MOPH

Nervous System Drugs Application

The below information is a summary of the FDA and NICE guidelines as accepted by the neurology committee at the ministry of public health

**For all applications:**

1- Detailed medical report showing the:
   - Onset of the disease.
   - Clinical symptoms and signs.
   - Evolution
   - Final diagnosis.
   - Medications history.
   - Body weight for pediatric cases.
   - Body weight for cases necessitating IVIG.
2- Neuro-imaging results including:
   - The last results.
   - Those that helped for establishing and confirming the appropriate diagnosis.
   - Signed official neuro-imaging report.

For Multiple Sclerosis drugs application:

1- Only accepted if given by neurologists.
2- The medical report should clearly define the clinical symptoms, and the course of the disease.
3- Should follow the international guidelines for the diagnosis (modified Mac Donald Criteria, appendix 1) and for the treatment (As given by Menactrims, Figure 1).
4- Therefore, a medical report saying only that the patient is having multiple sclerosis without the above-mentioned clarifications and information will be systematically refused.
5- Results of lumbar puncture including oligoclonal bands and IgG index are mandatory.
6- When MRI results are suggestive of another differential diagnosis such as systemic diseases, blood tests for autoimmune diseases are mandatory.

For Epilepsy cases

1- The epilepsy syndrome should be clearly defined in the medical report (partial, generalized, idiopathic, non idiopathic…etc)
2- Neuro-imaging results are mandatory for non idiopathic epilepsies
3- EEG results are mandatory in partial epilepsies and upon request.
4- AED's can be only prescribed by neurologists. Prescriptions from neurosurgeons are accepted in cases following surgery.
5- Should follow the guidelines as given in the attached table (table1).

For Inflammatory neuropathies

1- Detailed medical report showing the onset, location and the chronology of symptoms,
2- EMG results (+full EMG graphics) and lumbar puncture results.
3- Results of blood tests for autoimmune diseases in chronic cases.

For Botulinum toxin

1- Detailed medical report defining the indication, the muscles to be injected, and the underlying etiology.
2- Body weight for pediatric cases.
3- Should follow the FDA approved indications as per the attached table (table 2).

For dementia medications (memantine, donepezil, rivastigmine, and galantamine)

1- Detailed medical report
2- Mini-mental status exam score between 10 and 24 points (inclusive).
3- Are not accepted when prescribed by non-specialists, and neurosurgeons.

For the use of Rituximab in neurological disorders (see attached documents)

1- Should be kept as last resort after failure of other approved medications or in cases of contraindication to other medications.
2- The only approved indication in which it can be used as first line therapy is Neuromyelitis Optica (as per UK guidelines)
3- In multiple sclerosis and as per results from Salzer and colleagues published in Neurology in 2016, it can be used in special conditions such as progressive forms, however comparative data showed no better responses with 2000mg every 6 months as compared to 1000 mg every 6 months and therefore the accepted dose will be 1000mg every 6 months.

These are guidelines for approving applications for neurological medication at the Ministry of Health. Off label use of such medications may be approved in exceptional cases at the discretions of the neurology drugs committee, if the prescribing doctor can demonstrate a paramount need for such off label use of a medication.

Table 1: Antiepileptic drugs dosage and indication

| Generic Name | Trade Name | Indication | Adult dosage | Pediatric dosage | Remarks |
|---|---|---|---|---|---|
| Phenytoin | Epanutin | P and G | 300-400mg | 4-8 mg/kg | As per level |
| Valproic Acid | Depakine, Convulex | P, G, Absence | Till 60mg/kg | Till 60mg/kg | As per level |
| Phenobarbital | Gardenal | All | 100-300mg | 3-5mg/kg | As per level |
| Vigabatrin | Sabril | Infantile spasms Partial refractory | 3000mg/d maximal | Up to 150mg/kg | |
| Felbamate | | P, P&G in lennox Gastaut | Max: 3600mg | Max: 45mg/kg | Need regular LFT and CBCD to approve |
| Topiramate | Topamax, Topirate | Partial, generalized | 400mg | 5-9mg/kg not to exceed 400mg | - |
| Lamotrigine | Lamictal , Lepigine | P and G | 400mg | 1-5mg/kg | |
| Levetiracetam | Keppra, Levipram | Partial Generalized, JME | Optimal 3000mg | 20-60mg/kg | In special situations can accept higher doses. |
| Zonisamide | Zonegran | Partial, G | | | |
| Clobazam | Urbanyl | LG and epileptic encephalopathies. | | <30kg: 5-20mg >30kg 10-40mg | Other special conditions |
| Gabapentin | Neurontin | Partial | 2400mg | 3-4y: 40mg/kg 5-11y: 35mglkg | Higher should be discussed. |
| Pregabalin | Lyrica | Partial | 300mg | Max 10mg/kg- | Up to 600mg? |
| Lacosamide | Vimpat | Partial Add or mono | Up to 400mg | Above 17 years. | |
| Perampanel | Fycompa | P and G Refractory | Up to 8mg | Above 12 years | |
| Oxacarbazepine | Trileptal | Partial | Optimal 1200mg | Max: 60mg/kg | Can go up to 2400mg |
| Ethosuximide | Zarontin | Absence | | >3 years: 20mg/kg | Never to exceed 1500mg. |
| Carbamazepine | Tegretol | P, GTC, MIxed | max 1200mg | Max : 35mg/kg below 6years Max 1000mg 12-15 years | As per level. |
| Rifunamide | | Lennox Gastaut | | | |
| | | | | | |

Abbreviations: P=Partial, G=Generalized, GTC= Generalized tonico-clonic, JME=Juvenile myoclonic epilepsy, LG= Lennox-Gastaut.

