FIBROMYALGIA

CHI Formulary Development Project

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- October 2023
To the CHI Original Fibromyalgia Clinical Guidance- Issued March2020

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Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

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Abbreviations

AAPT	ACTTION-APS Pain Taxonomy
ACTTION	Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks
APS	American Pain Society
CHI	Council of Health Insurance
CPG	Clinical Practice Guideline
CWP	Persistent, Widespread Pain
EULAR	European Alliance of Associations for Rheumatology
FDA	Food and Drug Administration
FM	Fibromyalgia
FMS	Fibromyalgia Syndrome
IDF	CHI Drug Formulary
MSP	Pain Occurring in Multiple Sites
NICE	National Institute for Health and Care Excellence
NSAID	Non-Steroidal Anti-Inflammatory Grug
SFDA	Saudi Food and Drug Authority

Executive Summary

Fibromyalgia is a complex condition characterized by widespread musculoskeletal pain, accompanied by fatigue, sleep disturbances, memory issues, and mood fluctuations[1]. Researchers believe that fibromyalgia alters the processing of both painful and non-painful signals in the brain and spinal cord, heightening the perception of pain[1]. Symptoms can arise after events like physical trauma, surgery, infections, or significant psychological stress, or they may gradually accumulate over time without a specific trigger[1]. Key symptoms include widespread pain, persistent fatigue, and cognitive difficulties often referred to as "fibro fog."[1] Fibromyalgia frequently co-occurs with other conditions and has various contributing factors, including genetics, infections, and physical or emotional events[1]. This condition can significantly impact daily life, leading to functional impairments, depression, and health-related anxiety[1].

Epidemiological research findings on fibromyalgia (FM) in adult populations worldwide have shown an average global prevalence of FM of 2.7%[2]. Regional breakdowns revealed an average rate of 3.1% in the Americas, 2.5% in Europe, and 1.7% in Asia[2]. When considering gender differences, the mean prevalence was 4.2% in women and 1.4% in men, resulting in a female-to-male ratio of 3:1[2].

In Taif city, Saudi Arabia, a cross-sectional study conducted from June to August 2021 involving 1015 participants revealed that 7.6% had fibromyalgia syndrome (FMS)[3]. Notably, FMS was significantly more prevalent among females (9.3%) compared to males (3.1%), and individuals aged 40 or older (11.7%) had a significantly higher prevalence than those under 40 (6.0%)[3]. Additionally, occupational status had a significant impact, with employees (10.8%) and housewives (9.4%) showing higher rates than the unemployed (8.8%), students (5.0%), and retired participants (4.0%)[3].

CHI issued Fibromyalgia clinical guidelines after thorough review of renowned international and national clinical guidelines in March 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior **CHI Fibromyalgia** clinical guidance and seeks to offer guidance for the effective management of fibromyalgia. It provides an **update on the Fibromyalgia Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update were summarized, being **the addition of new guidelines to the report** such as the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION)-American

Pain Society (APS) Pain Taxonomy (AAPT): Diagnostic criteria for fibromyalgia (**2019**), the NICE guideline on Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain (**2021**), and the Consensus evidence-based clinical practice recommendations for the management of fibromyalgia (**2022**).

After carefully examining clinical guidelines and reviewing the SFDA drug list, there are no new drugs to be added to the CHI formulary, and there are no new drugs recently approved by the FDA. The following drug is no longer SFDA-registered, and it is advisable to delist them from CHI formulary: Amitriptyline Hydrochloride.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in Fibromyalgia therapeutic management.

Below is a table summarizing the major changes based on the different Fibromyalgia guidelines used to issue this report:

Table 1. General Recommendations for the Management of Fibromyalgia

Management of Fibromyalgia		
General Recommendations	**Level of Evidence/ Grade of Recommendation**	**Reference**
Management of fibromyalgia is a combination of non-pharmacological and pharmacological treatment modalities tailored according to pain intensity, function, associated features (such as depression), fatigue, sleep disturbance and patient preferences and comorbidities.	N/A	EULAR, 2016[4]
Initial management should focus on non-pharmacological therapies such as aerobic and strengthening exercise, cognitive behavioral therapies, multicomponent therapies, defined physical therapies: acupuncture, meditative movement therapies (qigong, yoga, tai chi) and mindfulness-based stress reduction.	N/A	EULAR, 2016[4]

Analgesic treatments, antidepressants, muscle relaxants, and anticonvulsants with pain modulating effects are recommended pharmacological management options.	N/A	Canadian Guidelines, 2012[5]
The primary hallmark of FM is persistent, widespread pain (CWP) or pain occurring in multiple sites (MSP), enduring for a minimum of three months.	N/A	AAPT, 2019[6]
The multitude of non-specific symptoms associated with FM can resemble a range of other medical conditions, underscoring the importance of considering alternative diagnoses when evaluating FM.	N/A	AAPT, 2019[6]
Consider using antidepressants (amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine, or sertraline) for individuals aged 18 and older with chronic primary pain after discussing the potential benefits and risks.	N/A	NICE, 2021[7]
When deciding whether to stop antidepressants, opioids, gabapentinoids, or benzodiazepines, discuss potential withdrawal issues with the patient.	N/A	NICE, 2021[7]
Non-pharmacological strategies that involve active patient participation should be an integral part of FMS treatment.	Level 1, Grade A	Italian Guidelines[8]
Physicians should encourage patients to adopt a regular lifestyle and gradually increase physical activity through motivation and/or maintain or enhance function through multi-modal therapy.	Level 4, Grade D	Italian Guidelines[8]
The use of non-steroidal anti-inflammatory drugs (NSAIDs) is conditionally discouraged because they primarily act peripherally and may have significant side effects	Level 1A recommendation	Egyptian Consensus, 2022[9]
For sleep disturbances, medications such as amitriptyline, cyclobenzaprine, or pregabalin may be considered.	Level 1A recommendation	Egyptian Consensus, 2022[9]

Strong opioids, corticosteroids, and growth hormone are strongly discouraged.	Level 1A recommendation	Egyptian Consensus, 2022[9]

At the end of the report, a key recommendation synthesis section is added highlighting the latest updates in **Fibromyalgia clinical and therapeutic management**.

