ΘΕΡΑΠΕΙΑ ΟΞΕΙΑΣ ΚΕΦΑΛΑΛΓΙΑΣ ΚΑΙ ΝΕΥΡΟΠΑΘΗΤΙΚΟΥ ΠΟΝΟΥ

Outline of International Classification of Headache Disorders II

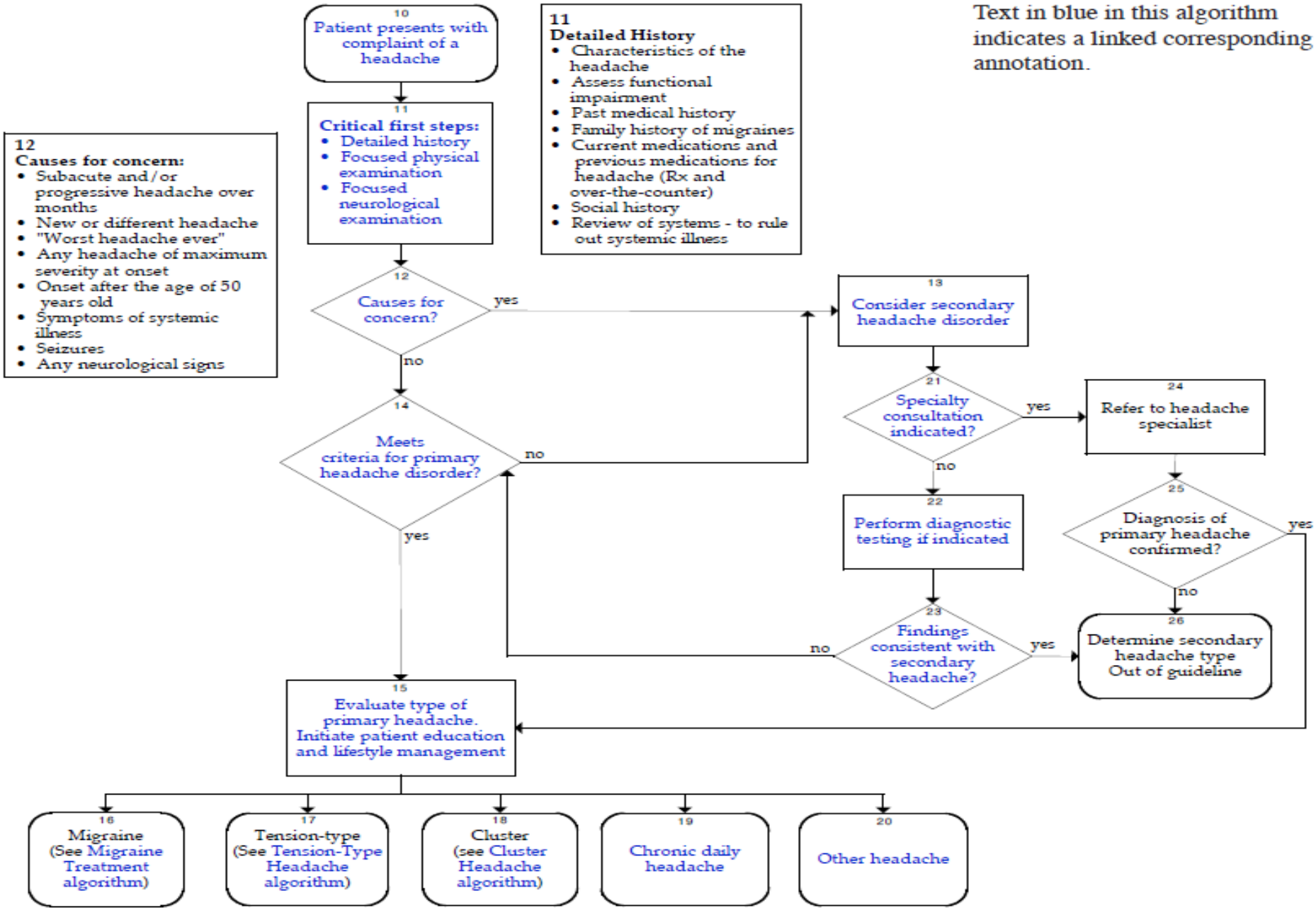
Primary Headache Disorders

- 1. Migraine
  - Migraine without aura
  - Migraine with aura
  - Childhood periodic syndromes that are precursors of migraine
  - Retinal migraine
  - Complications of migraine
  - Probable migraine
- 2. Tension-type headache
  - Infrequent episodic tension-type
  - Frequent episodic tension-type
  - Chronic tension-type
  - Probable tension-type
- 3. Cluster headache and other trigeminal autonomic cephalgia
  - Cluster headache
  - Paroxysmal hemicrania
  - Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
  - Probable trigeminal autonomic cephalgia
- 4. Other primary headaches
  - Primary stabbing headache
  - Primary cough headache
  - Primary exertional headache
  - Primary headache associated with sexual activity
  - Hypnic headache
  - Primary thunderclap headache
  - Hemicrania continua
  - New daily persistent headache

Secondary Headache Disorders

- 5. Headache attributed to head and neck trauma
- 6. Headache attributed to cranial or cervical vascular disorders
- 7. Headache attributed to nonvascular intracranial disorder
- 8. Headache atributed to substance or its withdrawal
- 9. Headache attributed to infection
- 10. Headache attributed to disturbance of homeostasis
- 11. Headache or facial pain attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cranial structures
- 12. Headache attributed to psychiatric disorders
- 13. Cranial neuralgias, central and primary facial pain and other headaches
- 14. Other headache, cranial neuralgia, central or primary facial pain

Diagnosis Algorithm



Text in blue in this algorithm indicates a linked corresponding annotation.

Προειδοποιητικά σημεία «συναγερμού» της Κεφαλαλγίας

Κόκκινες Επισημάνσεις (Red Flags)

