RECOMMENDATIONS ON THE PHARMACOLOGICAL MANAGEMENT OF TBI-RELATED IMPAIRMENTS
HEALTH CANADA INDICATIONS OF USE

AUTHORS	YEAR	REFERENCED CLINICAL PRACTICE GUIDELINES
Neurobehavioral Guidelines Working Group (NGWG) (Deborah L. Warden et al.)	2006	Guidelines for the Pharmacologic Treatment of Neurobehavioral Sequelae of Traumatic Brain Injury
Acquired Brain Injury Knowledge Uptake Strategy (ABIKUS)	2007	ABIKUS Evidence Based Recommendations for Rehabilitation of Moderate to Severe Acquired Brain Injury
New Zealand Guidelines Group (NZGG)	2007	Traumatic Brain Injury: Diagnosis, Acute Management and Rehabilitation
American Occupational Therapy Association (AOTA)	2009	Occupational Therapy Practice Guidelines for Adults with Traumatic Brain Injury
Stergiou-Kita, M. (KITA)	2011	A Guideline for Vocational Evaluation Following Traumatic Brain Injury: A Systematic and Evidence-based Approach
Scottish Intercollegiate Guidelines Network (SIGN)	2013	Brain Injury Rehabilitation in Adults
Royal College of Physicians (RCP)	2013	Prolonged Disorders of Consciousness National Clinical Guidelines
INCOG Team (INCOG)	2014	INCOG Recommendations for Management of Cognition Following Traumatic Brain Injury
INESSS-ONF	2015	INESSS-ONF Clinical Practice Guideline for the Rehabilitation of Adults with Moderate to Severe Traumatic Brain Injury

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N°	Recommendation	Indications according to Health Canada	Particularity	Level of evidence
J 3.1 **Priority**	Methylphenidate (initiated at a dose of approximately 0.10mg/kg and increased gradually to a target of 0.25–0.30 mg/kg bid) is recommended in adults with traumatic brain injury to enhance attentional function and speed of information processing. (Adapted from ABIKUS 2007, G44, p. 23 and INCOG 2014, Attention 9, p. 331)	Methylphenidate Used for the treatment of ADHD in adults and children 6 years of age and older. Methylphenidate is marketed under the brand names of BIPHENTIN, CONCERTA, RITALIN and RITALIN SR. and 16 generic methylphenidate products in Canada, at the time of this review (March 30, 2015).	Off-label use	B
J 3.2	Dextroamphetamine should be considered to enhance attentional function after traumatic brain injury when methylphenidate is not tolerated. (Adapted from NGWG 2006, p. 1483)	Dextroamphetamine Used for the adjunctive treatment of narcolepsy and for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).	Off-label use	C
J 3.3	Consider amantadine to improve attention in individuals with traumatic brain injury who are out of post-traumatic amnesia and who have not responded to other medication alternatives. (Adapted from NGWG 2006, p. 1483)	Amantadine Used to prevent and treat influenza A infections. Also used to treat of Parkinson's disease and for the short-term management of Parkinson-like symptoms caused by certain medications.	Off-label use	B
J 3.4 **Priority**	Amantadine may be considered to enhance arousal and consciousness and accelerate the pace of functional recovery in individuals in vegetative or minimally responsive state following traumatic brain injury. (Adapted from SIGN 2013, 9.2, p. 36) REFERENCE: Giacino et al. (2012)	Amantadine Used to prevent and treat influenza A infections. Also used to treat of Parkinson's disease and for the short-term management of Parkinson-like symptoms caused by certain medications.	Off-label use	A
NEW **J 6.1**	Rivastigmine may be considered for individuals with moderate-to-severe memory impairment in the subacute to chronic phase of recovery after traumatic brain injury. (INESSS-ONF, 2015) REFERENCE: Silver et al. (2009)	Rivastigmine Used for the symptomatic treatment of patients with mild to moderate dementia of the Alzheimer's type. Used for the symptomatic treatment of mild to moderate dementia associated with Parkinson's disease.	Off-label use	B

