serotonergic actions (NaSSA), selective serotonin reuptake inhibitors (SSRI), and serotonin reuptake inhibitors and norepinephrine (NSRI) [13]. Treatment can be started after the disease has been diagnosed based on symptoms (CWP-chronic widespread pain, a feeling of stiffness and swelling of the hands, feet, or face, and physical or emotional fatigue or sleep disturbance) or criteria of the American College of Rheumatology [14].

Figure 1. [15]



Duloxetine - SNRI in the treatment of Fibromyalgia

As a strong inhibitor of the 5-HT transporter (SERT) and norepinephrine transporter (NET), duloxetine is a serotonin-norepinephrine reuptake inhibitor. 5-HT receptors in the central and peripheral nervous systems are responsible for the modulation of antinociception and pronociception with pain [16]. Duloxetine raises dopamine levels, particularly in the prefrontal brain, in addition to its usual SNRI effects [17]. Like other SSRIs and SNRIs, duloxetine alters central nervous system receptors, which over time makes the effects of the medication stronger. After roughly four to six weeks, duloxetine's complete therapeutic action manifests [18].

Duloxetine is an antidepressant drug used to treat depression, chronic pain such as osteoarthritis, Chronic Low Back Pain (CLBP), diabetic peripheral neuropathy, neuropathy, FM, and also stress urinary incontinence [19,20]. Major metabolites of duloxetine have not been demonstrated to contribute to the pharmacological effects, despite the drug being extensively metabolized [21].

Clinical investigations have shown that duloxetine 60–120 mg/day effectively reduces major FM symptoms like discomfort, diminished functional ability, and poor quality of life. To lessen or avoid side effects, it is advised that the dose be started low and titrated gradually [22]. Patients complained of anorexia, diarrhea, nasopharyngitis, constipation, xerostomia (dry mouth), nausea, and decreased appetite [23]. The findings show that changes in depression and functional impairment, two other significant categories, as well as pain severity, are probable. These findings lend credence to the idea that, frequently, a multidisciplinary approach to treating chronic primary pain syndromes is necessary, referring to the biopsychosocial paradigm [24].

4 studies were conducted on patients diagnosed with fibromyalgia, which lasted 12 weeks. Pain was assessed by the Brief Pain Inventory (BPI) 24-hour average pain severity score. Beginning at week 1 and continuing through week 12, individuals treated with duloxetine showed significantly larger improvement in changes in the BPI (BPI = Brief Pain Inventory) 24-hour average pain severity scores over time compared to those given with placebo (all evaluations P <.001). Additionally, duloxetine showed noticeably more improvement than placebo on the mean of the pain interference ratings as well as the BPI severity scores for least pain, worst pain, and pain right now [25]. There is no question that lower dosages of duloxetine had superior tolerability, even if this meta-analysis was unable to determine the optimal dosage for fibromyalgia. Individual patients should have their doses adjusted accordingly [26].

Duloxetine or Pregabalin?

Pregabalin functions by attaching itself specifically to the α2δ-1 and α2δ-2 subunits. Pregabalin contributes to pain perception by binding to these subunits, which also decreases glutamate release in the spinal dorsal horn and insula and amygdala activation during emotional processing. Pregabalin is believed to lessen pain in fibromyalgia by blocking calcium channels and neurotransmitter release, which stops the sensory propagation of

nociception [27]. Pregabalin significantly reduced pain scores in a clinical investigation compared to a placebo. When compared to the placebo group, a 450 mg/day dose of pregabalin was found to help treat fibromyalgia, resulting in less fatigue, better sleep patterns, and less pain [28]. The most common side effects associated with pregabalin were noted, such as weight gain, dizziness, somnolence, and peripheral edema [29].

Compared to pregabalin initiators, duloxetine initiators experienced a significant decrease in outpatient and emergency department visits and hospitalizations, prescription medication use, and physical therapy appointments. Previous studies have shown that depression is a predictor of increased healthcare utilization. Because duloxetine is also an antidepressant, it may help people with fibromyalgia control their depressed mood, which may explain the study's finding that it is more effective than pregabalin [30]. Pregabalin should only be used sparingly in individuals with chronic heart failure and obesity, and it may be favored in patients with associated functional dyspepsia and irritable bowel syndrome. Patients who experience "fibro fog" as a primary complaint or who drive or operate machinery for personal or professional reasons may not be able to utilize pregabalin due to its neurocognitive adverse effects, which include confusion, focus problems, and euphoria [31].

Figure 2. [32,33]

	Duloxetine	**Pregabalin**
Dosage	60 -120 mg/day	300-450 mg/ day
Side effects	Nausea, somnolence, fatigue, constipation, diarrhea	Angioedema, weight gain, dizziness and somnolence, peripheral edema, hypersensitivity
Mechanism of action	5-HT transporter (SERT) and norepinephrine transporter (NET)	Alpha2-delta site in central nervous system tissues.