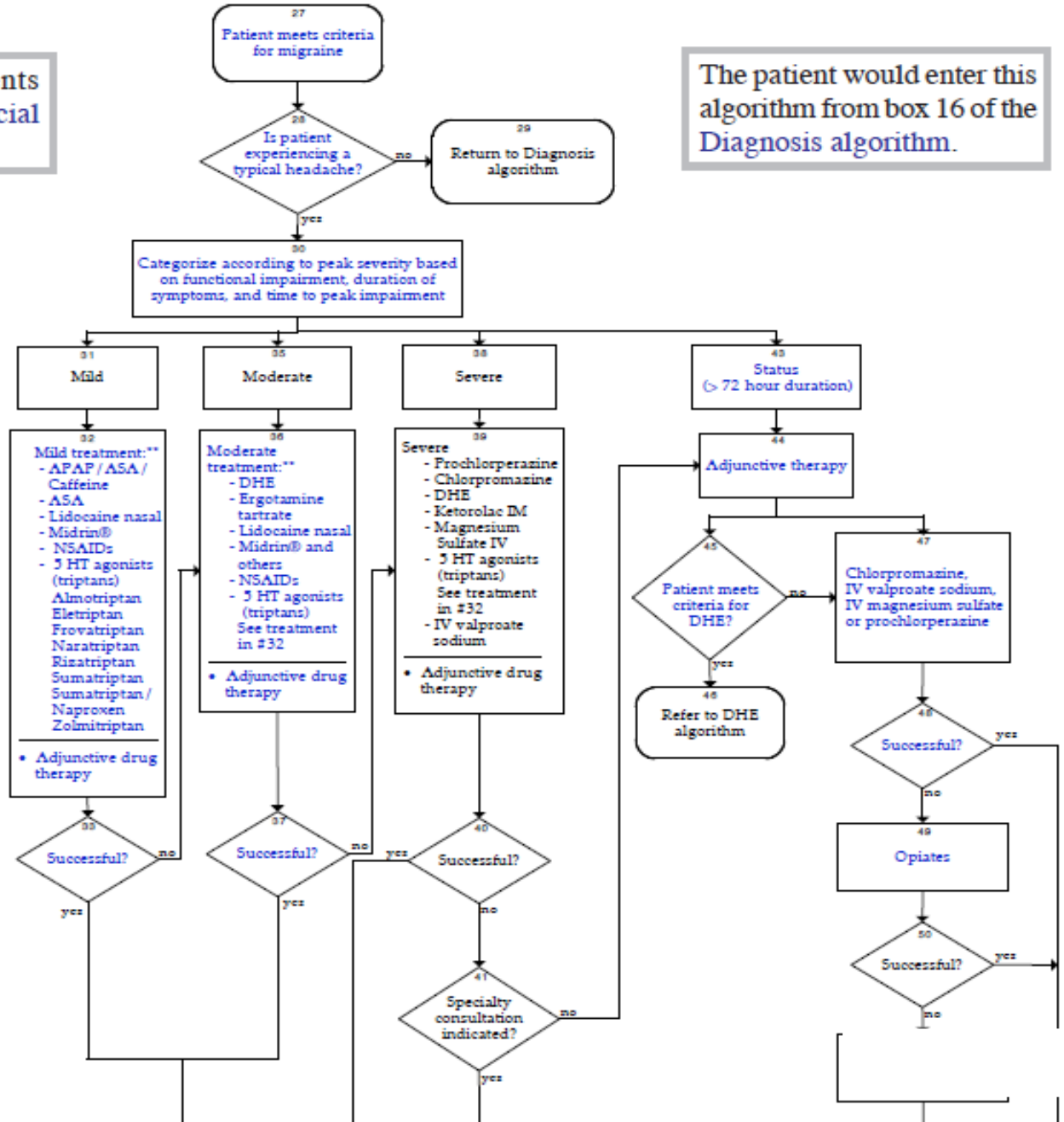
- «Κεραυνοβόλος» κεφαλαλγία (thunderclap headache)
- Έναρξη κεφαλαλγίας σε ηλικία > 50 ετών
- Νέα ένταση του άλγους («χειρότερο από ποτέ»)
- Υποξεία κεφαλγία με αυξανόμενη συχνότητα και ένταση
- Κεφαλαλγία με συνοδά συμπτώματα και σημεία (πυρετός, αυχενική δυσκαμψία)
- Κεφαλαλγία με εστιακά Ν/Λ συμπτώματα και σημεία (άλλα από την τυπική αύρα)
- Οίδημα οπτικών θηλών
- Νέας έναρξης κεφαλαλγία σε ασθενείς με παράγοντες κινδύνου (Ca, HIV)
- Κεφαλαλγία μετά από τραυματισμό κεφαλής ή αυχένα
- Έκλυση κεφαλαλγίας από σεξουαλική δραστηριότητα
- Κεφαλαλγία στην εγκυμοσύνη ή τη λοχεία
- Νέας έναρξης κεφαλαλγία, **αυστηρά** μονόπλευρης εντόπισης

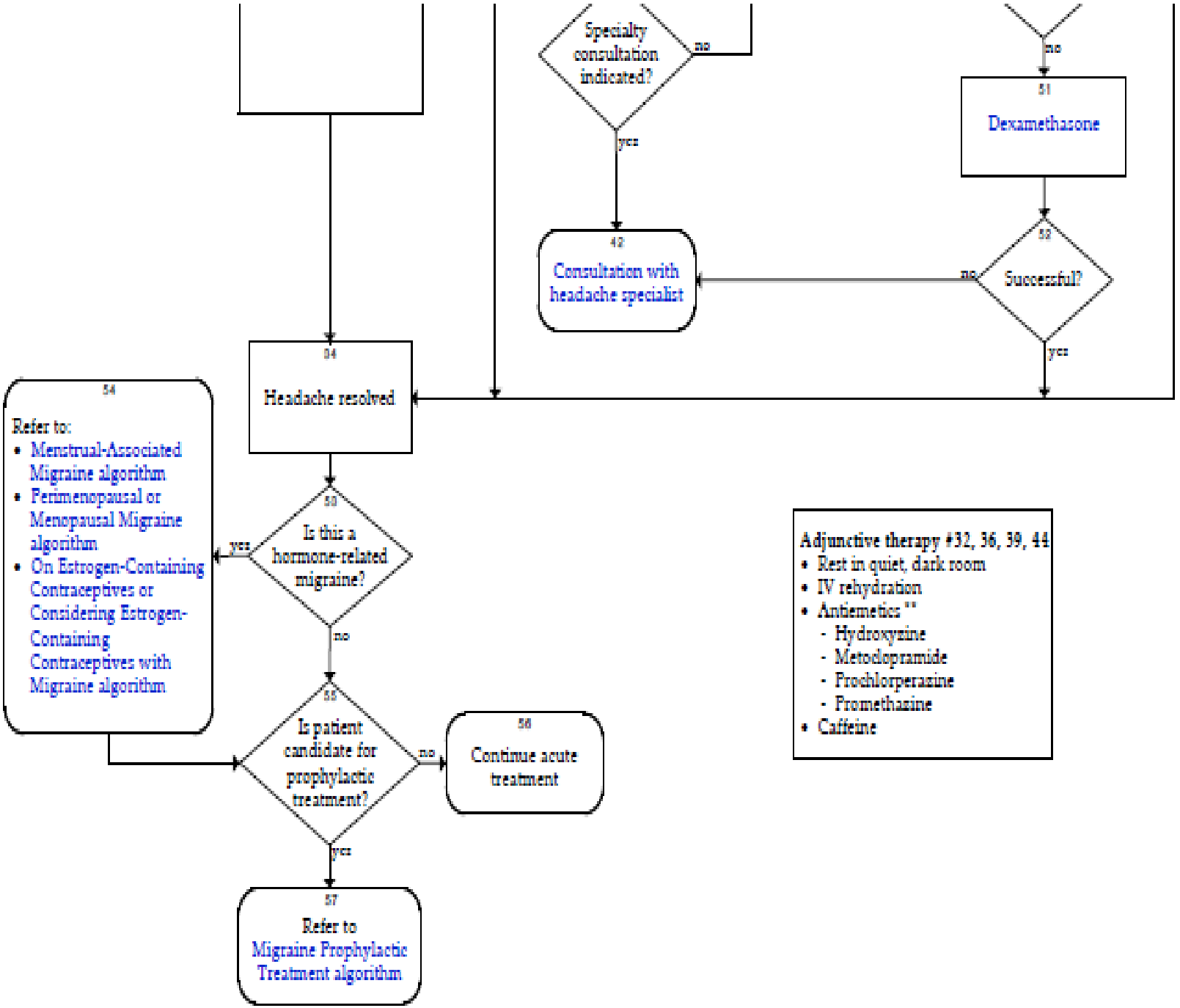
Migraine Treatment Algorithm

For information on adolescents (ages 12-17), refer to the "Special Circumstances" section.