N°	Recommendation	Indications according to Health Canada	Particularity	Level of evidence
J 6.2 **Priority**	Donepezil (5–10 mg/day) is recommended to enhance aspects of memory in individuals with traumatic brain injury. (Adapted from NGWG 2006, p. 1482)	Donepezil Used to treat the symptoms of Alzheimer's disease. Marketed in Canada under the brand names ARICEPT® since 1997 and ARICEPT® Rapidly Disintegrating Tablet (RDT) since 2006. As of November 2014, 16 companies have also received authorizations to sell generic donepezil in Canada.	Off-label use	B
M 3.1	Individuals with traumatic brain injury with spasticity should be assessed and provided with a coordinated plan for interdisciplinary management including: • Identification and management of aggravating factors such as pain, bladder or bowel distention, skin irritation and infection • Use of specific treatment modalities such as serial casting or removable splints • Use of anti-spasticity medications (See section M4 for more details) • Rehabilitation interventions that consider a range of motion, flexibility and positioning routine (Adapted from ABIKUS 2007, G63, p. 26)	Baclofen Used for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis. May also be of some value in patients with spinal cord injuries and other spinal cord diseases Dantrolen Indicated for controlling the manifestations of a chronic spasticity of skeletal muscle resulting from such conditions as spinal cord injury, cerebral palsy, multiple sclerosis, and stroke, whenever such spasticity results in a decrease in functional use of residual motor activity. Indicated for the pre-operative management of malignant hyperthermia-susceptible surgical patients. Indicated for the post-crisis follow-up management of patients stabilized with the intravenous product (for information regarding the intravenous product see the Dosage and Administration Section of the Dantrium Intravenous Product Monograph). Tizanidine Used to reduce the spasticity which may be caused by medical conditions such as spinal cord injury or multiple sclerosis. Botulinum toxin Used for the treatment of cervical dystonia, blepharospasm associated with dystonia, strabismus, dynamic equinus due to spasticity in pediatric cerebral palsy patients, hyperhidrosis of the axilla and focal spasticity.		C
M 4.1 **Priority**	Botulinum neurotoxin therapy (BoNT) may be considered to reduce tone and deformity in individuals with traumatic brain injury with focal spasticity. (Adapted from SIGN 2013, 4.2.2, p. 17)	Botulinum toxin Used for the treatment of cervical dystonia, blepharospasm associated with dystonia, strabismus, dynamic equinus due to spasticity in pediatric cerebral palsy patients, hyperhidrosis of the axilla and focal spasticity.		B

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M 4.2	Botulinum neurotoxin therapy (BoNT) for individuals with traumatic brain injury should be used in an interdisciplinary setting with physiotherapist / occupational therapist and orthotist inputs where appropriate. (Adapted from SIGN 2013, 4.2.2, p. 17)	Botulinum toxin Used for the treatment of cervical dystonia, blepharospasm associated with dystonia, strabismus, dynamic equinus due to spasticity in pediatric cerebral palsy patients, hyperhidrosis of the axilla and focal spasticity.		C
M 4.3	Oral baclofen, tizanidine or dantrolene sodium may be considered for treatment of spasticity in individuals with traumatic brain injury. (Adapted from SIGN 2013, 4.2.3, p. 18) Note: Physicians should consider and monitor the sedative and cognitive side effects when prescribing these medications.	Baclofen Used for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis. May also be of some value in patients with spinal cord injuries and other spinal cord diseases Dantrolen Indicated for controlling the manifestations of a chronic spasticity of skeletal muscle resulting from such conditions as spinal cord injury, cerebral palsy, multiple sclerosis, and stroke, whenever such spasticity results in a decrease in functional use of residual motor activity. Indicated for the pre-operative management of malignant hyperthermia-susceptible surgical patients. Indicated for the post-crisis follow-up management of patients stabilized with the intravenous product (for information regarding the intravenous product see the Dosage and Administration Section of the Dantrium Intravenous Product Monograph). Tizanidine Used to reduce the spasticity which may be caused by medical conditions such as spinal cord injury or multiple sclerosis.		C
M 4.4	A trial of intrathecal baclofen for the treatment of severe spasticity in individuals with traumatic brain injury may be considered after other treatment options have been exhausted, i.e. antispasticity medications (e.g. baclofen, dantrolene, tizanidine, botulinum toxin), casting, splinting or stretching. The trial should be carefully monitored for possible complications, including pump malfunction. Consideration must also be given to the individual's ability to access ongoing follow-up, for example to get refills, in case of a malfunction or for troubleshooting. (Adapted from NZGG 2006, 6.1.1, p. 90)	Baclofen Used for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis. May also be of some value in patients with spinal cord injuries and other spinal cord diseases Dantrolen Indicated for controlling the manifestations of a chronic spasticity of skeletal muscle resulting from such conditions as spinal cord injury, cerebral palsy, multiple sclerosis, and stroke, whenever such spasticity results in a decrease in functional use of residual motor activity. Indicated for the pre-operative management of malignant hyperthermia-susceptible surgical patients.		C