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Fibromyalgia report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This part contains the updated versions of the guidelines mentioned in the March 2020 CHI fibromyalgia report and the corresponding recommendations:

Table 2. Clinical Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated Versions**
Section 1.1 EULAR revised recommendations for the management of fibromyalgia (2016)[4]	N/A*
Section 1.2 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome (2012)[5]	N/A*

*: No updated versions available

1.1.1 EULAR Revised Recommendations for the Management of Fibromyalgia (2016)

*Please refer to **Section 1.1** of CHI Fibromyalgia Report.*
There are no new updates to the European Alliance of Associations for Rheumatology (EULAR) guidelines for the management of fibromyalgia. The recommendations remain unchanged[4].

1.1.2 Canadian Guidelines for the Diagnosis and Management of Fibromyalgia Syndrome (2012)

*Please refer to **Section 1.2** of CHI Fibromyalgia Report.*
There are no new updates. The recommendations of the Canadian guideline remain unchanged[5].

1.2 New Guidelines

This part includes the added guidelines to the previous CHI Fibromyalgia report, along with their recommendations.

Table 3. List of Additional Guidelines

Additional Guidelines
Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (**ACTTION**)-American Pain Society (**APS**) Pain Taxonomy (**AAPT**): Diagnostic Criteria for Fibromyalgia (**2019**)[6]
Chronic Pain (Primary and Secondary) in Over 16s: Assessment of All Chronic Pain and Management of Chronic Primary Pain, **NICE** Guideline (**2021**)[7]
The **Italian Society for Rheumatology** Clinical Practice Guidelines for the Diagnosis and Management of Fibromyalgia: Best Practices Based on Current Scientific Evidence **(2021)**[8]
Egyptian Guideline for Fibromyalgia: Consensus Evidence-Based Clinical Practice Recommendations for the Management of Fibromyalgia (**2022**)[9]

1.2.1 Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION)-American Pain Society (APS) Pain Taxonomy (AAPT): Diagnostic Criteria for Fibromyalgia (2019)

Evidence levels and recommendation grades are not stated in the clinical guidelines.

The following recommendations are provided by the AAPT on the Diagnostic criteria for Fibromyalgia[6]:

Medical History – A comprehensive medical history should be obtained, with specific attention directed towards the following aspects:

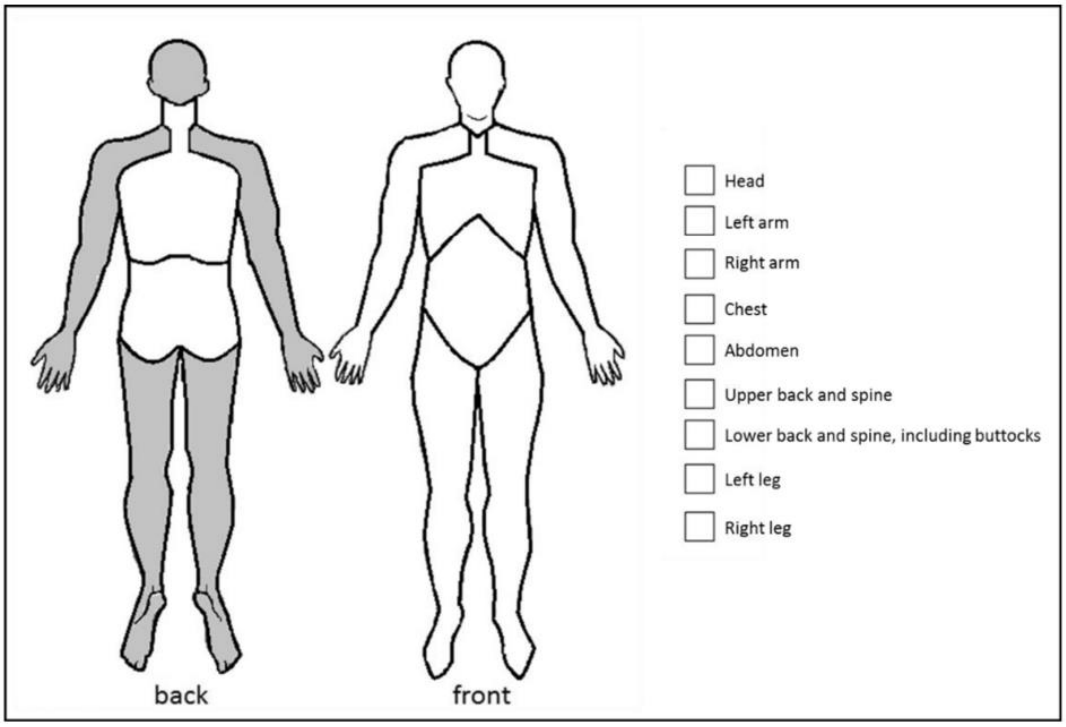
- **Pain Characteristics**: The primary hallmark of FM is persistent, widespread pain (CWP) or pain occurring in multiple sites (MSP), enduring for a minimum of three months. Documenting the location, duration, nature, and intensity of pain is essential. The recommended instrument for this purpose is the

Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks (ACTTION)-APS Pain Taxonomy (AAPT) from the American Pain Society (APS), which can be easily integrated into medical records.

- **Sleep, Fatigue, and Associated Symptoms**: Patients should undergo a detailed inquiry concerning their sleep patterns, mental and physical energy levels, cognitive disturbances, mood disorders, and other psychiatric conditions. Additionally, clinicians should explore other overlapping conditions that fall within the diagnostic spectrum of FM.
- **Other Disorders**: It's crucial to assess the patient's history for the presence of other medical conditions that may induce musculoskeletal pain, coexist with FM, or mimic its symptoms.
- **Differential Diagnosis** The multitude of non-specific symptoms associated with fibromyalgia (FM) can resemble a range of other medical conditions, underscoring the importance of considering alternative diagnoses when evaluating FM. Typically, the diagnostic process involves a comprehensive review of the patient's medical history, physical examination, and, in some cases, limited laboratory tests to effectively distinguish FM from these other conditions. These conditions may encompass systemic inflammatory arthropathies, spondyloarthritis, systemic autoimmune disorders, polymyalgia rheumatica, inflammatory myopathy, and hypothyroidism.

Table 4. AAPT Diagnostic Criteria for Fibromyalgia. Adapted from the AAPT 2019 Guidelines.