Text in blue in this algorithm indicates a linked corresponding annotation.

The patient would enter this algorithm from box 16 of the Diagnosis algorithm.

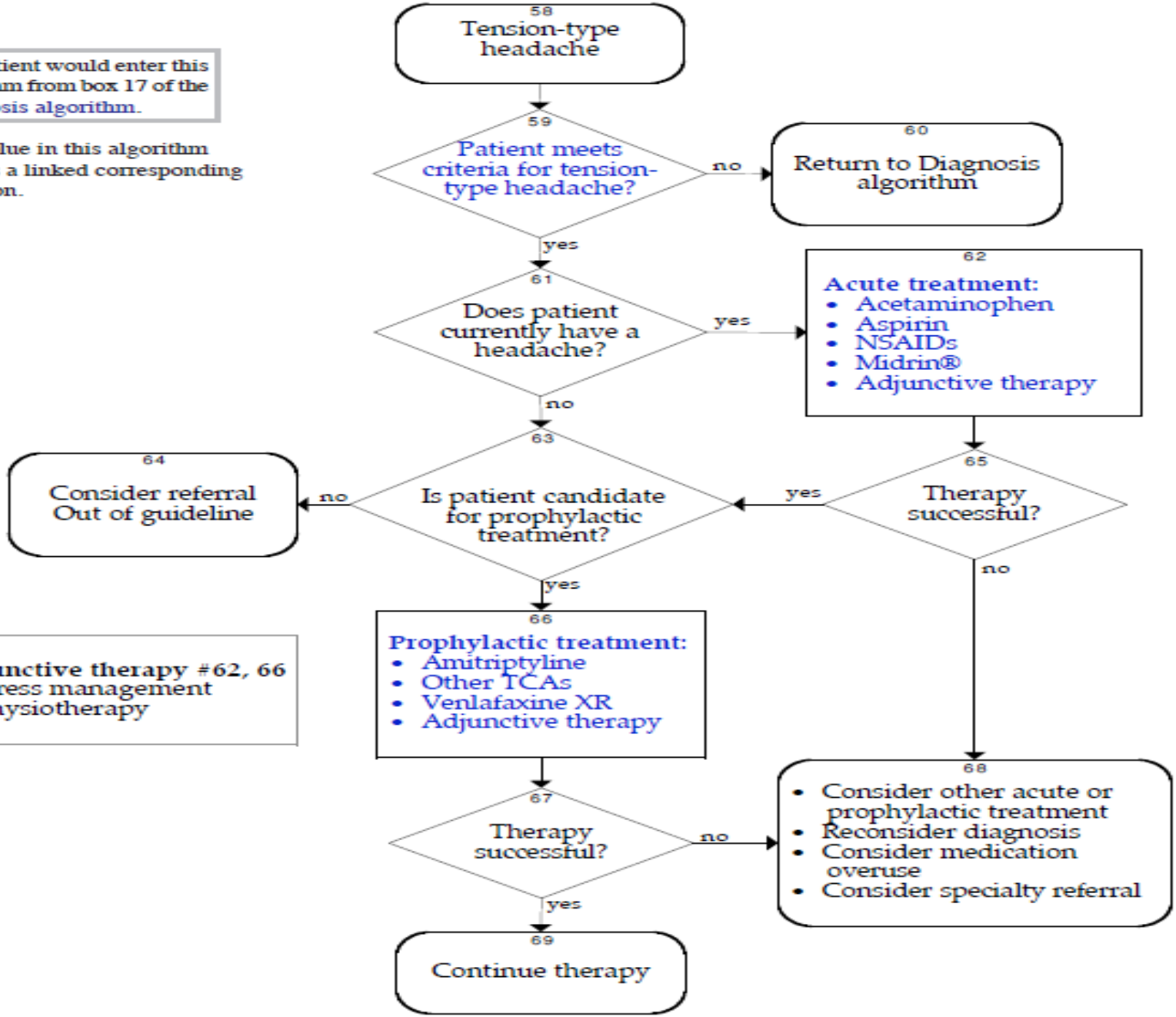



Specialty consultation indicated?
no
yes
42
Consultation with headache specialist
no
51
Dexamethasone
52
Successful?
no
yes
34
Headache resolved
54
Refer to:
• Menstrual-Associated Migraine algorithm
• Perimenopausal or Menopausal Migraine algorithm
• On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine algorithm
35
Is this a hormone-related migraine?
yes
no
55
Is patient candidate for prophylactic treatment?
no
56
Continue acute treatment
yes
57
Refer to Migraine Prophylactic Treatment algorithm
Adjunctive therapy #32, 36, 39, 44
• Rest in quiet, dark room
• IV rehydration
• Antiemetics **
- Hydroxyzine
- Metoclopramide
- Prochlorperazine
- Promethazine
• Caffeine