N°	Recommendation	Indications according to Health Canada	Particularity	Level of evidence
		Indicated for the post-crisis follow-up management of patients stabilized with the intravenous product (for information regarding the intravenous product see the Dosage and Administration Section of the Dantrium Intravenous Product Monograph). Tizanidine Used to reduce the spasticity which may be caused by medical conditions such as spinal cord injury or multiple sclerosis.		
NEW O 2.2	Consider use of melatonin 2–5 mg for insomnia following traumatic brain injury. (NESSS-ONF, 2015) REFERENCES: Shekleton et al. (2010) Kemp et al. (2004) Ponsford et al. (2012) Colantonio et al. (2010) Glassner et al. (2013)	Melatonin Helps to increase the total sleep time (aspect of sleep quality) in people suffering from sleep restriction or altered sleep schedule (e.g. shift-work, jet lag) Helps to prevent and/or reduce the effects of jet lag (e.g. daytime fatigue, sleep disturbance) for people travelling by plane easterly across two or more time zones. Helps to reduce the time it takes to fall asleep (sleep onset latency aspect of sleep quality) in people with delayed sleep phase disorder Helps to re-set the body's sleep-wake cycle (aspect of the circadian rhythm)		B
NEW O 2.3	Consider use of trazodone 25–100 mg for insomnia post traumatic brain injury. (INESSS-ONF, 2015) REFERENCE: Larson and Zollman (2010)	Trazodone Is an antidepressant used to treat the symptoms of depression in adults over 18 years old.	Off-label use	C
NEW O 2.4 **Priority**	Benzodiazepines (lorazepam) and other non-benzodiazepine hypnotic (zopiclone) medications should be considered as last resort for the treatment of sleep disorders in individuals with traumatic brain injury, and it should be prescribed for no longer than 7 days. (INESSS-ONF, 2015) REFERENCES: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 15-Fatigue and Sleep Disorders, p.22, 15.4.3 http://www.abiebr.com/sites/default/files/modules/Module15_Fatigue%20and%20Sleep%20Disorders.pdf	Lorazepam Used for the short-term relief of manifestations of excessive anxiety in patients with anxiety neurosis. Also useful as an adjunct for the relief of excessive anxiety that might be present prior to surgical interventions. Zopiclone Used for the short-term treatment and symptomatic relief of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakenings.	Off-label use	C

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	Li Pi Shan and Ashworth (2004) Kemp et al. (2004) Aton et al. (2009)			
NEW O 2.5	Consider short-term treatment with methylphenidate to reduce excess daytime sleepiness in individuals with traumatic brain injury. (INESSS-ONF, 2015) REFERENCE: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 15-Fatigue and Sleep Disorders, p.21, 15.4.2 http://www.abiebr.com/sites/default/files/modules/Module15_Fatigue%20and%20Sleep%20Disorders.pdf	Methylphenidate Used the treatment of ADHD in adults and children 6 years of age and older. Methylphenidate is marketed under the brand names of BIPHENTIN, CONCERTA, RITALIN and RITALIN SR. and 16 generic methylphenidate products in Canada, at the time of this review (March 30, 2015).	Off-label use	C
NEW P 2.4 **Priority**	Pregabalin may be considered for reducing central neuropathic pain caused by injuries to the brain or spinal column. (INESSS-ONF, 2015) REFERENCE: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 4-Motor & Sensory Impairment Remediation, p.58, 4.7.4.1 http://www.abiebr.com/sites/default/files/modules/Ch4_Motor%20and%20Sensory%20Impairment%20Remediation.pdf	Pregabalin Indicated for the management of neuropathic pain associated with diabetic neuropathy, postherpetic neuralgia and pain associated with fibromyalgia in adults, and it may be useful in the management of central neuropathic pain.		C
NEW R 6.1 **Priority**	Given their favourable side-effect profile, selective serotonin reuptake inhibitors (SSRIs) are recommended as a first-line treatment for depression following traumatic brain injury (TBI). A limited body of evidence supports the efficacy of sertraline (starting at 25 mg; aiming for 50–200 mg/day) and citalopram (starting at 10 mg; aiming for 20–40 mg/day). (INESSS-ONF, 2015) Note: Depression after TBI is amenable to pharmacologic interventions and such treatment may alleviate not only the mood disturbance but also be of benefit for other symptoms.	Sertraline Prescribed to you by your doctor to relieve your symptoms of the following conditions: • Depression (feeling sad, a change in appetite or weight gain, difficulty concentrating or sleeping, feeling tired, headaches, unexplained aches and pain) • Obsessive-Compulsive disorder • Panic Disorder (repeated, unexpected panic attacks) Citalopram Indicated for the symptomatic relief of depressive illness.		C