Dimension 1. Core Diagnostic Criteria
1. MSP defined as 6 or more pain sites from a total of 9 possible sites (see Fig 1) 2. Moderate to severe sleep problems OR fatigue 3. MSP plus fatigue or sleep problems must have been present for at least 3 months
NOTE. The presence of another pain disorder or related symptoms does not rule out a diagnosis of FM. However, a clinical assessment is recommended to evaluate for any condition that could fully account for the patient's symptoms or contribute to the severity of the symptoms.



Patients are asked to check the areas in which they experience pain on the 2-view manikins (ignoring the preshaded areas). Alternatively, patients may use the checklist of body sites. The number of separate sites are summed from a maximum of 9 body sites.

Figure 1. *Number of Painful Body Sites. Retrieved from the AAPT 2019 Guidelines.*

Table 5 summarizes some of the key medical disorders considered in the differential diagnosis of FM that require additional assessment, tests, and specific treatment.

Table 5. Differential Diagnoses of Fibromyalgia. Adapted from the AAPT 2019 Guidelines

Medical Disorder	Differentiating Signs and Symptoms
Rheumatologic	
Rheumatoid arthritis	Predominant joint pain, symmetric joint swelling, joint line tenderness, morning stiffness >1 hour
Systemic lupus erythematosus	Multisystem involvement, joint/muscle pain, rash, photosensitivity, fever
Polyarticular osteoarthritis	Joint stiffness, crepitus, multiple painful joints
Polymyalgia rheumatica	Proximal shoulder and hip girdle pain, weakness, stiffness, more common in the elderly

Polymyositis or other myopathies	Symmetric, proximal muscle weakness and pain
Spondyloarthropathy	Localization of spinal pain to specific sites in the neck, mid-thoracic, anterior chest wall, or lumbar regions, objective limitation of spinal mobility due to pain and stiffness
Osteomalacia	Diffuse bone pain, fractures, proximal myopathy with muscle weakness
Neurologic	
Neuropathy	Shooting or burning pain, tingling, numbness, weakness
Multiple sclerosis	Visual changes (unilateral partial or complete loss, double vision), ascending numbness in a leg or bandlike truncal numbness, slurred speech (dysarthria)
Infectious	
Lyme disease	Rash, arthritis or arthralgia, occurs in areas of endemic disease
Hepatitis	Right upper quadrant pain, nausea, decreased appetite
Endocrine	
Hyperparathyroidism	Increased thirst and urination, kidney stones, nausea/vomiting, decreased appetite, thinning bones, constipation
Cushing syndrome	Hypertension, diabetes, hirsutism, moon facies, weight gain
Addison disease	Postural hypotension, nausea, vomiting, skin pigmentation, weight loss
Hypothyroidism	Cold intolerance, mental slowing, constipation, weight gain, hair loss

1.2.2 Chronic Pain (Primary and Secondary) in Over 16s: Assessment of All Chronic Pain and Management of Chronic Primary Pain, NICE Guideline (2021)

Evidence levels and recommendation grades are outlined below[7]:

Table 6. NICE Grading Scheme for Recommendations

Grading Scheme for Recommendations			
Level	**Type of evidence**	**Grade**	**Evidence**
1	Evidence obtained from a single randomized controlled trial or a meta-analysis of randomized controlled trials	**A**	At least 1 randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level 1) without extrapolation
2a	Evidence obtained from at least 1 well-designed controlled study without randomization	**B**	Well conducted clinical studies but no randomized clinical trials on the topic of recommendation (evidence levels 2 or 3); or extrapolated from level 1 evidence
2b	Evidence obtained from at least 1 other well-designed quasi-experimental study	**–**	–
3	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies	**–**	–
4	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	**C**	Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level 4) or extrapolated from level 1 or 2 evidence. This grading indicates that directly applicable clinical studies of good quality are absent or not readily available
4	Evidence obtained from expert committee reports or opinions and/or clinical	**GPP**	Recommended good practice based on the clinical experience of the GDG.

	experiences of respected authorities		

Assessing all types of chronic pain (chronic primary pain, chronic secondary pain, or both):

Chronic Pain Management and Assessment Recommendations

Assessment:

- Conduct a person-centered assessment for individuals with chronic pain to determine the contributing factors and the pain's impact on their life.
- Emphasize:
    - Understanding the patient's unique experiences.
    - Encouraging patient participation through effective communication, provision of information, and joint decision-making.

Diagnosis:

- If no clear secondary cause exists, or if the pain’s severity seems disproportionate to an identified injury or illness, consider diagnosing chronic primary pain.
- Use clinical judgement in dialogue with the patient when determining the cause and extent of pain.
- Understand that a chronic primary pain diagnosis can evolve over time and may coexist with chronic secondary pain.

Discussion about Pain's Impact:

- Encourage patients to share how chronic pain influences their life, considering aspects like lifestyle, emotional well-being, relationships, socioeconomic status, and cultural background.
- Aim to grasp a patient’s strengths, understanding of their condition, and their expectations.
- Remember that chronic pain can cause distress; be empathetic.

Young Adults with Chronic Pain:

- When assessing young adults (16-25 years), consider the unique impact of pain on their family dynamics, education, and overall development.

Providing Information:

- Offer relevant advice tailored to individual preferences at every care stage.
- Discuss with patients (and their families/carers) about the potential unpredictability of pain, emphasizing that improvements in life quality can still occur.

Care Plan Development:

- Discuss a care and support plan with the patient, focusing on their goals, strengths, and desired treatment methods.
- Clearly explain potential benefits, risks, and uncertainties at all stages.
- For those with both chronic primary and secondary pain, use clinical judgement in decision-making.

Flare-ups:

- Re-evaluate patients presenting with pain flare-ups or changes in symptoms. Recognize that flare-ups may not always have identifiable causes.
- During flare-ups, revisit and potentially modify the care plan and explore potential contributing factors.

Managing Chronic Primary Pain:

Non-Pharmacological Management:

- Offer supervised group exercise programs for individuals aged 16 and older, tailored to their specific needs and preferences.
- Encourage long-term physical activity for general health benefits.
- Consider acceptance and commitment therapy (ACT) or cognitive-behavioral therapy (CBT) for chronic primary pain in individuals aged 16 and older, delivered by trained healthcare professionals.
- Avoid offering biofeedback to people aged 16 years and over to manage chronic primary pain.
- Consider acupuncture or dry needling in a community setting, delivered by band 7 (equivalent or lower) appropriately trained healthcare professionals, for those aged 16 and older.
- Do not recommend TENS, ultrasound, or interferential therapy.