Tension-Type Headache Algorithm

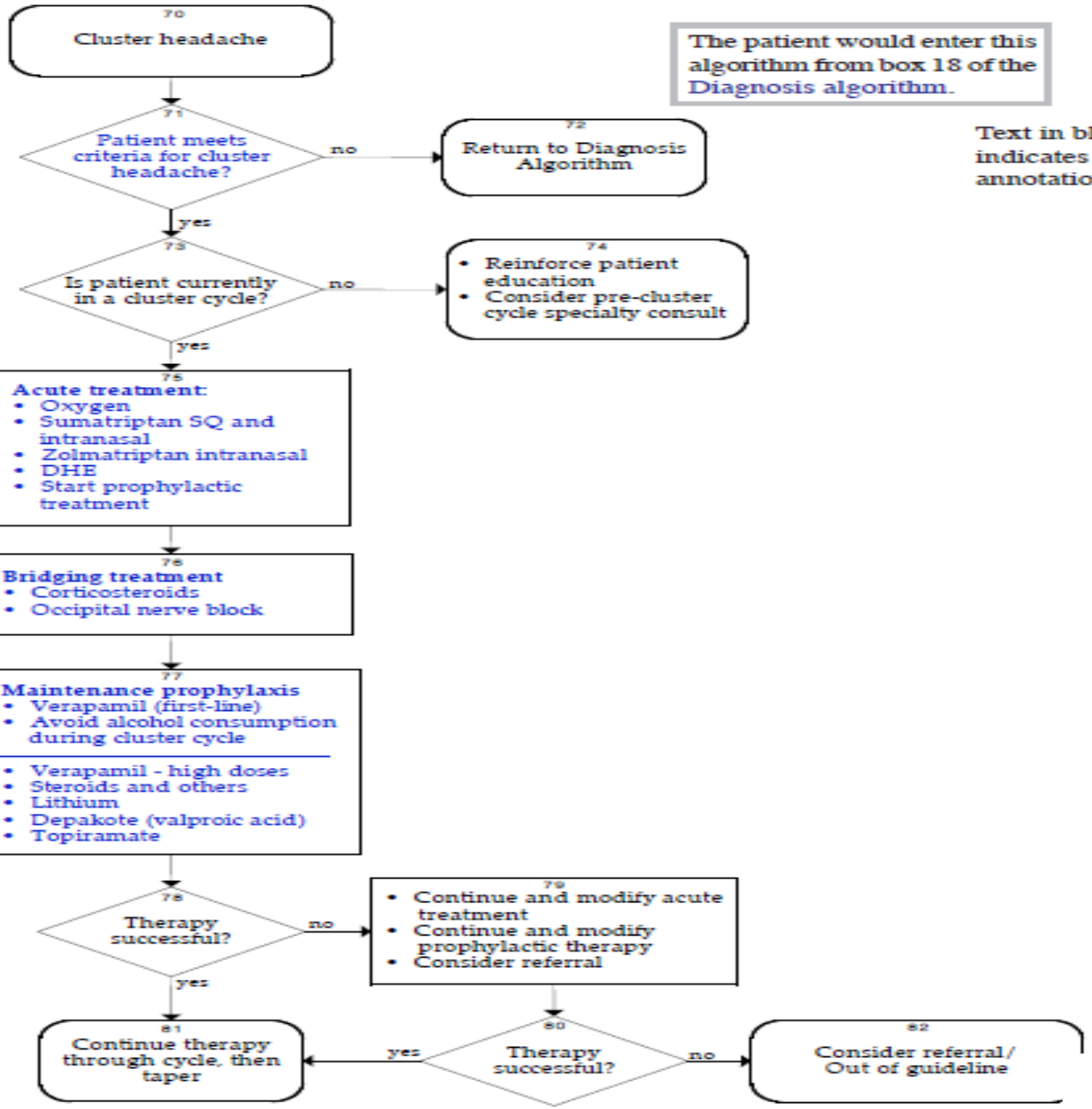
The patient would enter this algorithm from box 17 of the Diagnosis algorithm.

Text in blue in this algorithm indicates a linked corresponding annotation.



Adjunctive therapy #62, 66
- Stress management
- Physiotherapy

Cluster Headache Algorithm



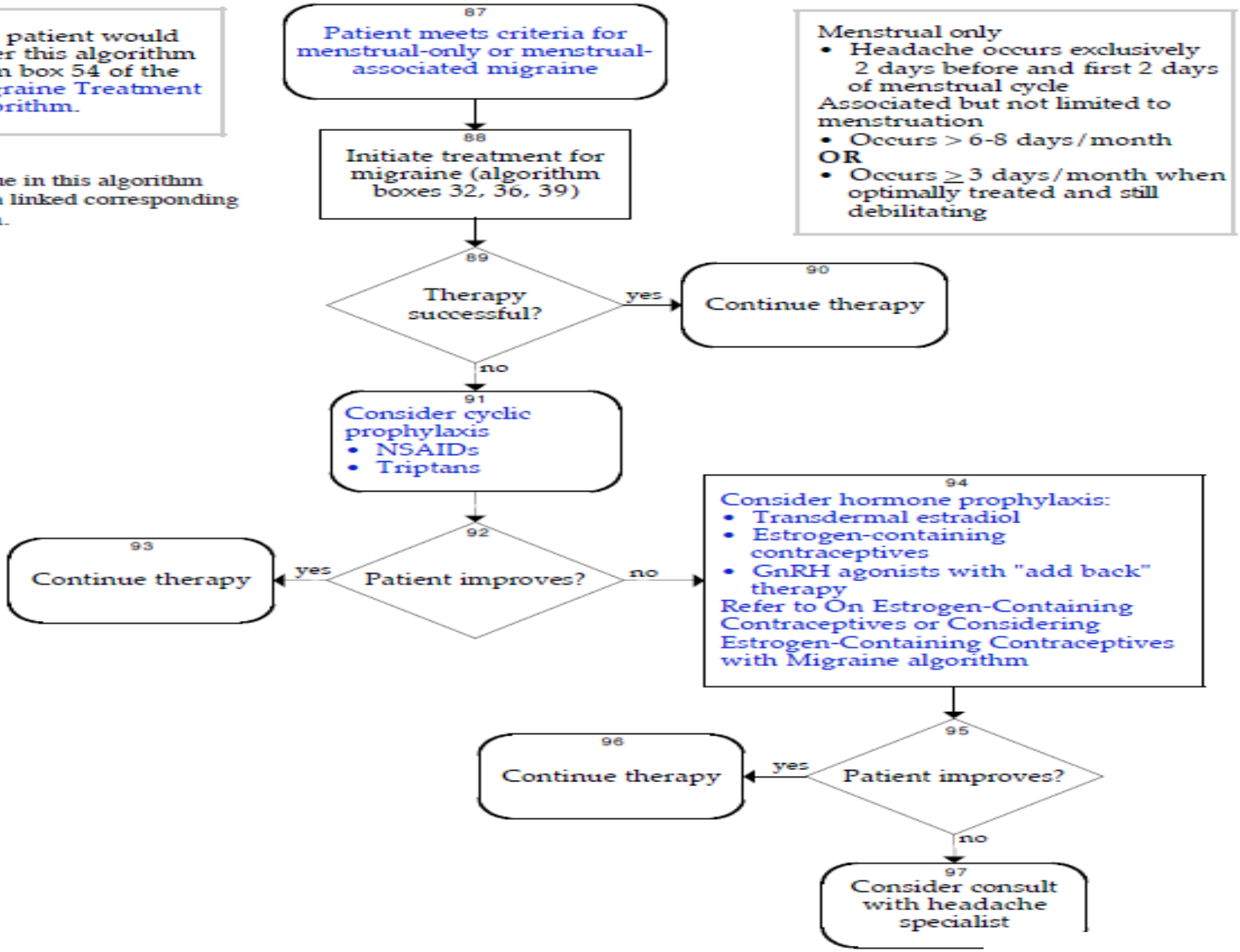
The patient would enter this algorithm from box 18 of the Diagnosis algorithm.

Text in blue in this algorithm indicates a linked corresponding annotation.