Table 2: Guidelines concerning the use of botulinum toxin

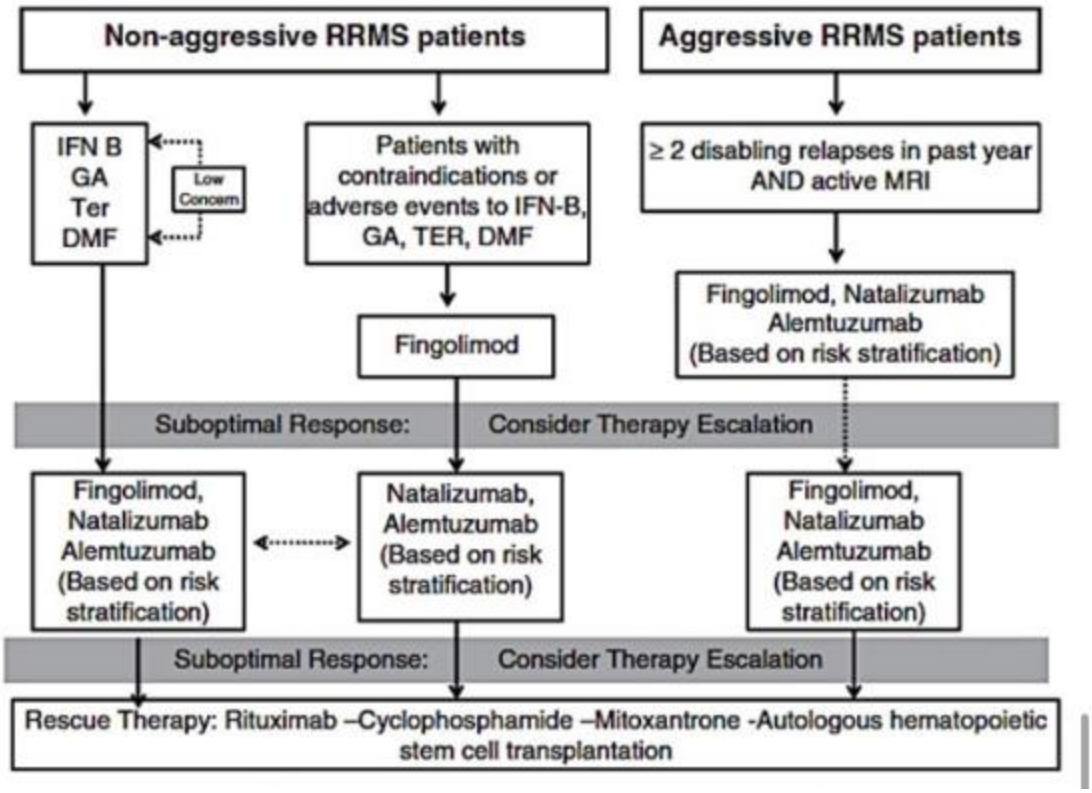
| **Onabotulinum toxin A (Botox):** | **Maximal Dose** |
|---|---|
| • Blepharospasm | less than 100u |
| • Cervical/Limb Dystonia | 300-400u |
| • Limbs spasticity | 300-400u |
| • Chronic Migraine | 155u |
| **Abobotulinum Toxin (Dysport):** | |
| • Cervical/Limb Dystonia | 500u-1500u |
| • Upper Limb spasticity | 500-1000u |
| • Pediatric Lower Limbs spasticity (2017) | 15u/Kg/Limb (max total |

*Doses can be repeated after 12 weeks.*

1-NICE guidelines for Botulinum toxin use in spasticity were updated in 2016, and corre above-mentioned indications.

2- For pediatric cases, body weight should be mentioned.

Figure 1: guidelines for the treatment of Multiple sclerosis as given by MENACTRIMS




Abbreviations: IFN B=Interferon B, GA=Glatiramer Acetate, Ter=Teriflunamide, DMF=Dimethyl Fumarate

Alemtuzumab use is reserved for very active cases not able to receive Fingolimod or Natalizumab.

Appendix 1

Modified Mc-Donald's criteria for the diagnosis of multiple sclerosis 2010

| Clinical Presentation | Additional Data Needed for MS Diagnosis |
|---|---|
| ≥2 attacks[a]; objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack[b] | None[c] |
| ≥2 attacks[a]; objective clinical evidence of 1 lesion | Dissemination in space, demonstrated by:<br>≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord)[d]; or<br>Await a further clinical attack[a] implicating a different CNS site |
| 1 attack[a]; objective clinical evidence of ≥2 lesions | Dissemination in time, demonstrated by:<br>Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or<br>A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or<br>Await a second clinical attack[a] |
| 1 attack[a]; objective clinical evidence of 1 lesion (clinically isolated syndrome) | Dissemination in space and time, demonstrated by:<br>For DIS:<br>≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord)[d]; or<br>Await a second clinical attack[a] implicating a different CNS site; and<br>For DIT:<br>Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or<br>A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or<br>Await a second clinical attack[a] |
| Insidious neurological progression suggestive of MS (PPMS) | 1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria[d]:<br>1. Evidence for DIS in the brain based on ≥1 T2 lesions in the MS-characteristic (periventricular, juxtacortical, or infratentorial) regions<br>2. Evidence for DIS in the spinal cord based on ≥2 T2 lesions in the cord<br>3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index) |