REFERENCE GUIDE FOR THE PHARMACY LICENSING EXAM Theory-Fourth Edition

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Part-I

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PREFACE

I am very happy to introduce the FOURTH edition of the Reference Guide for the Pharmacy Licensing Exam-Theory. It is specifically written for students preparing for NAPLEX® and QCE® exams. It contains over 70 chapters and includes well organized therapeutic classifications at the beginning of each chapter, with brand and generic names of medications.

This review guide also covers over 3000 drugs; a sound knowledge of these drugs is an important factor for passing NAPLEX® and QCE® exams. I would also recommend students to read the Reference Guide for the Pharmacy Licensing Exam - Questions and Answers (over 1200 NAPLEX-type questions) and the Reference Guide for Pharmaceutical Calculations (over 500 calculations).

I hope my efforts will help you to pass your key exams. I wish you the very best of luck, and any question or comment is always welcome.

Good luck,

Manan H. Shroff

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	Dose	Special Notes
Phenobarbital (C-IV) (Tablet) (Elixir)	1). Epilepsy: 50 to 100 mg 2 to 3 times daily. 2). Insomnia or sedative: 100 to 320 mg at bed time.	1). Phenobarbital (Luminal) is indicated for the following: a. Sedative b. Insomnia c. Preanesthetic d. Generalized tonic-clonic and cortical local seizures e. Seizure associated with status epilepticus, cholera, eclampsia, meningitis, tetanus, and toxic reactions to strychnine. 2). Phenobarbital (Luminal) has the lowest lipid solubility, lowest plasma binding, lowest brain protein binding, the longest delay in onset of activity, and the longest duration of action in the barbiturate class. 3). Phenobarbital (Luminal) is a weak acid that is absorbed and rapidly distributed to all tissues and fluids with high concentrations in the brain, liver, and kidneys. The more lipid soluble the drug is, the more rapidly it penetrates all tissues of the body. 4). The salts are more rapidly absorbed than are the acids. The rate of absorption is increased if the sodium salt is ingested as a dilute solution or taken on an empty stomach. 5). The normal therapeutic serum concentration of Phenobarbital (Luminal) should be between 10 and 25 mcg/ml. 6). The sedative, hypnotic and anticonvulsant effects of Phenobarbital (Luminal) are due to its ability to increase the concentrations of GABA in the brain. 7). Phenobarbital (Luminal) can induce hepatic microsomal enzymes resulting in increased metabolism and decreased pharmacological effects of a number of drugs. 8). Respiratory depression, ataxia, somnolence, sedation and lightheadedness are reported with the therapy.
Mephobarbital (Tablet)	1). Epilepsy: 400 to 600 mg daily in 3 or 4 divided doses.	1). Mephobarbital (Mebaral) is indicated for the following: a. Grand mal epilepsy. b. Petit-mal epilepsy. c. As a sedative for the relief of anxiety, tension, and apprehension.

	Dose	Special Notes
Mephobarbital (Tablet)	2) Sedative: 50 mg, 3 or 4 times daily.	2). Mephobarbital (Mebaral) is best taken at bedtime if seizures generally occur at night and during the day if attacks are diurnal. 3). Ataxia, somnolence, sedation and lightheadedness are reported side effects of Mephobarbital (Mebaral). 4). It can induce hepatic microsomal enzymes resulting in increased metabolism and decreased pharmacological effects of a number of drugs. 5). It exerts a strong sedative and anticonvulsant action but has a relatively mild hypnotic effect. It usually causes little or no drowsiness or lassitude. Hence, when it is used as a sedative or anticonvulsant, patients usually become calmer, more cheerful, and better adjusted to their surroundings without clouding of mental faculties. Mephobarbital (Mebaral) is reported to produce less sedation compared to phenobarbital. 6). About 75% of a single oral dose of Mephobarbital (Mebaral) is converted to phenobarbital in 24 hours. Therefore, chronic administration of Mephobarbital (Mebaral) may lead to an accumulation of phenobarbital (not Mephobarbital) in plasma.
Primidone (Tablet)	1). Epilepsy: 250 mg 3 or 4 times daily. Do not exceed 500 mg PO qid.	1). Primidone (Mysoline) is indicated for the following: a. Grand mal seizure b. Psychomotor and focal epileptic seizures 2). Primidone (Mysoline) is a prodrug that metabolites to Phenobarbital and phenylethylmalonamide (PEMA). Its anticonvulsant activity is due to its two metabolites, phenobarbital and phenylethylmalonamide (PEMA). 3). The most frequently occurring early side effects are ataxia and vertigo. These tend to disappear with continued therapy, or with reduction of initial dosage. 4). The sedative, hypnotic and anticonvulsant effects of Primidone (Mysoline) are due to its ability to increase the concentrations of GABA in the brain.