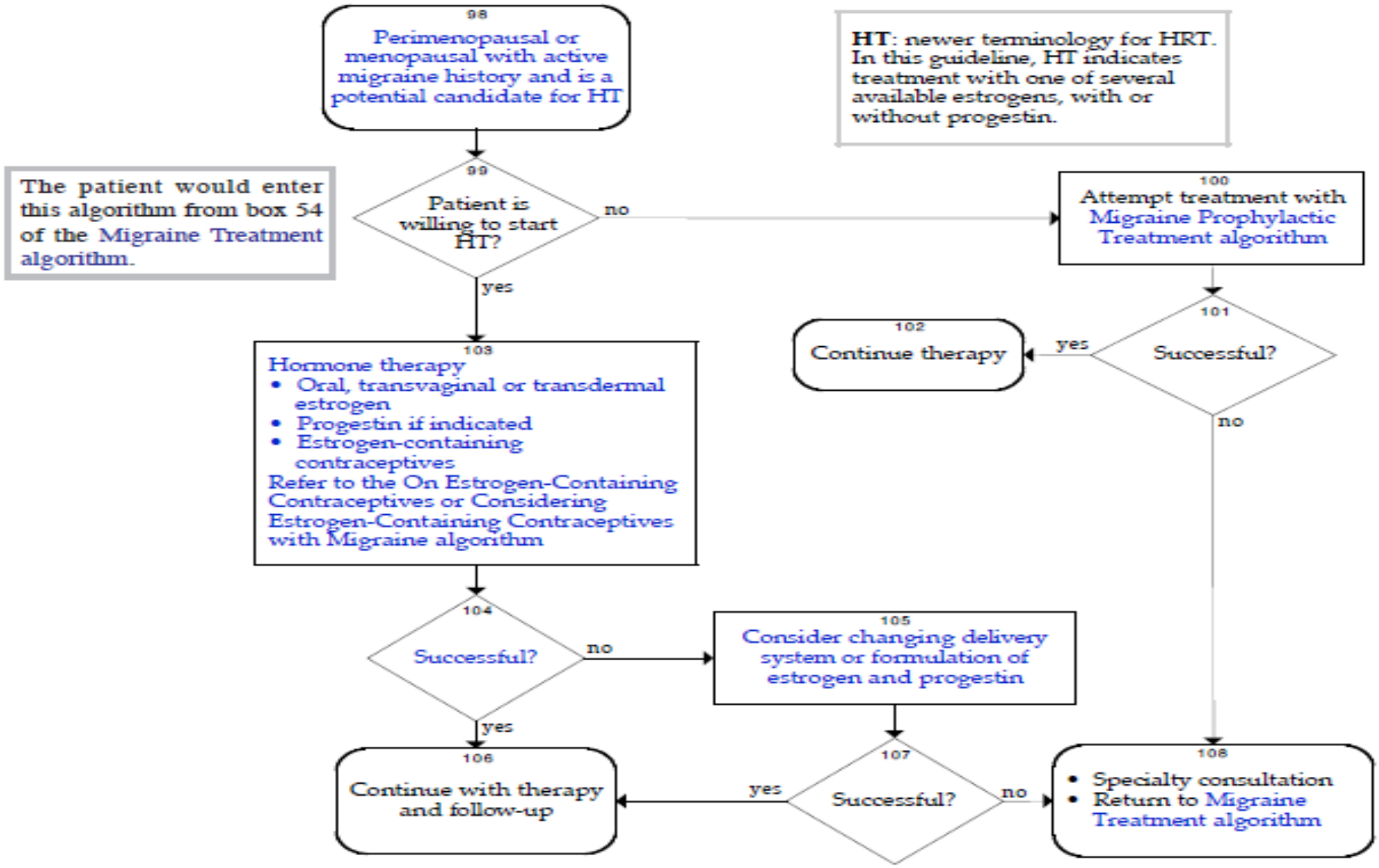
Menstrual-Associated Migraine Algorithm

The patient would enter this algorithm from box 54 of the Migraine Treatment algorithm.

Text in blue in this algorithm indicates a linked corresponding annotation.



Perimenopausal or Menopausal Migraine Algorithm



Text in blue in this algorithm indicates a linked corresponding annotation.

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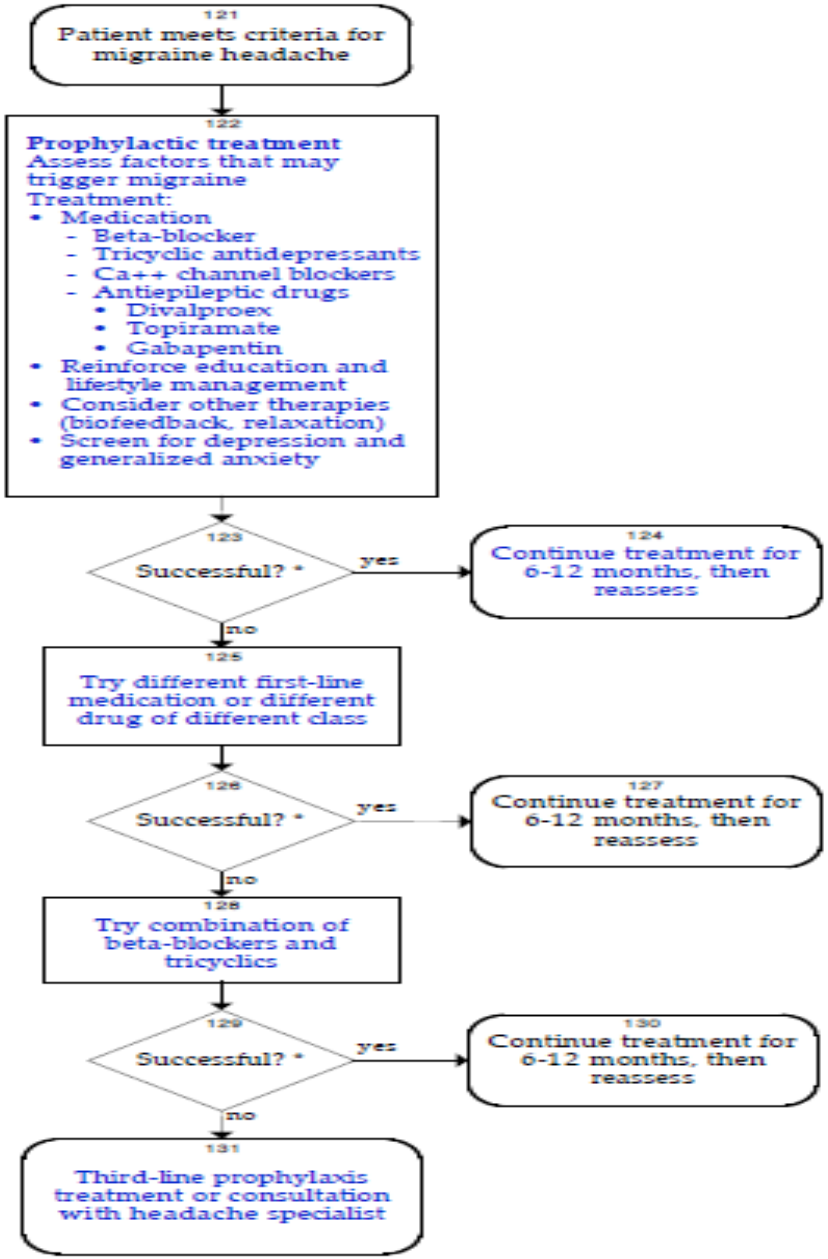
Migraine Prophylactic Treatment Algorithm



Text in blue in this algorithm indicates a linked corresponding annotation.