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	If selective serotonin reuptake inhibitors (SSRIs) have been trialed and are not effective, or have produced unwanted side effects or drug interactions, the individual with TBI should be referred for review to a psychiatrist with expertise in treating individuals with TBI. REFERENCE: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 8-Mental Health Issues, p.18, 8.2.3 http://www.abiebr.com/sites/default/files/modules/Module8_Mental%20Health%20Issues_0.pdf			
NEW R 6.2 **Priority**	Stimulants such as methylphenidate may be considered for depression after traumatic brain injury over the shorter term; they may also be used to augment a partial response to selective serotonin reuptake inhibitors (SSRIs), especially in the setting of cognitive impairments, apathy, and/or fatigue. (INESSS-ONF, 2015) REFERENCE: Lee et al. (2005)	Methylphenidate Used for the treatment of ADHD in adults and children 6 years of age and older. Is marketed under the brand names of BIPHENTIN, CONCERTA, RITALIN and RITALIN SR. and 16 generic methylphenidate products in Canada, at the time of this review (March 30, 2015). Sertraline Prescribed to you by your doctor to relieve your symptoms of the following conditions: • Depression (feeling sad, a change in appetite or weight gain, difficulty concentrating or sleeping, feeling tired, headaches, unexplained aches and pain) • Obsessive-Compulsive disorder • Panic Disorder (repeated, unexpected panic attacks) Citalopram Indicated for the symptomatic relief of depressive illness.	Off-label use	B
NEW R 6.3	Consider use of tricyclic antidepressants (TCAs) (desipramine) as a third-line option for depression following traumatic brain injury, although possible reduced efficacy and a higher risk of side effects (e.g., seizures) may limit their use. (INESSS-ONF, 2015) REFERENCE: Wroblewski et al. (1996)	Desipramine Help to elevate mood and eliminate or reduce other symptoms associated with depression.		C

N°	Recommendation	Indications according to Health Canada	Particularity	Level of evidence
NEW R 8.1 **Priority**	Given their favourable tolerability and broad utility, selective serotonin reuptake inhibitors (SSRIs) may be considered for anxiety treatment of individuals with traumatic brain injury (TBI). (INESSS-ONF, 2015) Level of evidence : C Note: There is a lack of research concerning medication treatment of anxiety disorders after TBI; however, much evidence exists supporting their treatment in the non-TBI population.	<u>Sertraline</u> Prescribed to you by your doctor to relieve your symptoms of the following conditions: • Depression (feeling sad, a change in appetite or weight gain, difficulty concentrating or sleeping, feeling tired, headaches, unexplained aches and pain) • Obsessive-Compulsive disorder • Panic Disorder (repeated, unexpected panic attacks) <u>Citalopram</u> Indicated for the symptomatic relief of depressive illness.	Off-label use	C
NEW R 8.2 **Priority**	The use of benzodiazepines as first-line therapy for anxiety in individuals with traumatic brain injury (TBI) is **NOT** recommended due to potential effects on arousal, cognition, and motor coordination. The potential for abuse/dependency associated with these agents is also of concern, given the elevated rates of pre-injury substance use disorders observed among individuals with TBI. Nonetheless, short-term use of these agents may be helpful during periods of crisis or acute distress. (INESSS-ONF, 2015) REFERENCE: Waldron-Perrine et al. (2008)			C
R 9.1	The use of second generation neuroleptics is recommended for the treatment of psychosis as they are associated with fewer extrapyramidal symptoms (EPS) than first generation neuroleptics and exert their effects at sites other than the D2 receptor. (Adapted from NGWG 2006, p. 1475) Note: First generation neuroleptics have also been associated with greater impact on neuronal recovery. The ongoing need for antipsychotic medications should be periodically reassessed, and ongoing monitoring of weight, metabolic parameters, and late-emerging extrapyramidal symptoms is required. As all neuroleptics lower the seizure threshold to varying degrees, an initial trial with an anticonvulsant should be considered when heightened risk of seizures is of substantial concern.			C

