DULOXETINA – propunere protocol

1. Denumire stiintifica : Duloxetinum
2. Clasa de medicamente : antidepresive
3. Profil farmacologic : SNRI (inhibitor al recaptarii serotoninei si noradrenalinei) (6)
4. Farmacocinetica : - timp de injumatatire 12 ore, varf plasmatic la 6 ore (in prezenta alimentelor pana la 10 ore), concentratii plasmatice stabile dupa 3 zile, metabolizare hepatica, substrat pentru CYP 1A2, inhiba CYP 2D6 (2 , 3 ,4 , 6 ,9)
5. Mecanism de actiune: potenteaza transmisia serotoninergica si noradrenergica, blocheaza slab pompa de recaptare a dopaminei (1 , 9)
6. Administrare si doze: 30 - 120 mg/zi.
   - Doza initiala:60 mg/zi . La pacientii cu o tolerabilitate scazuta se poate incepe cu 30 mg/zi sau se poate recomanda administrarea in timpul mesei. (9)
   - Forme de prezentare : capsule gastrorezistente 30mg, 60 mg

7. Indicatii principale :

   - Episod depresiv major (1, 2, 3, 5, 7, 9, 11, 12 ,14, 15 , 16 ,18)- aprobat EMA, FDA, ANMDM.
   -Tulburare de anxietate generalizata(1,2,5 ,7, 8, 9, 10, 11, 12, 13 , 18) - aprobat EMA, FDA, ANMDM.
   - Fibromialgie (1 , 2, 5 , 9, 11) - aprobat FDA.

8. Alte indicatii :

   - Tulburarea depresiva persistenta (Distimia si Depresia cronica) (16, 17, 20, 21)
   - Depresie cu simptome dureroase (1, 9, 16, 22)
   - Depresia în afectiuni somatice (scleroza multipla asociata cu simptome dureroase, depresia din diabet zaharat, afectiuni oncologice) (3 , 17, 15, 22)
   - Tulburare de anxietate sociala – linia a treia (13), Tulburare obsesiv-compulsiva – linia a treia (13), Tulburarea de panica – linia a treia (13), Tulburarea de stres posttraumatic – linia a treia (13,19)
   - Tulburare de somatizare /somatica dureroasa (1 , 5, 22)
   - Depresia la varstnici (1, 22)
   - Preventia depresiei post-stroke (3, 3ª)
   - Bulimie nervoasa (3, 5).

9. Efecte secundare :
   - Reacţiile adverse cel mai frecvent raportate la pacienţii trataţi cu duloxetina au fost greaţă, cefalee, xerostomie, somnolenţă şi ameţeli. Totuşi, majoritatea reacţiilor adverse frecvente a fost uşoară până la moderată, au apărut de

obicei precoce în cursul tratamentului şi cele mai multe au tins să se remită chiar dacă tratamentul a continuat. (12)
- constipatie sau diaree (12)
- disfunctii sexuale (3; 10)
- cresterea tensiunii arteriale, scaderea apetitului, hipersudoratie , retentie urinara
(3, 4 , 6)
-poate exacerba bolile hepatice (4)

10. Supradoza: toxicitate scazuta in supradoza; sindrom serotoninergic, sedare, voma, convulsii, coma, modificari ale tensiunii arteriale. (2 , 3)

11. Utilizare la grupe de pacienti cu risc crescut:
Afectare renala: nu este necesara modificarea dozei in insufucienta renala usoara /moderata, nu se recomanda in insuficienta renala in stadiu terminal (pacienti dializati) (3)
Afectare hepatica: nu se administreaza in insuficienta hepatica (3)
Afectare cardiaca: prudenta, se monitorizeaza tensiunea arteriala. (2)
Varstnici : unii pot beneficia de doze reduse
Sarcina: categorie de risc C, in general nu este recomandata administrarea in special in primul trimestru, dar tratamentul continuu poate fi necesar si nu s-a dovedit periculos pentru fat. Trebuie evaluate riscurile tratamentului pentru fat fata de riscurile absentei tratamentului atat pentru mama cat si pentru copil (2 , 3).
Alaptare: mici cantitati de medicament trec in laptele matern. Daca sugarul devine iritabil sau sedat, se recomanda trecerea la alimentatie artificiala, intreruperea tratamentului sau utilizarea unui antidepresiv cu un profil mai sigur. In toate cazurile se cantaresc riscurile tratamentului cu beneficiile tratarii depresiei atat pentru mama cat si pentru copil (2 , 3).
Epilepsie: se recomanda prudenta (3).

12. Interactiuni medicamentoase: poate creste riscul de hemoragii mai ales la pacientii cu anticoagulante; riscul este scazut (2 , 18). Atentie la asocierea cu fluvoxamina (inhibitor al enzimei CYP 450 1A2), (1) paroxetina , fluoxetina (inhibitori ai enzimei CYP 450 2D6)- pot creste nivelul plasmatic de duloxetina, necesitand micsorarea dozei. (2)

Alte interactiuni : fumatul poate reduce nivelul plasmatic cu pana la 50% (reducerea dozei daca se opreste fumatul, cresterea dozei daca se reincepe fumatul) (3)

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