Patients enter this algorithm from box 57 of the Migraine Treatment algorithm.

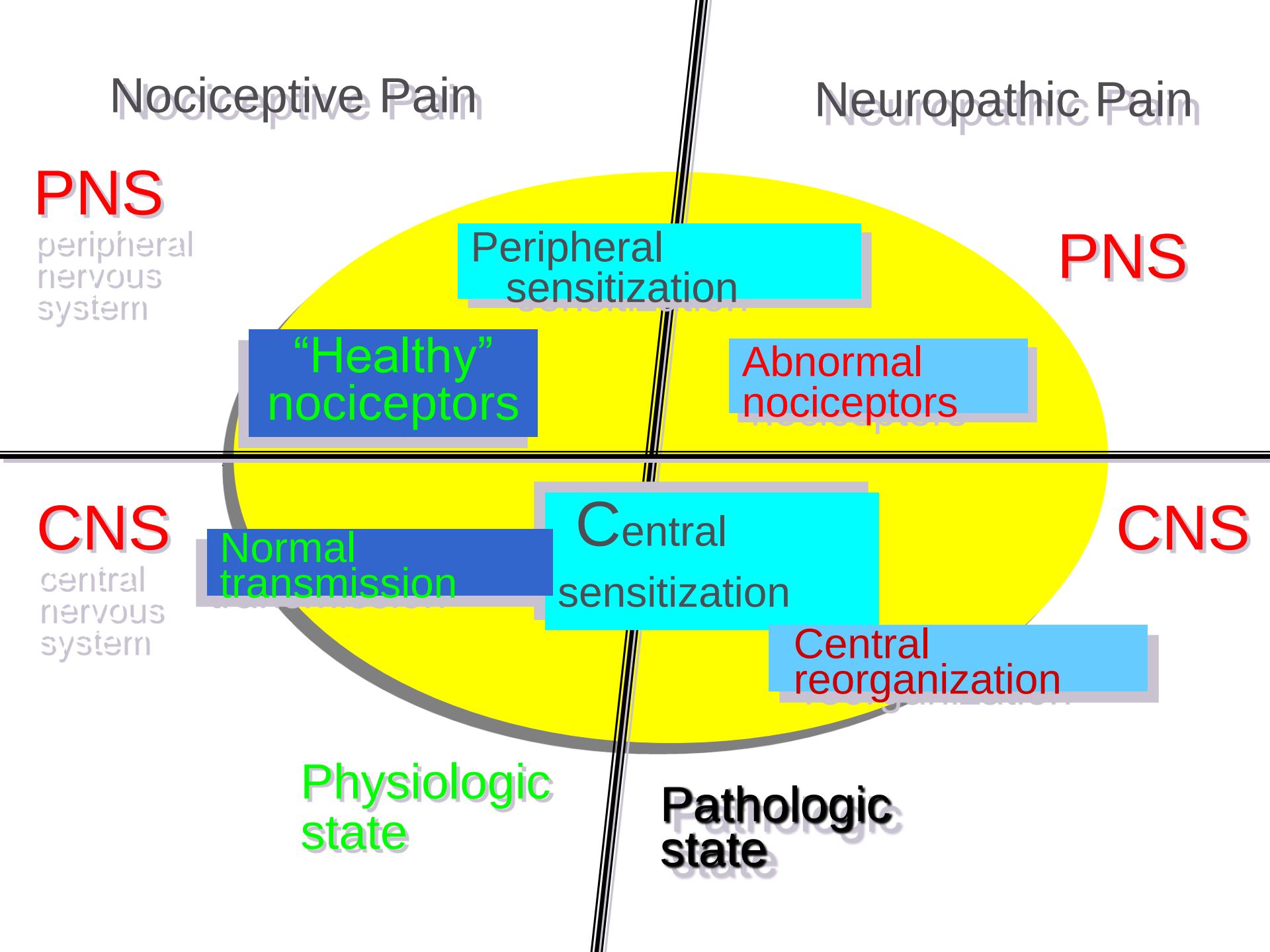
*123, 126, 129. Successful? Success as determined by:
- Headaches decrease by 50% or more
- An acceptable side effect profile

- **Αλγαισθητικός (noniceptive pain)**

- η δυσάρεστη αισθητική εμπειρία που σχετίζεται με **ιστική βλάβη** (π.χ τραύμα, έγκαυμα)
- η απόκριση σε μια παθοφυσιολογική διαδικασία που λαμβάνει χώρα **εντός των ιστών (π.χ φλεγμονή)**
- το σήμα παράγεται από άθικτες προσαγωγές νευρικές ίνες έπειτα από επώδυνο ερέθισμα στους υποδοχείς του πόνου (noniceptors)
- διαμεσολαβείται από **αλγογόνους παράγοντες** : κυτοκίνες , προστανγλαδίνες, βραδυκινίνη κ.α

- **Νευροπαθητικός (neuropathic pain)**

- η απάντηση σε μια **παθολογική διεργασία** που συμβαίνει **κατά μήκος ή εντός των σχετικών με τον πόνο οδών του νευρικού συστήματος**
- **Έκτοπη παραγωγή σήματος** συχνά απουσία ανάλογου ερεθίσματος
- Παριστά μια **παθολογική διεργασία εντός του ΠΝΣ ή του ΚΝΣ**


Nociceptive Pain
Neuropathic Pain
PNS
peripheral nervous system
Peripheral sensitization
PNS
"Healthy" nociceptors
Abnormal nociceptors
CNS
central nervous system
Normal transmission
Central sensitization
CNS
Central reorganization
Physiologic state
Pathologic state

Περιφερικός νευροπαθητικός πόνος

- **Διαβητική πολυνευροπάθεια**
- Επώδυνες νευροπάθειες (**αλκοολική,** από τοξικές ουσίες, **διατροφική ανεπάρκεια,** αμυλοειδική, αγγειίτιδας και άλλων συστηματικών νοσημάτων)
- **HIV νευροπάθεια**
- **Διήθηση Ca-λεμφώματος**
- Νευροπάθεια χημειοθεραπείας
- Μετακτινική πλεγματοπάθεια
- **Μεθερπητική νευραλγία**
- **Νευραλγία τριδύμου**
- **Παγιδευτικές νευροπάθειες-ριζοπάθειες**
- Post-taumatic και post-surgical

