ESCITALOPRAM – propunere protocol

1. Denumire stiintifica:
Escitalopramum

2. Clasa de medicamente:
Antidepresive; ISRS (inhibitori selectivi de recaptare a serotoninei)

3. Forme farmaceutice (ANMDM):
- comprimate filmate 5 mg, 10 mg, 15 mg, 20 mg escitalopram
- comprimate orodispersabile 5 mg, 10 mg, 15 mg, 20 mg escitalopram

4. Farmacocinetica:
- t1/2 = 27-32 h (3,4,5)
- Cncentratia de echilibru plasmatic = 1 saptamana
- debut actiune 2-4 saptamani
- inhibitor moderat al CYP2D6 (1-pag 22, 33 ; 6)

5. Mecanism de actiune: (3, 4, 5)
- creste eliberarea serotoninei
- blocheaza transportorul serotoninei (pompa de recaptare a serotoninei SERT)

6. Indicatii principale (ANMDM) (10):

Tratamentul episoadelor depresive majore. (3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14) (FDA)
Tratamentul tulburării de panică însoţită sau nu de agorafobie. (2, 5, 6, 8, 9, 10, 12, 13, 14, 15)
Tratamentul tulburării de anxietate socială (fobie socială). (2, 3, 4, 5, 8, 9, 10, 12, 13, 14, 15)
Tratamentul tulburării de anxietate generalizată. (2, 3, 4, 8, 10, 13, 14, 15) (FDA)
Tratamentul tulburării obsesiv-compulsive. (2, 3, 4, 5, 10, 12, 14, 15)

7. Alte indicatii:
a. Tulburare de stress posttraumatic (2, 3, 4, 9, 15)
b. Tulburare depresiva organica (16)
c. Tulburari fobice (16)
d. ISRS in Depresie si Comorbiditati somatice:

- Boli cardiovasculare – Boala cardiaca ischemica (1, 13, 17, 18) , AVC (1, 17)
- Afectiuni oncologice (13, 17)
- DZ (1, 13, 17)
- Epilpesie (1, 13)
- Demente (13, 17)
- Infectie HIV (1, 13)

e. Tulburarea depresiva persistenta (Distimia si Depresia cronica):

- ISRS (17, 18, 19, 20)

f. Antidepresivele in Tulburarea afectiva bipolara (21):

- In Episodul depresiv TAB I – ISRS:
  - linia a doua, adjuvant cu Litiu/Valproat sau Antipsihotic atipic
  - evitate, sau, daca e necesar, folosite cu precautie: la pacienti cu istoric de manie, hipomanie induse de antidepresive, in prezenta elementelor mixte, ciclare rapida recent.
  - contraindicata utilizarea in monoterapie.
- In Episodul depresiv din TAB II:
  - rezervate, mai ales in monoterapie, pacientilor cu depresie ”pura” (non-mixta)
  - de evitat la pacientii cu simptome mixte sau cu istoric de hipomanie indusa de antidepresive

- Tratament de mentinere in TAB II:
  - linia a doua: Escitalopram, Fluoxetina, alte antidepresive.
- Tulburari anxioase comorbide (TAG, TOC):
  - ISRS daca sunt utilizate trebuie asigurata profilaxia maniei cu unul sau mai multe stabilizatoare (eg. Litiu/Valproat sau Antipsihotic atipic).

g. Antidepresivele in Schizofrenie:

- depresia majora comorbida, depresia post-psihotica, TOC (13, 22, 23, 24, 25, 26, 27)
- simptome depresive severe, care determina disconfort semnificativ sau interfera cu functionarea (22, 27).

Doze: 10-20 mg/zi (3, 4, 5), Tulburare de panica +/- agorafobie 5-20mg/zi (5).