Pharmacological Management:

- Consider using antidepressants (amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine, or sertraline) for individuals aged 18 and older with chronic primary pain after discussing the potential benefits and risks.

- Seek specialist advice for pharmacological management with antidepressants for young people aged 16 to 17.
- Clarify that antidepressants may help with quality of life, pain, sleep, and psychological distress even without a depression diagnosis.
- Do not initiate the following medicines for chronic primary pain in individuals aged 16 and older:
    - Antiepileptic drugs (except in clinical trials for complex regional pain syndrome)
    - Antipsychotic drugs
    - Benzodiazepines
    - Corticosteroid trigger point injections
    - Ketamine
    - Local anesthetics (except in clinical trials for complex regional pain syndrome)
    - Local anesthetic/corticosteroid combination trigger point injections
    - Non-steroidal anti-inflammatory drugs
    - Opioids
    - Paracetamol.

Note on Gabapentinoids:

- Pregabalin and gabapentin (gabapentinoids) are Class C controlled substances. Evaluate patients for a history of drug misuse before prescribing and monitor for signs of misuse and dependence.

Review of Medications:

- If a person is already taking any of the medicines listed above (that are not recommended), review the prescribing as part of shared decision making. Discuss the lack of evidence for these medicines in treating chronic primary pain.
- Consider continuing if there is reported benefit at a safe dose with few harms or discuss reducing and stopping the medicine if little benefit or significant harm is reported.

Withdrawal and Shared Decision Making:

- When deciding whether to stop antidepressants, opioids, gabapentinoids, or benzodiazepines, discuss potential withdrawal issues with the patient.

1.2.3 The Italian Society for Rheumatology Clinical Practice Guidelines for the Diagnosis and Management of Fibromyalgia: Best Practices Based on Current Scientific Evidence (2021)

Evidence levels are outlined in the table below[8]:

Table 7. Categories of Evidence and Strength of Recommendations Based on the Oxford Levels of Evidence

Category	Evidence
1	From meta-analysis of randomized controlled trials or from at least one randomized controlled trial
2	From at least one controlled study without randomization or from at least one cohort study
3	From at least one case-control study
4	From case-series or poor-quality cohort and case-control studies
5	From expert committee reports or opinions and/or clinical experience of respected authorities

The following recommendations are provided by the Italian Society for Rheumatology on the diagnosis and management of fibromyalgia[8]:

- Fibromyalgia syndrome (FMS) necessitates a comprehensive evaluation encompassing pain, functionality, concurrent health conditions, and the psychological context. Generally, the management of FMS should adhere to a gradual approach (level 4, grade D). Diagnosis, severity assessment, and treatment coordination should be conducted by a rheumatologist who possesses expertise in FMS care. Patients with mild FMS can receive treatment in a primary care setting under the guidance of an experienced healthcare provider and participation in patient support groups (level 3, grade C). Specialized ongoing management should be reserved for patients who do not respond to initial treatment or those with complicated concurrent health issues (level 5, grade D). In some cases, a multidisciplinary team, which may include sleep specialists, nutritionists, or psychologists (level 1, grade A), may be required. As the treatment approach is based on self-management principles and employs a multi-modal strategy (level 1, grade A), it is advisable to tailor the approach to each patient and maintain diligent and regular monitoring, particularly during the initial stages (level 5, grade D).
- The management of fibromyalgia (FMS) should strive to enhance the quality of life by carefully weighing the advantages and drawbacks of treatment (level 4, grade D). At the beginning of treatment, patients should be encouraged to

establish specific health and quality of life objectives and assess their progress during follow-up (level 5, grade D).

- Clinical diagnosis of FMS relies on the presence of peculiar symptoms persisting for at least three months, while excluding those linked to other medical conditions (level 5, grade D). Although the 2016 review of the American College of Rheumatology (ACR) FMS diagnostic criteria (2011/2010) can aid in the initial assessment, it should be noted that symptoms can fluctuate over time (level 3, grade B). Physical examination should generally appear normal except for heightened sensitivity to soft tissue pressure (level 5, grade D). However, examining 'tender points' based on the 1990 ACR diagnostic criteria holds little clinical significance and does not confirm an FMS diagnosis (level 5, grade D).
- Key symptoms of FMS encompass:
    - Chronic and widespread musculoskeletal pain
    - Fatigue and weakness
    - Sleep disturbances
    - Neurocognitive issues.

  Psycho-emotional changes (anxiety, depression, etc.) may correlate with various somatic and neurovegetative symptoms that vary in intensity (level 5, grade D). Healthcare providers should be aware that pain can be linked to other medical or psychological conditions, and patients with other medical ailments may also have concurrent FMS (level 5, grade D).
- FMS should be diagnosed primarily through clinical assessment without the need for confirmatory laboratory tests (level 5, grade D). Repeated tests after diagnosis should be avoided unless prompted by new symptoms or clinical findings (level 5, grade D). Additional laboratory or imaging analyses should be based on the patient's individual clinical evaluation, which may suggest other medical conditions (level 5, grade D).
- After an FMS diagnosis, patients should be informed about recommended and non-recommended treatments (level 4, grade A). Healthcare providers should educate patients about the condition's pathogenesis in an empathetic, open, and honest manner, devoid of negative attitudes, and should facilitate shared decision-making (level 3, grade D). Patients should be informed that FMS primarily affects the functional sphere without clear evidence of organic damage. Healthcare providers should affirm the legitimacy of the disorder, offer information regarding long-term prognosis (i.e., life expectancy assessment), and provide a clear explanation of symptoms (level 3, grade D). Emphasis should be placed on the patient's ability to alleviate symptoms

through coping strategies, with the understanding that outcomes can be favorable despite symptom fluctuations (level 3, grade B). Patient associations can play an active role in promoting educational and support activities (e.g., self-help groups, informational materials) (level 5, grade D).