Κεντρικός νευροπαθητικός πόνος

- Συνεπεία **ΑΕΕ (post-stroke pain) π.χ θαλαμικός πόνος**
- **Τραυματική** βλάβη-διατομή Ν.Μ
- Μυελοπάθειες (μετακτινική, συριγγομυελία , αυχενική σπονδύλωση κ.α)
- **Πολλαπλή σκλήρυνση**
- **Parkinson-related pain**

NOVARTIS

Κριτήρια επιλογής θεραπείας

- Αποτελεσματικότητα (αποδεδειγμένη και αναπαραγόμενη σε καλά σχεδιασμένες-υψηλής ποιότητας τυχαιοποιημένες μελέτες)
- Διατήρηση αποτελέσματος (παρατεταμένη ανακούφιση του πόνου)
- Ανοχή-ασφάλεια
- Αποτέλεσμα στη ποιότητα ζωής του ασθενούς
- Κόστος/Όφελος

NOVARTIS

	Total daily dose and dose regimen	Recommendations
Strong recommendations for use		
Gapabentin	1200–3600 mg, in three divided doses	First line
Gabapentin extended release or enacarbil	1200–3600 mg, in two divided doses	First line
Pregabalin	300–600 mg, in two divided doses	First line
Serotonin-noradrenaline reuptake inhibitors duloxetine or venlafaxine*	60–120 mg, once a day (duloxetine); 150–225 mg, once a day (venlafaxine extended release)	First line
Tricyclic antidepressants	25–150 mg, once a day or in two divided doses	First line†
Weak recommendations for use		
Capsaicin 8% patches	One to four patches to the painful area for 30-60 min every 3 months	Second line (peripheral neuropathic pain)‡
Lidocaine patches	One to three patches to the region of pain once a day for up to 12 h	Second line (peripheral neuropathic pain)
Tramadol	200–400 mg, in two (tramadol extended release) or three divided doses	Second line
Botulinum toxin A (subcutaneously)	50–200 units to the painful area every 3 months	Third line; specialist use (peripheral neuropathic pain)
Strong opioids	Individual titration	Third line§

GRADE=Grading of Recommendations Assessment, Development, and Evaluation (see appendix for details about the GRADE classification). *Duloxetine is the most studied, and therefore recommended, of the serotonin-noradrenaline reuptake inhibitors. †Tricyclic antidepressants generally have similar efficacy (appendix); tertiary amine tricyclic antidepressants (amitriptyline, imipramine, and clomipramine) are not recommended at doses greater than 75 mg/day in adults aged 65 years and older because of major anticholinergic and sedative side-effects and potential risk of falls;[33] an increased risk of sudden cardiac death has been reported with tricyclic antidepressants at doses greater than 100 mg daily.[34] ‡The long-term safety of repeated applications of high-concentration capsaicin patches in patients has not been clearly established, particularly with respect to degeneration of epidermal nerve fibres, which might be a cause for concern in progressive neuropathy. §Sustained release oxycodone and morphine have been the most studied opioids (maximum doses of 120 mg/day and 240 mg/day, respectively, in clinical trials; appendix); long-term opioid use might be associated with abuse, particularly at high doses, cognitive impairment, and endocrine and immunological changes.[35-37]

Table 1
Combined numbers needed to treat (with 95% confidence interval) to obtain one patient with more than 50% pain relief

	Neuropathic pain[a]	Central pain	Peripheral pain	Painful polyneuropathy	Post-herpetic neuralgia	Peripheral nerve injury	Trigeminal neuralgia	HIV neuropathy	Mixed neuropathic pain	NNH in neuropathic pain
Antidepressants										
TCA	3.1 (2.7–3.7)	4.0 (2.6–8.5)	2.3 (2.1–2.7)	2.1 (1.9–2.6)	2.8 (2.2–3.8)	2.5 (1.4–11)	ND	ns	NA	14.7 (10–25)
SSRI	6.8 (3.4–441)	ND	6.8 (3.4–441)	6.8 (3.4–441)	ND	ND	ND	ND	ND	ns
SNRI	5.5 (3.4–14)	ND	5.5 (3.4–14)	5.5 (3.4–14)	ND	NA	ND	ND	ND	ns
DNRI	1.6 (1.3–2.1)	ND	ND	ND	ND	ND	ND	ND	1.6 (1.3-2.1)	ns
Antidepressants	3.3 (2.9–3.8)	4.0 (2.6–8.5)	3.1 (2.7–3.7)	3.3 (2.7–4.1)	2.8 (2.2–3.8)	2.5 (1.4–11)	ND	ns	1.6 (1.3–2.1)	16.0 (12–[illegible]
Anticonvulsants										
Carbamazepine	2.0 (1.6–2.5)	3.4 (1.7–105)	2.3 (1.6–3.9)	2.3 (1.6–3.9)	ND	ND	1.7 (1.3–2.2)	ND	NA	21.7 (13–[illegible]
Phenytoin	2.1 (1.5–3.6)	ND	2.1 (1.5–3.6)	2.1 (1.5–3.6)	ND	ND	ND	ND	ND	ns
Lamotrigine	4.9 (3.5–8.1)	ns	4.0 (2.1–42)	4.0 (2.1–42)	ND	ND	2.1 (1.3–6.1)	5.4 (3.1–20)	ns	ns
Valproate	2.8 (2.1–4.2)	ns	2.4 (1.8–3.4)	2.5 (1.8–4.1)	2.1 (1.4–4.2)	ND	ND	ND	ND	ns
Gabapentin, pregabalin	4.7 (4.0–5.6)	NA	4.3 (3.7–5.2)	3.9 (3.2–5.1)	4.6 (3.7–6.0)	NA	ND	ND	8.0 (4.8–24)	17.8 (12–[illegible]
Topiramate	7.4 (4.3–28)	ND	7.4 (4.3–28)	7.4 (4.3–28)	ND	ND	NA	ND	ND	6.3 (5–8)
Anticonvulsants	4.2 (3.8–4.8)	ns	4.1 (3.6–4.8)	3.9 (3.3–4.7)	4.4 (3.6–5.6)	NA	1.7 (1.4–2.2)	5.4 (3.1–20)	10.0 (5.9–32)	10.6 (9–1[illegible]
Opioids										
Opioids	2.5 (2.0–3.2)	ND	2.7 (2.1–3.6)	2.6 (1.7–6.0)	2.6 (2.0–3.8)	3.0 (1.5–74)	ND	ND	2.1 (1.5–3.3)	17.1 (10–[illegible]
Tramadol	3.9 (2.7–6.7)	ND	3.9 (2.7–6.7)	3.5 (2.4–6.4)	4.8 (2.6–27)	ND	ND	ND	ND	9.0 (6–18[illegible]
NMDA antagonists										
Dextromethorphan	4.4 (2.7–12)	ND	3.4 (2.2–7.6)	2.5 (1.6–5.4)	ns	ND	ND	ND	ns	8.8 (6–21[illegible]
Memantine	ns	ND	ns	ns	ns	ns	ND	ND	ND	ns
NMDA antagonists	7.6 (4.4–27)	ND	5.5 (3.4–14)	2.9 (1.8–6.6)	ns	ns	ND	ND	ns	12.5 (8–36)
Various										
Mexiletine	7.8 (4.0–129)	NA	5.2 (2.9–26)	ns	ND	2.2 (1.3–8.7)	ND	ns	NA	ns
Topical lidocaine	4.4 (2.5–17)	ND	NA	ND	NA	ND	ND	NA	4.4 (2.5–17)	ns
Cannabinoids	ns	3.4 (1.8–23)	ND	ND	ND	ND	ND	ND	9.5 (4.1–∞)	ns
Topical capsaicin	6.7 (4.6–12)	ND	6.7 (4.6–12)	11 (5.5–317)	3.2 (2.2–5.9)	6.5 (3.4–69)	ND	NA	NA	11.5 (8–20)