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NEW R 10.1	For severe acute life threatening agitation and aggression that threatens staff or patient safety, the use of neuroleptic medications or intramuscular benzodiazepine can be considered. (INESSS-ONF, 2015) REFERENCE: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 12-Neuropharmacology, p.25;36;38 http://www.abiebr.com/sites/default/files/modules/Module12_Neuropharmacological%20Interventions%20_0.pdf	Midazolam Useful: • As intramuscular premedication prior to surgical or diagnostic procedures. • As an intravenous agent for patients requiring sedation/anxiolysis/amnesia prior to and during short endoscopic or short diagnostic procedures and direct-current cardioversion. • As an alternative intravenous agent for the induction of anesthesia.	Off-label use	C
NEW R 10.2	For severe agitation and aggression that threatens staff or patient safety, consider the use of oral neuroleptic medications (while taking into consideration the onset of action). Second generation neuroleptic medications like quetiapine, ziprasidone, olanzapine and risperidone are preferred as older agents may have more side effects though methotrimeprazine have been used with limited side effects. (INESSS-ONF, 2015) REFERENCES: Chew and Zafonte (2009) Bhatnagar et al. (2016) Elovic et al. (2008)	Quetiapine Used to : • Treat the symptoms of schizophrenia, such as hallucinations (hearing or seeing things which are not there), fixed false beliefs, unusual suspiciousness, or emotional withdrawal. Patients may also feel depressed, anxious or tense. • Treat the symptoms of mania associated with bipolar disorder, such as racing thoughts, irritability, aggressiveness, agitation, impulsive behaviour or excessively elevated mood. • Treat the symptoms of depression associated with bipolar disorder, such as sadness, feeling guilty, lack of energy, loss of appetite and/or sleep disturbance. Ziprasidone Used to treat symptoms of schizophrenia and related psychotic disorders, and symptoms of acute manic or mixed episodes associated with bipolar disorder. Olanzapine Used to treat symptoms of schizophrenia and related psychotic disorders as well as those of bipolar disorder. Risperidone Use in Schizophrenia : • Used to treat the symptoms of schizophrenia and related psychotic disorders, which may include hallucinations (hearing or seeing things that are not there), delusions, unusual suspiciousness, emotional withdrawal. Patients suffering from schizophrenia may also feel depressed, anxious or tense.	Off-label use	C

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		Use in Severe Dementia related to Alzheimer's disease : • May also be used for the short-term treatment in dementia related to Alzheimer's disease specifically to control aggression or psychotic symptoms (such as believing things that are not true or seeing, feeling or hearing things that are not there) when there is a risk of harm to self or others. Use in Acute Mania Associated with Bipolar Disorder : • May be used for the acute treatment of manic episodes associated with bipolar disorder. Signs and symptoms of bipolar mania include but are not limited to: feeling invincible or all powerful, inflated self-esteem, racing thoughts, easily lose your train of thought, overreaction to what you see or hear, misinterpretation of events, speeded-up activity, talking very quickly, talking too loudly, or talking more than usual, decreased need for sleep, and poor judgment. Methotrimeprazine Used for: • Mental illnesses including schizophrenia, disorders in the elderly, manic-depressive syndromes • Conditions associated with anxiety and tension • Pain due to cancer, shingles, trigeminal neuralgia, neurocostal neuralgia, phantom limb pains and muscular discomforts • Before and after surgery as a sedative and to control pain • Nausea and vomiting • Insomnia.		
NEW R 10.3 **Priority**	Either propranolol or pindolol is recommended for the treatment of aggression after traumatic brain injury, particularly for individuals in post-traumatic amnesia (PTA). Studies have reported the efficacy of both propranolol (maximum dose 420–520 mg/day) and pindolol (maximum dose 40–100 mg/day) in the treatment of aggression in this population, if there are no medical contraindications. (INESSS-ONF, 2015) REFERENCE: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 8-Mental Health Issues, p.37-38 http://www.abiebr.com/sites/default/files/modules/Module8_Mental%20Health%20Issues_0.pdf	Propranolol hydrochloride Used as: • Maintenance treatment for patients with high blood pressure; • Preventive treatment of angina pectoris (a condition associated with sharp chest pain and difficulty breathing, often associated with exercise). Pindolol Used to treat high blood pressure, also called hypertension. It is also used to prevent a type of chest pain called Angina Pectoris. Hydrochlorothiazide : Used for edema (swelling) associated with heart failure, cirrhosis of the liver, corticosteroid and estrogen therapy and for edema originating from the kidneys; or hypertension; or toxemia (hypertension) due to pregnancy.	Off-label use	A