Carbamate Anticonvulsants

	Dose	Special Notes
Felbamate (Tablet) (Oral suspension)	1). Epilepsy: 1200 to 3600 mg per day given in 3 to 4 divided doses.	1). Felbamate (Felbatol) is indicated for the following: a. Partial seizure b. Partial and generalized seizures associated with Lennox-Gastaut syndrome in children 2). Hepatic failure and aplastic anemia are principal side effects of Felbamate (Felbatol). Therefore, Felbamate is not indicated as a first line antiepileptic treatment. 3). Anorexia, vomiting, insomnia, nausea, and headache are also reported with the therapy. 4). Patients, their caregivers, and families should be counseled that antiepileptic drugs, including Felbamate (Felbatol), may increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm.
Acetazolamide (Tablet)	1). Epilepsy: 8 to 30 mg/kg in divided doses.	1). Acetazolamide (Diamox) is indicated for the treatment of centrencephalic epilepsies. (e.g Petit mal and unlocalized seizure). 2). Caution is advised for patients receiving concomitant high-dose aspirin and acetazolamide, as anorexia, tachypnea, lethargy, coma and death have been reported.
Topiramate (Tablet) (Capsule)	1). Epilepsy: 200 to 400 mg per day in two divided doses without regard to meals. 2. Migraine: 100 mg per day administered in two divided doses without regard to meals.	1). Topiramate (Topamax) is indicated for the following: a. Partial onset or primary generalized tonic-clonic seizures in patients 10 years of age and older b. Seizures associated with Lennox-Gastaut syndrome in patients 2 years of age and older c. Prophylaxis of Migraine 2). Acute myopia and secondary angle closure glaucoma have been reported during Topiramate (Topamax) therapy. The symptoms include an acute onset of decreased visual activity and ocular pain.

	Dose	Special Notes
Topiramate (Tablet) (Capsule)		3). Paresthesia, weight decrease, somnolence, anorexia, dizziness, depression and mood swings are reported side effects of the drug. 4). Oligohidrosis (decreased sweating), infrequently resulting in hospitalization, has been reported in association with Topiramate (Topamax) use. Patients, especially pediatric patients, treated with Topiramate (Topamax) should be monitored closely for evidence of decreased sweating and increased body temperature, especially in hot weather. 5). Data from pregnancy registries indicate that infants exposed to Topiramate (Topamax) in utero have an increased risk for cleft lip and/or cleft palate (oral clefts). It is therefore classified under Pregnancy Category D.
Zonisamide (Capsule)	1). Epilepsy: 100 to 600 mg per day in a single or two divided doses with or without food.	1). Zonisamide (Zonegran) is indicated for the treatment of partial seizure in adults (age 16 or over). 2). Somnolence, anorexia, dizziness, ataxia, agitation / irritability, and difficulty with memory and/or concentration are commonly reported side effects of the drug. 3). Concomitant use of Zonisamide (Zonegran), a carbonic anhydrase inhibitor, with any other carbonic anhydrase inhibitor (e.g., topiramate, acetazolamide or dichlorphenamide), may increase the severity of metabolic acidosis and may also increase the risk of kidney stone formation. 4). Zonisamide (Zonegran) is a sulfonamide. It should be strictly avoided in patients hypersensitive to sulfa drugs. 5). Zonisamide (Zonegran) may produce drowsiness, especially at higher doses. Patients should be advised not to drive a car or operate other complex machinery until they have gained experience on Zonisamide (Zonegran) sufficient to determine whether it affects their performance. 6). Because of the potential of Zonisamide (Zonegran) to cause CNS depression, as well as other cognitive and/or neuropsychiatric adverse events, Zonisamide (Zonegran) should be used with caution if used in combination with alcohol or other CNS depressants.