NNH, combined numbers needed to harm (95% confidence interval) to obtain one patients to withdraw because of side effects. TCA, tricyclic antidepressants; SNRI, serotonin noradrenaline reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors; DNRI, dopamine noradrenaline reuptake inhibitors; ND, no studies done; NA, dichotomized data are not available; ns, relative risk not significant.

[a] Heterogeneity across different pain conditions.

	First-line drugs			Second-line drugs			Third-line drugs	
	Serotonin-noradrenaline reuptake inhibitors duloxetine and venlafaxine	Tricyclic antidepressants	Pregabalin, gabapentin, gabapentin extended release or enacarbil	Tramadol	Capsaicin 8% patches	Lidocaine patches	Strong opioids	Botulinum toxin A
Quality of evidence	High	Moderate	High	Moderate	High	Low	Moderate	Moderate
Balance between desirable and undesirable effects								
Effect size	Moderate	Moderate	Moderate	Moderate	Low	Unknown	Moderate	Moderate
Tolerability and safety*	Moderate	Low-moderate	Moderate-high	Low-moderate	Moderate-high	High	Low-moderate	High
Values and preferences	Low-moderate	Low-moderate	Low-moderate	Low-moderate	High	High	Low-moderate	High
Cost and resource allocation	Low-moderate	Low	Low-moderate	Low	Moderate-high	Moderate-high	Low-moderate	Moderate-high
Strength of recommendation	Strong	Strong	Strong	Weak	Weak	Weak	Weak	Weak
Neuropathic pain conditions	All	All	All	All	Peripheral	Peripheral	All	Peripheral

GRADE=Grading of Recommendations Assessment, Development, and Evaluation (see appendix for details about the GRADE classification). *Common side-effects: antidepressants: somnolence, constipation, dry mouth (particularly with tricyclic antidepressants), and nausea (particularly duloxetine); pregabalin or gabapentin: somnolence, dizziness, and weight gain; opioids (including tramadol): constipation, nausea, vomiting, tiredness, somnolence, dizziness, dry mouth, and itch; lidocaine patches: local irritation; capsaicin patches: local pain, oedema, and erythema; botulinum toxin A: local pain; see the appendix for further information about safety issues.

Table 3: Summary of GRADE recommendations

Panel: Drugs or drug classes with inconclusive recommendations for use or recommendations against use based on the GRADE classification

Inconclusive recommendations

- Combination therapy
- Capsaicin cream
- Carbamazepine
- Clonidine topical
- Lacosamide
- Lamotrigine
- NMDA antagonists
- Oxcarbazepine
- SSRI antidepressants
- Tapentadol
- Topiramate
- Zonisamide

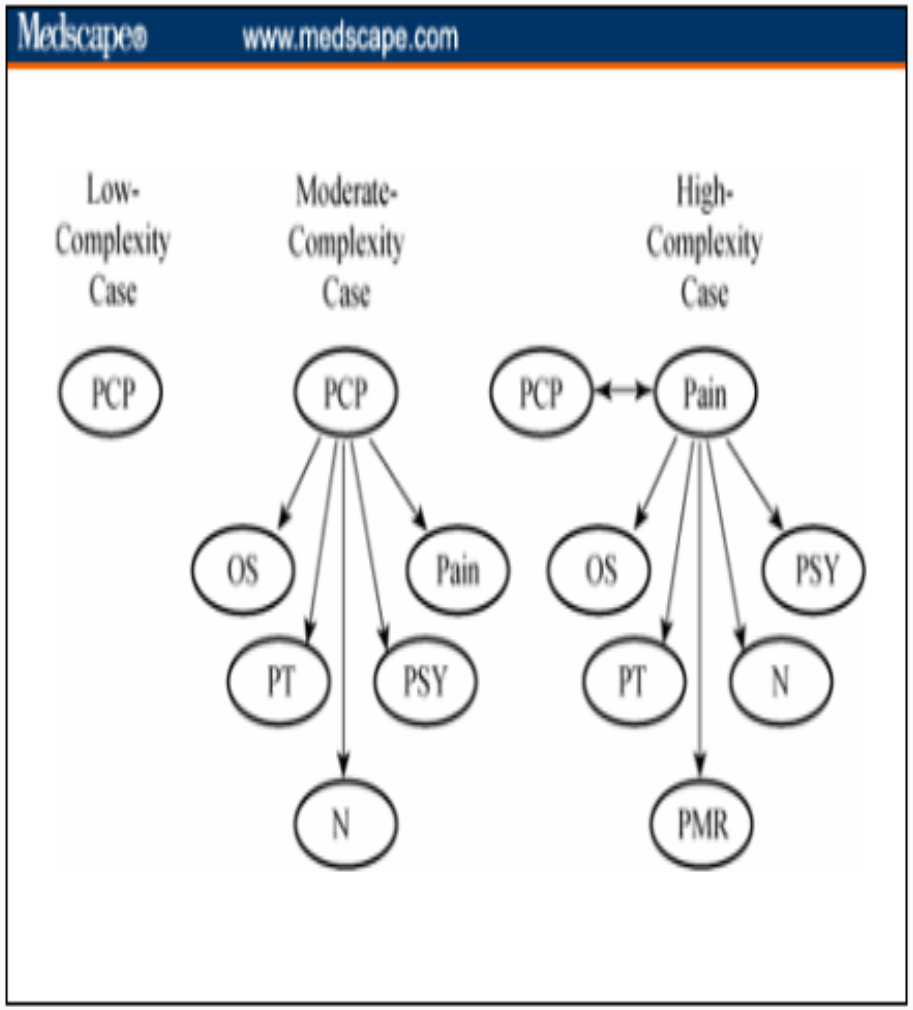
Weak recommendations against use

- Cannabinoids
- Valproate

Strong recommendations against use

- Levetiracetam
- Mexiletine

GRADE=Grading of Recommendations Assessment, Development, and Evaluation (see appendix for details about the GRADE classification).



Referral model for the care of chronic pain. Adapted with permission from the American Pain Society.[21]
PCP, primary care physician; OS, orthopedic surgeon; PT, physical therapist; PSY, psychotherapist; Pain, pain specialist; N, neurologist; PMR, physical medicine and rehabilitation specialist.