	Duloxetine	Pregabalin
Pharmacokinetics	Elimination mainly through hepatic metabolism involving two P450 isozymes, CYP1A2 and CYP2D6, half-life: 12 hours	Elimination largely by renal excretion, half-life: 6 hours

One 14-week, double-blind, placebo-controlled, multicenter research, and one 6-month, randomized withdrawal study demonstrated the effectiveness of pregabalin in treating fibromyalgia.

Pregabalin total daily dosages of 300, 450, and 600 mg were compared with a placebo in a 14-week research. Patients were recruited if their baseline mean pain score was at least 40 mm on the 100 mm pain visual analog scale (VAS) and greater than or equal to 4 on an 11-point numerical pain rating scale. The study is summarized in Table 2. In a 6-month study, patients receive the same daily dose as in 14- a 14-week study. By Week 26 of the research, 53% of the people receiving pregabalin remained on the medication and continued to show a therapeutic response, compared to 33% of patients receiving a placebo [32].

Figure 3. [32]

Pregabalin mg/ day	Improvement
Placebo	47.6 %
300	68.1 %
450	77.8 %
600	66. 1%

Conclusion

This work explores the pharmacological and non-pharmacological treatment options for FM. Duloxetine, an SNRI, has been shown to effectively reduce pain, improve functional outcomes, and enhance the quality of life in FM patients. Clinical trials highlight significant benefits from duloxetine, with improvements observed early in treatment and sustained over time. Pregabalin, another effective medication, targets calcium channels to modulate pain and improve sleep and fatigue. However, its neurocognitive side effects may limit its use in some populations. Comparative analysis suggests duloxetine may have broader benefits, particularly in reducing healthcare utilization due to its dual action on pain and depression.

Non-pharmacological therapies, including physical exercise, cognitive-behavioral therapy, acupuncture, and dietary interventions, play a crucial role in a multidisciplinary approach to FM management. Personalized treatment strategies tailored to individual patient needs are essential for optimizing outcomes and improving the overall quality of life.

This review underscores the necessity of a biopsychosocial framework in managing FM and highlights the potential of combining pharmacological treatments like duloxetine and pregabalin with lifestyle interventions to address the multifaceted nature of this condition.

Author's contribution

Conceptualization: Magdalena Bujak, Magdalena Waśniowska

Methodology: Natalia Rulewska, Filip Grabowski, Jakub Siemko

Software: not applicable

Verification: Justyna Stadler- Szajda, Adrianna Czyżnikiewicz

Formal analysis: Dominika Prystacka- Szar, Natalia Rulewska

Research: Filip Grabowski, Magdalena Bujak, Wenancjusz Stołowski, Magdalena Waśniowska

Resources: Jakub Siemko, Justyna Stadler- Szajda,

Writing- rough preparation: Dagmara Neska, Adrianna Czyżnikiewicz

Writing- review and editing: Magdalena Bujak, Natalia Rulewska, Dominika Prystacka- Szar

Visualization: Magdalena Waśniowska, Jakub Siemko, Wenancjusz Stołowski

Supervision: Magdalena Bujak

Project administration: Magdalena Bujak

Funding acquisition: not applicable

All authors have read and agreed with the published version of the manuscript.

Funding statement
The study did not receive special funding.

Informed Consent Statement
Not applicable.

Conflict of Interest Statement:
The authors report no conflict of interest.

Reference:

1. Rosalba Siracusa , Rosanna Di Paola , Salvatore Cuzzocrea , Daniela Impellizzeri. Fibromyalgia: Pathogenesis, Mechanisms, Diagnosis and Treatment Options Update. doi: 10.3390/ijms22083891
2. Massimo E Maffei. Fibromyalgia: Recent Advances in Diagnosis, Classification, Pharmacotherapy and Alternative Remedies. doi: 10.3390/ijms21217877
3. Winfried Häuser, Mary-Ann Fitzcharles. Facts and myths pertaining to fibromyalgia. doi: 10.31887/DCNS.2018.20.1/whauser
4. Tobias Schmidt-Wilcke, Martin Diers. New Insights into the Pathophysiology and Treatment of Fibromyalgia. doi: 10.3390/biomedicines5020022
5. Chanika Assavarittirong, Włodzimierz Samborski, Bogna Grygiel-Górniak. Oxidative Stress in Fibromyalgia: From Pathology to Treatment. doi: 10.1155/2022/1582432
6. Liraz Cohen-Biton, Dan Buskila, Rachel Nissanholtz-Gannot. Review of Fibromyalgia (FM) Syndrome Treatments. doi: 10.3390/ijerph191912106
7. Hajra Khurshid, Israa A Qureshi, Nasrin Jahan, Terry R Went, Waleed Sultan, Alisha Sapkota, Michael Alfonso. A Systematic Review of Fibromyalgia and Recent Advancements in Treatment: Is Medicinal Cannabis a New Hope?. doi: 10.7759/cureus.17332
8. Roie Tzadok, Jacob N Ablin. Current and Emerging Pharmacotherapy for Fibromyalgia. doi: 10.1155/2020/6541798
9. Seoyoung C Kim, Joan E Landon, Daniel H Solomon. Clinical characteristics and medication uses among fibromyalgia patients newly prescribed amitriptyline, duloxetine, gabapentin or pregabalin. doi: 10.1002/acr.22071