Dibenzazepine Anticonvulsants:

	Dose	Special Notes
Carbamazepine (Tablet), (Chewable tablet), (Oral suspension), (Tablet, ER)	1. Epilepsy: 800 to 1200 mg per day given in 2 to 4 divided doses. 2. Trigeminal neuralgia: 400 to 800 mg per day given in 2 to 4 divided doses. Do not exceed 1200 mg per day. 3. Bipolar disorder (Equetro only) 400 to 1600 mg per day in two divided doses with or without meals.	1). Carbamazepine (Tegretol) is indicated for the following: a. Partial seizure b. Generalized tonic-clonic seizure c. Trigeminal neuralgia 2). Carbamazepine (Tegretol) is NOT indicated for the treatment of absence seizure (Petit mal). 3). It is structurally related to tricyclic antidepressants and should NOT be used in patients hypersensitive to TCAs (tricyclic antidepressants). 4). CYP 3A4 inhibitors inhibit Carbamazepine (Tegretol) metabolism and can thus increase plasma Carbamazepine (Tegretol) levels whereas CYP 3A4 inducers can increase the rate of Carbamazepine (Tegretol) metabolism and reduce plasma Carbamazepine (Tegretol) levels. 5). The normal therapeutic serum concentration of Carbamazepine (Tegretol) should be between 10 and 20 mcg/ml. 6). Aplastic anemia and agranulocytosis are principal side effects of the drug. 7). Coadministration of carbamazepine and nefazodone may result in insufficient plasma concentrations of nefazodone and its active metabolite to achieve a therapeutic effect. Coadministration of carbamazepine with nefazodone is contraindicated. 8). Because Carbamazepine (Tegretol) induces its own metabolism, the half-life is also variable. Auto induction is completed after 3-5 weeks of a fixed dosing regimen. Initial half-life values range from 25-65 hours, decreasing to 12-17 hours on repeated doses. 9). It is indicated in the treatment of the pain associated with true trigeminal neuralgia. 10). Equetro, extended release tablet form of Carbamazepine, is indicated for the treatment of acute manic and mixed episodes associated with Bipolar I Disorder.

	Dose	Special Notes
Carbamazepine (Tablet), (Chewable tablet), (Oral suspension), (Tablet, ER)		11). Serious and sometimes fatal dermatological reactions, including toxic epidermal necrolysis (TEN) and Steven-Johnson Syndrome (SJS), have been reported during treatment with Carbamazepine (Tegretol). Studies in patients of Chinese Ancestry have found a strong association between the risk of developing TEN/SJS and the presence of HLA-B 1502, an inherited variant of the HLA-B gene. Therefore, patients with Ancestry in genetically at risk populations should be screened for the presence of HLA-B 1502 prior to initiating therapy with Carbamazepine (Tegretol). 12). Carbamazepine (Tegretol) suspension in combination with liquid chlorpromazine or thioridazine results in precipitate formation, and, in the case of chlorpromazine, there has been a report of a patient passing an orange rubbery precipitate in the stool following coadministration of the two drugs. Therefore, it is advisable not to administer Carbamazepine (Tegretol) suspension with other liquid medications or diluents.
Oxcarbazepine (Tablet), (Oral suspension)	1. Epilepsy 600 to 1200 mg per day, given in a twice a day regimen with or without food.	1). Oxcarbazepine (Trileptal) is indicated for the treatment of partial seizure. 2). The pharmacological activity of Oxcarbazepine (Trileptal) is primarily exerted through the 10-monohydroxy metabolite (MHD) of Oxcarbazepine (Trileptal). 3). Dizziness, diplopia, somnolence, nausea and vomiting, tremor, hyponatremia, ataxia and abnormal vision are reported side effects of the drug. 4). It can inhibit CYP2C19 and induce CYP3A4/5 with potentially important effects on plasma concentrations of other drugs. 5). Clinically significant hyponatremia (sodium < 125 mmol/L) can develop during Oxcarbazepine (Trileptal) use. Measurement of serum sodium levels should be considered for patients during maintenance treatment with Oxcarbazepine (Trileptal). 6). Patients should be advised to report symptoms of low sodium like nausea, tiredness, lack of energy, confusion, and more frequent or more severe seizures.