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R 10.4	The use of valproate (750–2250 mg/day and/or carbamazepine (200–1200 mg/day) to reach therapeutic range should be considered as an option for the treatment of aggression in individuals with traumatic brain injury, particularly those who have a concomitant seizure disorder. (Adapted from NGWG 2006, p.1492)	Sodium valproate Used to control the epilepsy. Carbamazepine Used to : • Reduce your number of seizures; • Relieve the pain of trigeminal neuralgia • Treat your acute mania or bipolar disorder	Off-label use	C
NEW R 10.5 **Priority**	The use of amantadine 100 mg bid or methylphenidate can be considered for individuals with traumatic brain injury when impaired arousal and attention is suspected as a factor in agitation. (INESSS-ONF, 2015) REFERENCES: Hammond et al. (2014) Hammond et al. (2015)	Amantadine Used to prevent and treat influenza A infections. Also used to treat of Parkinson's disease and for the short-term management of Parkinson-like symptoms caused by certain medications. Methylphenidate Used for the treatment of ADHD in adults and children 6 years of age and older. Methylphenidate is marketed under the brand names of BIPHENTIN, CONCERTA, RITALIN and RITALIN SR. and 16 generic methylphenidate products in Canada, at the time of this review (March 30, 2015).	Off-label use	B
NEW R 10.6	The use of sertraline may be considered as an option for the treatment of individuals with moderate agitation and irritability following traumatic brain injury. The use of other selective serotonin reuptake inhibitors (SSRIs) may be considered as an alternative if sertraline is not tolerated. (INESSS-ONF, 2015) REFERENCES: ABIKUS (2007), G29, p.21 http://www.abiebr.com/pdf/abikus_aug_07.pdf Kant et al. (1998)	Sertraline Prescribed to you by your doctor to relieve your symptoms of the following conditions : • Depression (feeling sad, a change in appetite or weight gain, difficulty concentrating or sleeping, feeling tired, headaches, unexplained aches and pain) • Obsessive-Compulsive disorder • Panic Disorder (repeated, unexpected panic attacks) Citalopram Indicated for the symptomatic relief of depressive illness.	Off-label use	B
NEW R 10.7	Tricyclic antidepressants may be considered as a third-line option for the treatment of aggression following traumatic brain injury, particularly for those who have an associated sleep-wake disorder. When used, nortriptyline or desipramine are preferable based upon their tolerability. (INESSS-ONF, 2015) REFERENCE: Warden et al. (2006), p.1492	Desipramine Help to elevate mood and eliminate or reduce other symptoms associated with depression. Nortriptyline hydrochloride Used to treat depression.	Off-label use	C

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NEW R 10.8	The use of first generation neuroleptics and benzodiazepines to treat agitation or aggression in individuals with traumatic brain injury should be minimized, as these medications may slow recovery after brain injury and may have a negative effect on cognition. (INESSS-ONF, 2015) REFERENCE: ABIKUS (2007),G15, p.19 http://www.abiebr.com/pdf/abikus_aug_07.pdf			C
NEW R 11.1	The use of commonly used medications such as lithium, anticonvulsants and neuroleptics in the management of symptoms resembling bipolar disorder (i.e., mania and depressed mood) should be considered, although insufficient evidence supports or refutes their use in individuals with traumatic brain injury. Lithium requires careful monitoring, as side effects may limit its use in this population. (INESSS-ONF, 2015) REFERENCES: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016) ERABI Module 12-Neuropharmacology, p.25;36;38 http://www.abiebr.com/sites/default/files/modules/Module12_Neuropharmacological%20Interventions%20_0.pdf Chew and Zafonte (2009)	Lithium carbonate Indicated in the lithium treatment of manic episodes of manic-depressive illness. Maintenance therapy has been found to be useful in preventing or diminishing the frequency of subsequent relapses in bipolar manic-depressive patients (with a history of mania).		C
T 2.3	Anticholinergic medication for continence problems for individuals with traumatic brain injury should **only** be prescribed after demonstration of an overactive bladder. Use of urodynamic assessment is considered optimal. (Adapted from NZGG 2006, 6.1.3, p. 93) Note: Anticholinergic medications are associated with complications including memory and cognitive impairments.			C