10. Mark I Johnson, Leica S Claydon, G Peter Herbison, Gareth Jones, Carole A Paley.Transcutaneous electrical nerve stimulation (TENS) for fibromyalgia in adults. doi: 10.1002/14651858.CD012172.pub
11. Maja Hasterok, Magdalena Piegza, Paweł Dębski. Fibromyalgia from a psychiatric point of view. DOI: 10.15557/PiPK.2021.0014
12. Caroline Metyas, Tun Tun Aung, Jennifer Cheung, Marina Joseph, Andrew M Ballester, Samy Metyas. Diet and Lifestyle Modifications for Fibromyalgia. doi: 10.2174/0115733971274700231226075717
13. Włodzimierz Szamborski. Fibromyalgia — the current concepts in diagnosis and new approaches to the pathogenesis and.
14. Winfried Häuser, Wolfgang Eich, Markus Herrmann, Detlev O Nutzinger, Marcus Schiltenwolf, Peter Henningsen. Fibromyalgia Syndrome. doi: 10.3238/arztebl.2009.0383
15. https://www.niams.nih.gov/health-topics/fibromyalgia
16. Daniela Rodrigues-Amorim, José Manuel Olivares, Carlos Spuch, Tania Rivera-Baltanás.A Systematic Review of Efficacy, Safety, and Tolerability of Duloxetine. doi: 10.3389/fpsyt.2020.554899
17. Duloxetine. Jaberpreet S. Dhaliwal; Benjamin C. Spurling; Mohammed Molla.
18. Przemysław Bieńkowski. Pharmacological properties of serotonin and norepinephrine reuptake inhibitors — case of duloxetine.
19. Kelly D Karpa , Jane E Cavanaugh, Joan M Lakoski. Duloxetine pharmacology: profile of a dual monoamine modulator. DOI: 10.1111/j.1527-3458.2002.tb00234.x
20. Herlinda Bonilla-Jaime, José Armando Sánchez-Salcedo, M Maetzi Estevez-Cabrera, Tania Molina-Jiménez, José Luis Cortes-Altamirano, Alfonso Alfaro-Rodríguez. Depression and Pain: Use of Antidepressants. doi: 10.2174/1570159X19666210609161447
21. Scott D Mist, Rebecca L Ross, Kim D Jones. Duloxetine for the treatment of fibromyalgia. doi: 10.1586/eci.10.64
22. Howard S Smith, Donna Bracken, Joshua M Smith. Duloxetine: A Review of Its Safety and Efficacy in the Management of Fibromyalgia Syndrome. doi: 10.4137/JCNSD.S4127
23. Nurcan Üçeyler, Martin Offenbächer, Frank Petzke, Winfried Häuser, Claudia Sommer. New treatment options for fibromyalgia: critical appraisal of duloxetine. doi: 10.2147/ndt.s3164

24. Helen Koechlin , Anna Kharko, Tamara Probst, Julia Pradela, Stefan Buechi, Cosima Locher. Placebo Responses and Their Clinical Implications in Fibromyalgia: A Meta-Analysis Using SSRI and SNRI Trials. doi: 10.3389/fpain.2021.750523
25. Lesley M Arnold, Daniel J Clauw, Madelaine M Wohlreich, Fujun Wang, Jonna Ahl, Paula J Gaynor, Amy S Chappell. Efficacy of Duloxetine in Patients With Fibromyalgia: Pooled Analysis of 4 Placebo-Controlled Clinical Trials. doi: 10.4088/PCC.08m00680
26. Filippo Migliorini , Nicola Maffulli, Jörg Eschweiler, Alice Baroncini, Andreas Bell, Giorgia Colarossi . Duloxetine for fibromyalgia syndrome: a systematic review and meta-analysis. doi: 10.1186/s13018-023-03995-z
27. Eric A Jones, Farrah Asaad, Nishil Patel, Esha Jain, Alaa Abd-Elsayed. Management of Fibromyalgia: An Update. DOI: 10.3390/biomedicines12061266
28. Pothuri R Ram, Madhan Jeyaraman, Naveen Jeyaraman, Arulkumar Nallakumarasamy, Manish Khanna, Ashim Gupta, Sankalp Yadav. Beyond the Pain: A Systematic Narrative Review of the Latest Advancements in Fibromyalgia Treatment. doi: 10.7759/cureus.48032
29. v Sheena Derry, Malene Cording, Philip J Wiffen, Simon Law, Tudor Phillips, R Andrew Moore. Pregabalin for pain in fibromyalgia in adults. doi: 10.1002/14651858.CD011790.pub2
30. Seoyoung C Kim, Joan E Landon, Yvonne C Lee. Patterns of health care utilization related to initiation of amitriptyline, duloxetine, gabapentin, or pregabalin in fibromyalgia. doi: 10.1186/s13075-015-0530-8
31. Winfried Häuser , Frank Petzke, Claudia Sommer. Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. DOI: 10.1016/j.jpain.2010.01.002
32. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021446s035,022488s013lbl.pdf
33. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022516lbl.pdf