Fatty acid Derivatives Anticonvulsants

	Dose	Special Notes
Valproic acid / Divalproex Na (Capsule) (Oral solution), (Tablet, DR) (Capsule, DR) DR = Delayed Release.	Epilepsy: 10 to 60 mg/kg/day. Mania: 60 mg/kg/day given in divided doses. Migraine: 250 mg PO B.I.D.	1). Valproic acid/Divalproex Na (Depakene/Depakote) is indicated for the following: a. Complex partial seizures. b. Simple and complex absence seizures. c. Multiple seizures including absence seizure. d. Manic episodes associated with bipolar disorder (only Depakote and Stavzor). e. Prophylaxis of migraine headaches (only Depakote and Stavzor). 2). It may increase the concentration of GABA (Gamma-Amino Butyric Acid). GABA is an inhibitory neurotransmitter. By increasing the concentration of GABA, antiepileptic action is produced. 3). It can produce neural tube defects (e.g., spina bifida). 4). Severe liver toxicity, pancreatitis, thrombocytopenia, bleeding, aplastic anemia and agranulocytosis are reported with the therapy. 5). Patients should be monitored for symptoms such as malaise, lethargy, facial edema, nausea and vomiting. Liver function tests should be performed prior to therapy and at frequent intervals thereafter especially during the first 6 months. Patients who experience G.I. irritation may benefit from administration of the drug with food or by slowly building up the dose from an initial low level. 6). Divalproex sodium is a stable co-ordination compound comprised of sodium valproate and valproic acid in a 1:1 molar relationship and formed during the partial neutralization of valproic acid with 0.5 equivalent of sodium hydroxide. 7). Valproic acid/Divalproex Na (Depakene/Depakote) generally inhibits the aggregation of platelets and thus increases the risk of bleeding when used alone or in combination with anticoagulants. Prothrombin time (PT) should be monitored when used with anticoagulants. 8). It inhibits the metabolism of barbiturates and Primidone, and increases the risks of neurological toxicity when used in combination with these drugs.

Gamma-Aminobutyric Acid (GABA) Analogs

	Dose	Special Notes
Pregabalin (Capsule) (Oral solution)	Epilepsy: 150 to 600 mg per day, given in 2 or 3 divided doses. DPN pain: 100 mg three times a day. Postherpetic neuralgia: 75 to 150 mg two times a day, or 50 to 100 mg three times a day. Fibromyalgia: 300 to 450 mg per day in 2 divided doses.	1). Pregabalin (Lyrica) is indicated for the following: a. Partial onset seizures. b. Management of neuropathic pain associated with diabetic peripheral neuropathy (DPN). c. Management of postherpetic neuralgia. d. Management of fibromyalgia. 2). Ataxia, somnolence, weight gain, edema, abnormal thinking and blurred vision are reported side effects of the drug. 3). It is a Schedule V controlled substance. Pregabalin (Lyrica) can be taken with or without food. 4). Since Pregabalin (Lyrica) is predominantly excreted unchanged in the urine, undergoes negligible metabolism in humans, and does not bind to plasma proteins, its pharmacokinetics are unlikely to be affected by other agents through metabolic interactions or protein binding displacement. For the same reason, the risk of toxic reactions to Pregabalin (Lyrica) may be greater in patients with impaired renal function.
Gabapentin (Capsule) (Tablet) (Oral solution) (Tablet, ER) (Oral suspension)	1. Partial seizure (Neurontin): 900 to 1800 mg per day in three divided doses. 2. PHN (Neurontin): 300 mg on day 1; 600 mg per day on day 2 (divided BID); 900 mg per day on day 3 (divided TID), titrated up as needed for pain relief to a daily dose of 1800 mg (divided TID). 3. PHN (Gralise): Titrate Gralise to an 1800 mg dose taken orally once daily with the evening meal.	1). Gabapentin is indicated for the following: a. Partial seizure (Only Neurontin) b. Management of pain associated with postherpetic neuralgia (Neurontin, Horizant and Gralise). d. Management of Restless legs syndrome (RLS) (Only Horizant). 2). Its oral suspension is available under the brand name of Fanatrex. 3). Gabapentin, available under the brand name of Gralise, is ONLY indicated for the treatment of post herpetic neuralgia (PHN). Gralise is not interchangeable with other gabapentin products because of differing pharmacokinetic profiles that affect the frequency of administration. 4). Gabapentin enacarbil, available under the brand name of Horizant, is indicated for the treatment of restless legs syndrome (RLS) and PHN. It is NOT recommended for patients who are required to sleep during the daytime and remain awake at night.