8. Reactii adverse:

a. gastrointestinale (greata, varsaturi, dispepsie, dureri abdominale, diaree) (3, 4,5)
b. Disfunctii sexuale (3,4,5)
c. Transpiratii
d. Hemoragii (3,4,5)
e. Hiponatremie (3,4,5 - rara, mai ales la varstnici, reversibila la discontinuarea tratamentului)
f. Galactoree cu PRL normal (5)
g. Crestere ponderala (5)
h. Insomnie, sedare, agitatie, tremor, cefalee, ameteala
i. Manie-rar (5)
j. Activarea ideatiei suicidare si comportamentului suicidar(mai ales la varsta <24 ani)(5)
k. Rash(3,4).
l. Sindrom de discontinuare (3,4)

9. Supradoza:

- rar intalnita

- greata, varsaturi, transpiratii, tulburari de ritm cardiac, sedare, ameteala, tremor, amnezie, convulsii, confuzie, coma (3, 4, 5-cardiotoxicitate modesta, nesemnificativa pag 313)

10. Grupe speciale de pacienti:

- afectare cardiaca– scade frecventa cardiaca, scade TA, creste QTc dependent de doza, torsada vf mai ales in supradoza, nu determina tulburari de conducere, post IMA (precautie, unele evidente de siguranta in boala cardiovasculara) (5)
- de evitat la pacientii cu aritmii severe, IC, HVS, IMA (5)
- afectare renala- usoara/moderata (nu e necesara ajustarea dozei), severa(RFG<30ml/min), se incepe cu doza scazuta si se creste lent (3 ,4, 5)
- afectare hepatica- 10mg/zi (3, 4, 5 - afectare minima a enzimelor hepatice, hepatotoxicitate ocazionala)
- vârstnici: doze 5-10mg/zi (5)
- sarcina: categoria risc C (unele studii pe animale au aratat efecte adverse, nu sunt studii controlate pe oameni (3,4). Nu se recomanda mai ales in primul trimestru. Riscuri la administrarea in timpul sarcinii: Creste riscul de defecte septale cardiace. Trebuie pus in balanta riscul tratamentului pentru copil si riscul absentei tratamentului pentru mama si copil. La nastere creste riscul de hemoragii la mama si iritabilitate sau sedare a nou-nascutului. Utilizarea SSRI dupa saptamana 20 creste riscul de Hipertensiune pulmonara la nou nascut iar expunerea la SSRI in sarcina inaintata creste riscul de HTA de sarcina si preeclampsie.

Nou-nascutii expusi la SSRI sau SNRI in trimestrul III- complicatii: prelungirea spitalizarii, suport respirator, alimentatie pe sonda naso-gastrica, efect direct toxic al SSRI sau SNRI sau sindrom de discontinuitate (distress respirator, cianoza, apnee, convulsii, instabilitate termica, dificultati de alimentatie, varsaturi, hipoglicemie, hipotonie, hipertonie, hipereflexie, tremor, iritabilitate, plans constant)

- alaptarea: iritabilitate sau sedare, trebuie puse in balanta beneficiile alaptarii cu riscurile si beneficiile tratamentului antidepresiv vs. nontratament la copil si mama.

11. Interactiuni medicamentoase:

- cele mai putine interactiuni medicamentoase mediate de CYP 450 (3, 4, 5, 9)
- interactiuni majore: IMAO, Sunatoarea (5), Alcool, AINS, Triptofan, Warfarina. Creste concentratia de metoprolol (6). Creste concentratia antipsihoticelor, opiaceelor si antidepresivelor triciclice (7)

12. Contraindicatii (3):

- Alergie dovedita la escitalopram sau citalopram
- Tratament cu IMAO
- Tratament cu Pimozid

Referinte:

1. American Psychiatric Association, Practice Guideline for the Treatment of Patients with Major Depressive Disorder 3rd ed November 2010.
2. Katzman M.A. et al., Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders, BMC Psychiatry 2014, 14 (Suppl 1):S1.
3. Stahl SM., Stahl's Essential Psychopharmacology: Prescriber's Guide 5th ed 2014.
4. Stahl SM., Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Application 4th edition. New York: Cambridge University Press 2013.
5. David Taylor, Carol Paton, Shitij Kapur, The Maudsley Prescribing Guidelines in Psychiatry 12th ed 2015.
6. Kaplan and Sadock's Synopsis of Psychiatry-Behavioral Sciences/Clinical Psychiatry 11th ed 2015.
7. BAP Fundamentals of Clinical Psychopharmacology 4th ed 2016 (pag 83,84,97)
8. Simon A.B., Mount Sinai Expert Guides Psychiatry, Wiley Blakwell, 2017.
9. Glen O. Gabbard, Gabbard's Treatments of Psychiatric Disorders DSM-5 ed 5th 2014.
10. ANMDM - Nomenclatorul medicamentelor pentru uz uman
    https://www.anm.ro/_/_RCP/RCP_6649_15.07.14.pdf
    https://www.anm.ro/_/_RCP/RCP_8284_29.10.15.pdf
11. U.S. Food and Drug Administration
    https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021323s047lbl.pdf
12. MHRA Medicines&Healthcare products Regulatory Agency
    http://www.mhra.gov.uk/home/groups/par/documents/websiteresources/con480089.pdf
13. Bon Usage des Medicaments Antidepresseurs dans le Traitement des Troubles Depressifs et des Troubles Anxieus de L'Adulte, Agence Française de Sécurité Sanitaire des Produits de Santé, octobre 2006, www.afssaps.sante.fr
14. British Medical Association and the Royal Pharmaceutical Society, British National Formulary 73 March 2017, Royal Pharmaceutical Society, BMJ Group.
15. Bandelow B. et al., World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Pharmacological Treatment of Anxiety, Obsessive-Compulsive and Post-Traumatic Stress Disorders - First Revision, The World Journal of Biological Psychiatry, 2008; 9(4): 248-312.
16. Lista Protocoalelor terapeutice aprobate prin Ordinul MS/CNAS nr 1301/500/2008 cu modificarile si completarile ulterioare - actualizate la 16.11.2017, http://www.cnas.ro/media/pageFiles/LISTA%20PROTOCOALELOR%20TERAPEUTICE%20CU%20MODIFICARILE%20SI%20COMPLETARILE%20ULTERIOARE-%20NOIEMBRIE%202017.pdf
17. German Society for Psychiatry and Psychotherapy, Psychosomatics and Neurology, S3 Guideline Unipolar Depression, 2015/ DGPPN, BÄK, KBV, AWMF, S3-Leitlinie/Nationale VersorgungsLeitlinie Unipolare Depression, Langfassung 2. Auflage, Version 5, 2015.

18. Mahli G.S., Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders, Australian and New Zealand Journal of Psychiatry 2015, Vol. 49(12) 1-185.

19. Canadian Network for Mood and Anxiety Treatments (CANMAT) Guidelines for the management of adults with major depressive disorder, The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie 2016, Vol. 61(9) 504-505.

20. Bauer M. et al., World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Unipolar Depressive Disorders in Primary Care, The World Journal of Biological Psychiatry, 2007; 8(2): 67-104.

21. Yatham et al., Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder, Bipolar Disorders. 2018;1–74.

22. Lehman A.F. et al., American Psychiatric Association, Practice Guideline for the Treatment of Patients with Schizophrenia Second Edition, 2004.

23. Remington G. et al., Canadian Schizophrenia Guidelines, Guidelines for the Pharmacotherapy of Schizophrenia in Adults, The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie 2017, Vol. 62(9) 604-616.

24. Hasan A. et al., World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia. Part 3: Update 2015 Management of special circumstances: Depression, Suicidality, substance use disorders and pregnancy and lactation, The World Journal of Biological Psychiatry, 2015; 16: 142–170.

25. Galletly C. et al., Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders, Australian and New Zealand Journal of Psychiatry 2016, Vol. 50(5) 1-117.

26. Scottish Intercollegiate Guidelines Network, Management of schizophrenia, A national clinical guideline, March 2013.

27. Clinical Practice Guidelines In the NHS Ministry Of Health And Consumer Affairs, Clinical Practice Guideline for Schizophrenia and Incipient Psychotic Disorder, Published by: Catalan Agency for Health Technology Assessment and Research , 1st ed., 2009.