- Physicians should select pharmacological strategies (including combinations of drugs) based on symptoms and take care to avoid drug interactions (level 5, grade D). Pharmacological treatments should commence at low doses, with a cautious and gradual dose escalation to minimize poor tolerance and potential side effects (level 5, grade D). In complex cases unresponsive to standard therapies, adopting a 'multi-modal' approach (combining physical activity with psychotherapeutic support) is advisable, with patient involvement (level 1, grade A).
- According to the WHO step-up analgesic scale, paracetamol may be beneficial in some patients; however, clinicians should be aware of the effective and toxic doses (level 5, grade D). Weak opioids, particularly tramadol, should be considered for patients with moderate to severe pain unresponsive to other treatments (level 1, grade A). Close monitoring of pharmacological effects, especially drug-related side effects or behavioral issues, is essential (level 5, grade D). Opioid use should be discouraged if there is no improvement in symptoms (level 5, Grade D).
- Anticonvulsant drugs, especially pregabalin, can be valuable for their pain-modulating properties. Treatment should begin with the lowest feasible dose and be gradually increased, with attention to adverse effects (level 1, grade A).
- In FMS treatment, serotonin reuptake inhibitors (such as fluoxetine and paroxetine) and norepinephrine (duloxetine), or tricyclic antidepressant drugs (like amitriptyline) may be employed (level 1, grade A). Treatment with cyclobenzaprine (level 1, grade A) and cannabinoids (level 3, grade C) could be considered, particularly for patients with significant sleep disturbances.
- Non-pharmacological strategies that involve active patient participation should be an integral part of FMS treatment (level 1, grade A). Physicians should encourage patients to adopt a regular lifestyle and gradually increase physical activity through motivation and/or maintain or enhance function through multi-modal therapy (level 4, grade D). Physicians should recognize the negative impact of psychological distress associated with FMS (level 3, grade D) and promote psychological assessment or counseling (level 5, grade C).
- Physical therapies, tailored to individual patient capabilities, should be considered for FMS, including aerobic resistance training, strength exercises,

water-based activities like water jogging, and thermal therapy (e.g., thermal spring baths) (level 1, grade A).

- Psychological therapies like behavioral-cognitive therapy and occupational therapy, including patient education, should be considered, even for short durations (level 1, grade A). Techniques like hypnosis, guided imagery, or therapeutic writing may also be explored (level 3, grade C).
- Non-conventional therapies that may be considered include:
    - Meditative movement therapies (qigong, yoga, tai chi), mindfulness-based stress reduction programs, and relaxation training (combined with exercise) (level 1, grade A).
    - Acupuncture (level 1, grade A).
    - Hydrotherapy (level 1, grade C).
- Clinical follow-up should be guided by the rheumatologist's judgment, with more frequent visits during the initial phase or until symptoms stabilize (level 5, grade E). The development of new symptoms may necessitate clinical evaluation to rule out other conditions (level 5, grade E). Patient goals and achievement levels should be documented as a useful outcome measure (level 5, grade E). Physicians should consider that factors such as passivity, lack of self-control, and mood disturbances can negatively impact outcomes (level 5, grade E). Tender point examinations should not be used as an outcome measure (level 3, grade C).
- Treatment benefits should be regularly assessed by both patients and physicians, and therapy should continue only if positive effects are experienced. In cases where drug therapy yields a response, a gradual withdrawal should be considered after an appropriate treatment duration (level 2, grade A). Patients who experience improvement with aerobic endurance training should continue to incorporate it into their routines (level 1, grade A). Physicians should encourage patients to maintain optimal productivity, as outcomes tend to be more favorable for those who are employed (level 3, grade D). FMS patients on long-term sick leave should be encouraged to participate in appropriate rehabilitation programs aimed at improving function, including returning to work if possible (level 5, grade D). For long-term therapy, patients should be educated on self-managed procedures that can be performed independently (e.g., individualized resistance or strength training, stretching, or heat therapy) (level 2, grade A).

1.2.4 Egyptian Guideline for Fibromyalgia Consensus Evidence-Based Clinical Practice Recommendations for the Management of Fibromyalgia (2022)

Evidence levels and recommendation grades are outlined below[9]:

Table 8. Grading Scheme for Recommendations

Levels of evidence according to the Oxford Center of Evidence-Based Medicine	
1a	Systematic review (with homogeneity) of randomized controlled trials
1b	Individual randomized controlled trial (with narrow confidence interval)
1c	All or none
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low-quality randomized controlled trials, e.g., < 80% follow-up)
2c	"Outcomes" research; ecological studies
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series (and poor-quality cohort and case-control studies)
5	Expert opinion without an explicit critical appraisal or based on physiology, bench research, or "first principles"

The following recommendations are provided on the management of fibromyalgia[9]:

- **How is fibromyalgia (FM) diagnosed?** The diagnosis of FM involves considering a combination of reported symptoms along with standard investigations. To confirm the diagnosis, healthcare professionals can refer to the ACR preliminary diagnostic criteria for FM from 2010, which primarily relies on assessing Widespread Pain Index (WPI) and Symptom Severity Scale (SSS). It's important to note that the specific tender point examination outlined in the 1990 ACR diagnostic criteria is not mandatory for confirming a clinical diagnosis of FM. Patients are diagnosed with FM if they meet the following three conditions: (i) WPI ≥ 7 and SS Scale score ≥ 5, or WPI 3–6 and SS Scale score ≥ 9, (ii) symptoms have been consistently present at a similar level for at least three months, and (iii) there is no other underlying disorder that would explain the pain. (Level 1A recommendation)
- In 2016, ACR further revised the FM diagnostic criteria (ACR 2016 Cr) by adding the generalized pain criterion, which was defined as pain in at least four of five regions (excluding jaw, chest, and abdominal pain) specifying somatic symptoms as headache, pain or cramps in lower abdomen, and depression,

and confirming the framework of PDS. These criteria state specifically that 'a diagnosis of FM is valid irrespective of other diagnoses[10].