N°	Recommendation	Indications according to Health Canada	Particularity	Level of evidence
NEW T 2.8	Asymptomatic bacteriuria should only be treated with antibiotic therapy in exceptional circumstances following traumatic brain injury (i.e., pregnancy, pending urologic procedure, worsening cognitive status). (INESSS-ONF, 2015) REFERENCES: Lin and Fajardo (2008) Colgan et al. (2006)			C
NEW T3.2	Anticonvulsants, particularly phenytoin and levetiracetam, are indicated to reduce the incidence of post-traumatic seizures in the first 7 days post-injury. Routine use of anticonvulsants to prevent late post-traumatic seizures after 7 days post-injury is not recommended. (INESSS-ONF, 2015) REFERENCE: Brain Trauma Foundation (2007)	<u>Phenytoin</u> Used to control seizures, specially used for: • The control of generalized tonic-clonic seizures, and psychomotor seizures • The prevention and treatment of seizures that may begin during or after surgery to the brain or nervous system. <u>Levetiracetam</u> Is indicated as adjunctive therapy in the management of patients with epilepsy who are not satisfactorily controlled by conventional therapy.		C
NEW T 3.3 **Priority**	In the event that use of anticonvulsant medications is indicated in the acute and chronic phases of traumatic brain injury, consideration should be given to choosing medications with the most favourable side effect profiles, as these medications have significant neuropsychological and other side effects. (INESSS-ONF, 2015) Note: For example, phenytoin may have negative effects on cognitive performance and recovery, although phenytoin may still be considered a first-line drug for early seizures in the acute period in view of ease of administration and monitoring. Clinicians should be particularly vigilant for adverse cognitive side effects of anticonvulsant medications and not assume that these drugs are without risk of impairment of cognitive, behavioural, physical, and neuroendocrine function, as well as having potential negative impacts on long-term recovery. REFERENCE: Evidence-Based Review of Moderate To Severe Acquired Brain Injury (ERABI) (2016)	<u>Phenytoin</u> Used to control seizures, specially used for: • The control of generalized tonic-clonic seizures, and psychomotor seizures • The prevention and treatment of seizures that may begin during or after surgery to the brain or nervous system.		C

N°	Recommendation	Indications according to Health Canada	Particularity	Level of evidence
	ERABI Module 10- Post-Traumatic Seizure Disorder, p.12, 10.4 http://www.abiebr.com/sites/default/files/modules/Ch10_Post-Traumatic%20Seizure%20Disorder%20.pdf			
T 4.2	Low-molecular-weight heparin (LMWH) is preferred over unfractionated heparin (UFH) for venous thromboprophylaxis after traumatic brain injury (TBI). (Adapted from ABIKUS 2007, G77, p. 28) Note: Much of the evidence supporting this recommendation is derived from the trauma/medical literature not specifically focused on individuals with TBI.	Heparin Used for: • Treatment to stop your blood from clotting in many surgical and non-surgical situations • Preventing and stopping the spread of blood clots in your veins • Preventing and stopping the spread of blood clots to your lungs • Treatment of some disorders of blood clotting • Prevention of blood clotting during surgery • Prevention and treatment of blood clots in your arteries		C
T 8.1	Once heterotopic ossification (HO) has developed in individuals with traumatic brain injury, treatment should include etidronate and/or non-steroidal anti-inflammatory drugs. (Adapted from ABIKUS 2007, G75, p. 28)	Étidronate disodium Used for: • Treatment of symptomatic Paget's disease of the bone • Short-term (30-90 days) maintenance of blood calcium levels following treatment with etidronate I.V Infusion for patients with hypercalcemia of malignancy (i.e. high blood calcium secondary to malignancy disease)	Off-label use	C