	Dose	Special Notes
Gabapentin (Capsule) (Tablet) (Oral solution) (Tablet, ER) (Oral suspension)	4. PHN (Horizant): 600 mg PO BID. 5. RLS (Horizant): 600 mg once daily taken with food at about 5 PM.	5). Gabapentin enacarbil (Horizant) is a prodrug of Gabapentin. 6). Somnolence, dizziness, ataxia, fatigue, nystagmus, nausea and vomiting are the most common adverse effects reported with therapy.
Vigabatrin (Tablet) (Oral solution)	1. Complex partial seizure: 500 mg to 1500 mg PO BID with or without food.	1). Vigabatrin (Sabril) is indicated for the treatment of refractory Complex Partial seizures in adults. 2). Vision loss is the principal side effect of Vigabatrin (Sabril). The onset of vision loss from Vigabatrin (Sabril) is unpredictable, and can occur within weeks of starting treatment or sooner, or at any time during treatment, even after months or years. 3). Because of the risk of vision loss, it should be withdrawn from patients who fail to show substantial clinical benefit within 3 months of initiation, or sooner if treatment failure becomes obvious. 4). Because of the risk of permanent vision loss, it is available only through a special restricted distribution program called SHARE. Only prescribers and pharmacies registered with SHARE may prescribe and distribute Vigabatrin (Sabril). 5). Somnolence, fatigue, peripheral neuropathy anemia, edema and weight gain are also reported with the therapy.
GABA Reuptake Inhibitors		
Tiagabine (Tablet)	1. Partial seizure 4 to 56 mg per DAY given in 2 to 4 divided doses.	1). Tiagabine (Gabitril) is indicated for the treatment of partial seizure (patient 12 years and older). Dizziness, somnolence, depression, confusion, and asthenia are major side effects of the drug. 2). Tiagabine (Gabitril) inhibits reuptake of GABA through highly selective binding to the GAT-1 transporter and therefore, it is classified as a selective GABA reuptake inhibitor (SGRI). 3). Post-marketing reports have shown that Tiagabine (Gabitril) use has been associated with new onset seizures and status epilepticus in patients without epilepsy. Seizures and status epilepticus are also known to occur with overdosage.

Hydantoin Anticonvulsants:

	Dose	Special Notes
Phenytoin 1.Tablet 2. Chewable tablet - Infatab 3. Oral suspension 4. Capsule – Kapseals 5. Capsule, ER	1. Grand-mal and complex partial seizure: 1. 100 mg three times daily or 300 mg (extended release) once daily. 2. 125 mg (suspension) three times daily.	1). Phenytoin (Dilantin) is indicated for the treatment of generalized tonic-clonic (grand mal) seizure and complex partial seizure. 2). Hydantoin derivatives may cause membrane stabilization either by increasing the efflux of Na^+ ions or by decreasing the influx of Na^+ ions across the cell membrane of neurons. 3). The normal therapeutic serum concentration of Phenytoin (Dilantin) should be between 10 and 20 mcg/ml. A serum concentration above this may result in various adverse effects and toxicities. a. A serum concentration greater than 20 mcg/ml but less than 30 mcg/ml may cause nystagmus. b. A serum concentration greater than 30 mcg/ml but less than 40 mcg/ml may cause ataxia. c. A serum concentration greater than 40 mcg/ml may cause dysarthria and lethargy. 4). Serum concentrations should be monitored and care should be taken when switching a patient from the sodium salt to the free acid form. Dilantin Kapseals is formulated with the sodium salt of phenytoin. The free acid form of Phenytoin is used in Dilantin-125 Suspension and Dilantin Infatabs. Because there is approximately an 8% increase in drug content with the free acid form over that of the sodium salt, dosage adjustments and serum level monitoring may be necessary when switching from a product formulated with the free acid to a product formulated with the sodium salt and vice versa.
Fosphenytoin (Injection)	1. Status Epilepticus: Loading dose: 15 to 20 mg PE/Kg given at 100 to 150 mg PE/min.	1). Fosphenytoin sodium (Cerebyx) is indicated for the treatment of generalized convulsive status epilepticus. 2). Each Fosphenytoin sodium (Cerebyx) vial containing 75 mg\ml Fosphenytoin sodium is equivalent to 50mg\ml Phenytoin sodium after administration.