- A diagnosis of FM does not exclude the presence of other clinically important illnesses.' This comment was inserted into the ACR 2016 Cr to make clear that FM criteria were valid in the presence of other clinically important illnesses, including those diagnosed using the ACR 2010 and 2011 criteria[10].
- **Should tender points be considered in the diagnosis of FM?** Tender points can be considered as part of the diagnostic process for FM, especially when evaluated in conjunction with other functional disorders as outlined in the ACR 2010 criteria. The count of tender points may be associated with the severity of somatic symptoms, particularly those related to emotional stress. (Level 2A recommendation)
- **What investigations should be conducted for a patient with widespread pain?** There are no specific laboratory tests that can definitively confirm a clinical diagnosis of FM. FM should not be viewed as a diagnosis of exclusion. Laboratory testing should be limited to a basic panel, including a complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid-stimulating hormone (TSH), hepatitis C virus antibody (HCV Ab), vitamin D levels, and anti-tissue transglutaminase IgA antibody testing. Additionally, creatine kinase levels should be checked to rule out conditions that might mimic FM, such as endocrine disorders (e.g., hypothyroidism), rheumatic conditions (e.g., early inflammatory arthritis or polymyalgia rheumatica), celiac disease, or neurological diseases (e.g., myopathy or multiple sclerosis), depending on the clinical evaluation. Musculoskeletal ultrasound (MSUS) can be employed where relevant to rule out inflammatory arthritic conditions. Psychological evaluations may also be considered for selected patients. (Level 2B recommendation)
- **Can patient-reported outcomes be used as a diagnostic tool and for evaluating FM patients?** Patients with FM often experience higher risks of somatic symptoms, depression, and panic syndrome compared to those with rheumatoid arthritis. Additionally, they may have more pronounced pain, sleep disturbances, and reduced quality of life. Patient-reported outcomes provide a patient-friendly method to gather all these relevant data. (Level 1A recommendation)
- **What are the treatment strategies for FM?** The treatment approach for FM should be comprehensive and patient-centered, involving a multidisciplinary team. It should include a gradual, multimodal, and individually tailored approach to management, with close monitoring and regular follow-up, especially during the early stages of treatment. (Level 1A recommendation)

- **What are the recommended non-pharmacologic treatments?** Initial management should prioritize non-pharmacological therapies based on factors like availability, cost, and patient preferences. Patients should be encouraged to engage in gradually increasing aerobic and strength-building exercises to maintain or enhance their function. If necessary, cognitive behavioral therapies can be added, along with multicomponent therapies (comprising at least one educational or psychological therapy and at least one exercise therapy). Specific physical therapies like acupuncture or hydrotherapy, meditative movement therapies such as yoga and tai chi, and mindfulness-based stress reduction can also be considered. Dietary recommendations for FM patients should include quitting tobacco use and avoiding chemically processed foods, aspartame, and monosodium glutamate (MSG). Encouraging a gluten-free diet, slowly reducing caffeine intake, and promoting overall healthy nutrition, appropriate vitamin supplementation, bone health, and weight management, if needed, are also advisable. It is partially recommended to avoid prolonged exposure to electromagnetic field devices. (Level 2A recommendation)
- **Which type of exercise is most effective: strength and/or aerobic training?** There are no significant differences, although supervised aerobic exercise may lead to greater improvements in physical capacity and FM symptoms. Water-based exercises can also enhance both physical and emotional aspects of FM. Since subjective muscle pain can be a barrier to exercise, patients should be encouraged to choose enjoyable and convenient activities, whether land-based or water-based, that fit their budget to improve adherence. (Level 1A recommendation)
- **What are the recommended pharmacologic treatments?** If non-pharmacological approaches do not provide adequate relief, a symptom-based pharmacological approach can be considered after reevaluating the patient. For patients experiencing severe pain, medications like duloxetine or milnacipran and pregabalin can be considered, while tramadol may be suitable for certain patients. The use of non-steroidal anti-inflammatory drugs (NSAIDs) is conditionally discouraged because they primarily act peripherally and may have significant side effects, so their use should be limited to conditions like osteoarthritis. For sleep disturbances, medications such as amitriptyline, cyclobenzaprine, or pregabalin may be considered. Medications should be initiated at low doses with gradual titration to minimize side effects, and regular follow-up is essential to monitor both efficacy and side effects, as some medication side effects may resemble FM symptoms. If multiple symptoms coexist, a combination of medications may be necessary, requiring careful consideration of potential drug interactions. Strong opioids,

corticosteroids, and growth hormone are strongly discouraged. (Level 1A recommendation)

- **Are combined pharmacological and non-pharmacological approaches to management more effective than single modality management?** The ideal approach involves a combination of both non-pharmacological and pharmacological treatments in a multimodal approach. Both approaches have been shown to be effective in improving key FM symptoms, including pain, fatigue, depression, and quality of life. (Level 1A recommendation)
- **How should FM be managed when it occurs as a comorbidity with inflammatory arthritis?** When FM occurs as a comorbidity with inflammatory arthritis, the management should follow the same principles as primary FM treatment. It should be combined with appropriate management of the underlying inflammatory disease, taking into consideration potential drug interactions and side effects. (Level 1B recommendation)
- **What factors may help predict the outcome in FM?** FM symptoms can persist and fluctuate over time, even with treatment. However, an early response to a specific medication may serve as an indicator of treatment effectiveness. Factors that could negatively influence the outcome include passivity, a poor internal locus of control, cognitive dysfunction, prominent mood disorders, perfectionism, meticulous and obsessive personalities, and uncontrolled underlying diseases, if present. (Level 2A recommendation)
- **How should patients with FM be followed regarding function, global status, and quality of life?** Clinical follow-up should be tailored to the individual case and evaluated by the physician. More frequent visits may be recommended during the initial phase of management or until symptoms stabilize. In case new symptoms develop, clinical evaluation is necessary to ensure they are not attributable to another medical condition. (Level 1A recommendation)
- **What is the role of self-management in the treatment of patients with FM?** Self-management plays a crucial role in the treatment of FM. It involves patient education and active participation, with a focus on reassuring patients that physical activity will not harm them, especially if they tend to be passive. Encouraging self-efficacy and providing social support can facilitate the adoption of health-promoting lifestyles. This is achieved through graded incremental activity aimed at maintaining or improving function. (Level 1B recommendation)

Section 2.0 Drug Therapy in Fibromyalgia

This section comprises three subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, and the third one outlines the drugs that have been withdrawn from the market.

2.1 Additions

There are no new drugs added to the treatment of Fibromyalgia. The drugs used in the management of Fibromyalgia are still the same.

2.2 Modifications

Remove the PE ST for Gabapentin.

Add the PE ST for CYCLOBENZAPRINE HYDROCHLORIDE and PARACETAMOL, to be used as 2nd line therapy.

2.3 Delisting

The medications below are no longer SFDA registered[11], therefore, it is advisable to delist the following drugs from CHI formulary. *Please refer to* ***Drug Therapy in Fibromyalgia - Section 2*** *of CHI Fibromyalgia original clinical guidance.*

- Amitriptyline Hydrochloride

Section 3.0 Key Recommendations Synthesis

- Management of Fibromyalgia is a combination of non-pharmacological and pharmacological treatment modalities tailored according to pain intensity, function, associated features (such as depression), fatigue, sleep disturbance and patient preferences and comorbidities. (N/A, EULAR, 2016[4])
- Initial management should focus on non-pharmacological therapies such as aerobic and strengthening exercise, cognitive behavioral therapies, multicomponent therapies, defined physical therapies: acupuncture, meditative movement therapies (qigong, yoga, tai chi) and mindfulness-based stress reduction. (N/A, EULAR, 2016[4])
- EULAR recommends using Duloxetine, Pregabalin, or tramadol (in combination with paracetamol) in severe pain, and that Amitriptyline, cyclobenzaprine, or Pregabalin should be considered at night for sleep problems. (N/A, EULAR, 2016[4])
- Analgesic treatments, antidepressants, muscle relaxants, and anticonvulsants with pain modulating effects are recommended pharmacological management options. (N/A, Canadian Guidelines, 2012[5])
- The primary hallmark of FM is persistent, widespread pain (CWP) or pain occurring in multiple sites (MSP), enduring for a minimum of three months. Documenting the location, duration, nature, and intensity of pain is essential. (N/A, AAPT, 2019[6]).
- Patients should undergo a detailed inquiry concerning their sleep patterns, mental and physical energy levels, cognitive disturbances, mood disorders, and other psychiatric conditions (N/A, AAPT, 2019[6]).
- The multitude of non-specific symptoms associated with fibromyalgia (FM) can resemble a range of other medical conditions, underscoring the importance of considering alternative diagnoses when evaluating FM (N/A, AAPT, 2019[6]).
- Consider acceptance and commitment therapy (ACT) or cognitive-behavioral therapy (CBT) for chronic primary pain in individuals aged 16 and older, delivered by trained healthcare professionals (N/A, NICE, 2021[7]).
- Consider using antidepressants (amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine, or sertraline) for individuals aged 18 and older with chronic primary pain after discussing the potential benefits and risks (N/A, NICE, 2021[7]).

- When deciding whether to stop antidepressants, opioids, gabapentinoids, or benzodiazepines, discuss potential withdrawal issues with the patient (N/A, NICE, 2021[7]).
- According to the WHO step-up analgesic scale, paracetamol may be beneficial in some patients; however, clinicians should be aware of the effective and toxic doses (level 5, grade D, Italian Guidelines[8]).
- Weak opioids, particularly tramadol, should be considered for patients with moderate to severe pain unresponsive to other treatments (level 1, grade A). Opioid use should be discouraged if there is no improvement in symptoms (level 5, Grade D). (Italian Guidelines[8])
- Anticonvulsant drugs, especially pregabalin, can be valuable for their pain-modulating properties. Treatment should begin with the lowest feasible dose and be gradually increased, with attention to adverse effects (level 1, grade A, Italian Guidelines[8]).
- In FMS treatment, serotonin reuptake inhibitors (such as fluoxetine and paroxetine) and norepinephrine (duloxetine), or tricyclic antidepressant drugs (like amitriptyline) may be employed (level 1, grade A, Italian Guidelines). Treatment with cyclobenzaprine (level 1, grade A) and cannabinoids (level 3, grade C) could be considered, particularly for patients with significant sleep disturbances (Italian Guidelines[8]).
- Non-pharmacological strategies that involve active patient participation should be an integral part of FMS treatment (level 1, grade A, Italian Guidelines[8]). Physicians should encourage patients to adopt a regular lifestyle and gradually increase physical activity through motivation and/or maintain or enhance function through multi-modal therapy (level 4, grade D, Italian Guidelines[8]).
- The use of non-steroidal anti-inflammatory drugs (NSAIDs) is conditionally discouraged because they primarily act peripherally and may have significant side effects, so their use should be limited to conditions like osteoarthritis. For sleep disturbances, medications such as amitriptyline, cyclobenzaprine, or pregabalin may be considered. Strong opioids, corticosteroids, and growth hormone are strongly discouraged. (Level 1A recommendation, Egyptian, 2022[9])

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Fibromyalgia report** and aims to provide recommendations to aid in the management of Fibromyalgia. It is important to note that these recommendations should be utilized to support clinical

decision-making and not replace it in the management of individual patients with Fibromyalgia. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

II. Adult and Pediatric Quantity Limit?

This is either the adult or pediatric maximum amount of a drug that can be administered per day based on a maximum daily dose. If there is no clinical evidence supporting the quantity limit for that relevant indication, this column will be left as Blank.

III. What information is available in the notes?

"Notes" section provides details of the prescribing edits, extra important drug information and special warning and precautions.

IV. Drug interactions

- A: No known interaction
- B: No action needed
- C: Monitor therapy
- D: Consider therapy modification
- X: Avoid combination

V. Defined Daily Dose

The Defined Daily Dose (DDD) is to be set based on the WHO recommendations https://www.whocc.no/ddd/definition_and_general_considera/

VI. REMS

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.

Appendix B. Fibromyalgia Scope

Comparison of the 2020 and the 2023 Report

2020	Changes Performed	2023	Rationale
Section 1.0 Fibromyalgia Clinical Guidelines			
EULAR revised recommendations for the management of fibromyalgia 2016[4]	**N/A**	**N/A**	
Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome 2012[5]	**N/A**	**N/A**	
	Missing	**Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION)- American Pain Society (APS) Pain Taxonomy (AAPT): Diagnostic criteria for fibromyalgia (2019)**[6]	Insert table on diagnosis of fibromyalgia.
	Missing	**Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain NICE guideline (2021)**[7]	Insert recommendations on assessing chronic primary pain (includes fibromyalgia), as well as the recommendations on the management of chronic primary pain. No new drugs.

	Missing	**Consensus evidence-based clinical practice recommendations for the management of fibromyalgia (2022)**[9]	Insert consensus recommendations.

Appendix C. MeSH Terms PubMed

The following is the result of the PubMed search conducted for guideline search:

Query	Filters	Search Details	Results
((((((((((((((((((((((((Fibromyalgia [MeSH Terms]) OR (Fibromyalgias[Title/Abstract])) OR (Fibromyalgia-Fibromyositis Syndrome[Title/Abstract])) OR (Fibromyalgia Fibromyositis Syndrome[Title/Abstract])) OR (Fibromyalgia-Fibromyositis Syndromes[Title/Abstract])) OR (Syndrome, Fibromyalgia-Fibromyositis[Title/Abstract])) OR (Syndromes, Fibromyalgia-Fibromyositis[Title/Abstract])) OR (Rheumatism, Muscular[Title/Abstract])) OR (Muscular Rheumatism[Title/Abstract])) OR (Fibrositis[Title/Abstract])) OR (Fibrositides[Title/Abstract])) OR (Myofascial Pain Syndrome, Diffuse[Title/Abstract])) OR (Diffuse Myofascial Pain Syndrome[Title/Abstract])) OR (Fibromyositis-Fibromyalgia Syndrome[Title/Abstract])) OR (Fibromyositis Fibromyalgia Syndrome[Title/Abstract])) OR (Fibromyositis-Fibromyalgia Syndromes[Title/Abstract])) OR (Syndrome, Fibromyositis-Fibromyalgia[Title/Abstract])) OR (Syndromes, Fibromyositis-Fibromyalgia[Title/Abstract])) OR (Fibromyalgia, Secondary[Title/Abstract])) OR (Fibromyalgias, Secondary[Title/Abstract])) OR (Secondary Fibromyalgia[Title/Abstract])) OR (Secondary	Guideline, in the last 5 years, English	("Fibromyalgia"[MeSH Terms] OR "Fibromyalgias"[Title/Abstract] OR ("Syndrome"[Title/Abstract]) OR ((("Fibromyalgia"[MeSH Terms] OR "Fibromyalgia"[All Fields] OR "Fibromyalgias"[All Fields]) AND ("Fibromyalgia"[MeSH Terms] OR "Fibromyalgia"[All Fields] OR "fibromyositis"[All Fields])) AND "Syndrome"[Title/Abstract]) OR ("Syndromes"[Title/Abstract]) OR "rheumatism muscular"[Title/Abstract] OR "muscular rheumatism"[Title/Abstract] OR "Fibrositis"[Title/Abstract] OR (("Myofascial"[All Fields] AND ("Pain"[MeSH Terms] OR "Pain"[All Fields])) AND "syndrome diffuse"[Title/Abstract]) OR (("diffusable"[All Fields] OR "diffusant"[All Fields] OR "diffusants"[All Fields] OR "Diffuse"[All Fields] OR "diffusely"[All Fields] OR "diffuses"[All Fields] OR "diffusibility"[All Fields] OR "diffusible"[All Fields] OR "diffusion"[MeSH Terms] OR "diffusion"[All Fields] OR "diffused"[All Fields] OR "diffusing"[All Fields] OR "diffusions"[All Fields] OR "diffusive"[All Fields] OR "diffusively"[All Fields] OR "diffusivities"[All Fields] OR "diffusivity"[All Fields]) AND "myofascial pain syndrome"[Title/Abstract]) OR ("Syndrome"[Title/Abstract]) OR	444

Fibromyalgias[Title/Abstract])) OR (Fibromyalgia, Primary[Title/Abstract])) OR (Fibromyalgias, Primary[Title/Abstract])) OR (Primary Fibromyalgia[Title/Abstract])) OR (Primary Fibromyalgias[Title/Abstract])		(("Fibromyalgia"[MeSH Terms] OR "Fibromyalgia"[All Fields] OR "fibromyositis"[All Fields]) AND "fibromyalgia syndrome"[Title/Abstract]) OR ("Syndromes"[Title/Abstract]) OR "fibromyalgia secondary"[Title/Abstract] OR (("Fibromyalgia"[MeSH Terms] OR "Fibromyalgia"[All Fields] OR "Fibromyalgias"[All Fields]) AND "Secondary"[Title/Abstract]) OR "secondary fibromyalgia"[Title/Abstract] OR "secondary fibromyalgias"[Title/Abstract] OR "fibromyalgia primary"[Title/Abstract] OR (("Fibromyalgia"[MeSH Terms] OR "Fibromyalgia"[All Fields] OR "Fibromyalgias"[All Fields]) AND "Primary"[Title/Abstract]) OR "primary fibromyalgia"[Title/Abstract] OR "primary fibromyalgias"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]) AND (english[Filter]))	

Appendix D. Treatment Algorithm

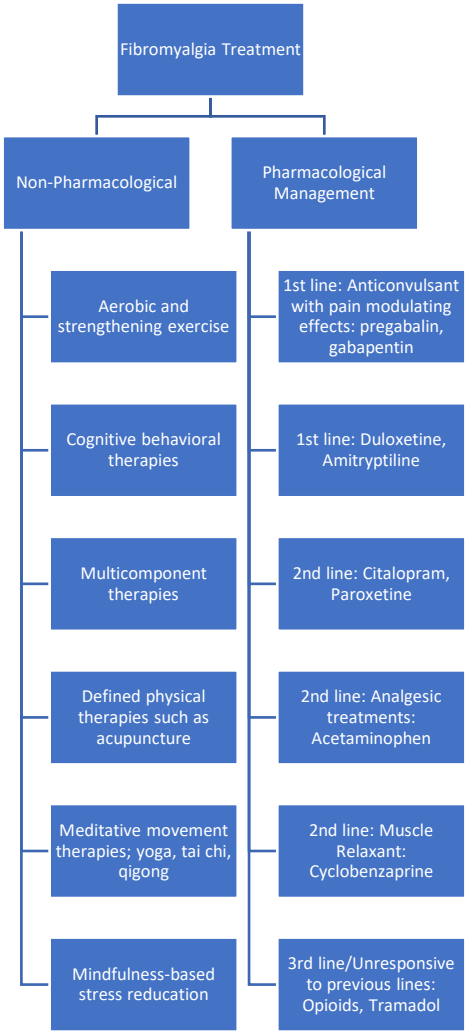

Figure 2. *Treatment Algorithm for the Management of Fibromyalgia*