	Dose	Special Notes
Fosphenytoin (Injection)	Maintenance dose: 4 to 6 mg PE/kg/day. *PE = Phenytoin Na Equivalent.	3). Fosphenytoin sodium (Cerebyx) is a prodrug of Phenytoin. Fosphenytoin sodium is completely converted to Phenytoin after an I.V. administration. The recommended I.V. dose of Fosphenytoin sodium for the treatment of status epileptics is 15 to 20 mg Phenytoin Na equivalent/kg. The maximum recommended rate at which Fosphenytoin sodium can be administered in a patient is 150 mg Phenytoin equivalent/min. 4). Because of the risk of hypotension, Fosphenytoin sodium (Cerebyx) should be administered no faster than 150 mg PE/min. Continuous monitoring of the electrocardiogram, blood pressure, and respiratory function is essential and the patient should be observed throughout the period where maximal serum phenytoin concentrations occur, approximately 10 to 20 minutes after the end of Fosphenytoin sodium injection infusions. 5). An IM Fosphenytoin sodium (Cerebyx) injection should not be used in the treatment of status epilepticus because of its slow onset of action.
Neuronal Potassium Channel Opener		
Ezogabine (Tablet)	1. Partial seizure: 100 mg to 400 mg three times daily with or without food.	1). Ezogabine (Potiga) is indicated for the treatment of partial onset seizure in patients aged 18 years and older. 2). Ezogabine (Potiga) enhances transmembrane potassium currents mediated by the KCNQ family of ion channels. By activating KCNQ channels, Ezogabine (Potiga) is thought to stabilize the resting membrane potential and reduce brain excitability. In vitro studies suggest that Ezogabine (Potiga) may also exert therapeutic effects through augmentation of GABA-mediated currents. 3). Urinary retention, neuro-psychiatric symptoms, and dizziness are reported side effects of the drug. 4). Carbamazepine and Phenytoin may reduce the serum concentration and pharmacological effects of Ezogabine (Potiga) by enzyme induction. When simultaneously prescribed, Ezogabine (Potiga) dose should be increased.

Succinimide Anticonvulsants

	Dose	Special Notes
Ethosuximide (Capsule) (Oral solution) **Methsuximide** (Capsule)	Ethosuximide: 250 mg to 1500 mg per day in divided doses. Methsuximide 300 mg to 1200 mg per day in divided doses.	1). All succinimide derivatives are indicated for the treatment of absence seizure (petit mal) and have been associated with risks of blood dyscrasia. Complete blood counts should be performed during succinimide therapy. Signs of a sore throat and fever may be initial signs of blood dyscrasia. 2). The normal therapeutic serum concentration of Methsuximide (Celontin) is 10 to 40 mcg/ml; whereas for Ethosuximide (Zarontin), it is 40 to 100 mcg/ml.

Pyrrolidine Anticonvulsants:

Levetiracetam (Tablet) (Tablet, ER) (Oral solution) (Injection) ER = Extended Release	1. Epilepsy: 1. 500 mg to 1500 mg (Immediate Release) PO BID. 2. 1000 mg to 3000 mg once daily (ER).	1). Levetiracetam (Keppra) is indicated for the following: a. Partial onset seizure. b. Myoclonic seizure. c. Generalized tonic-clonic seizure. d. Idiopathic generalized epilepsy. 2). The extended release tablet formulation of Levetiracetam (Keppra) is ONLY indicated for the treatment of partial seizure. 3). When switching from oral Levetiracetam (Keppra), the initial total daily intravenous dosage of Levetiracetam should be equivalent to the total daily dosage and frequency of oral Levetiracetam and should be administered as a 15-minute intravenous infusion following dilution in 100 mL of a compatible diluent. 4). At the end of the intravenous treatment period, the patient may be switched to Levetiracetam (Keppra) oral administration at the equivalent daily dosage and frequency of the intravenous administration. 5). Side effects: Somnolence, fatigue, asthenia, agitation and depression.

Triazine Anticonvulsants:

	Dose	Special Notes
Lamotrigine (Tablet) (Tablet, chewable) (Tablet, orally disintegrating), (Tablet, ER)	1. Seizure: 225 to 375 mg per day in two divided doses. 2. Bipolar disorder: 200 mg per day.	1). Lamotrigine (Lamictal) is indicated for the following: a. Partial seizure. b. Tonic-clonic seizure. c. Seizure associated with Lennox-Gastaut syndrome. d. Bipolar disorder. 2). Lamotrigine (Lamictal) can cause serious rashes requiring hospitalization and discontinuation of treatment. The incidence of these rashes, which have included Stevens Johnson syndrome, is approximately 0.8% in pediatric patients (2 to 16 years of age) receiving Lamotrigine as adjunctive therapy for epilepsy and 0.3% in adults on adjunctive therapy for epilepsy. 3). The risk of rash may also be increased by: a). Coadministration of Lamotrigine with Valproate. b). Exceeding the recommended initial dose of Lamotrigine. c). Exceeding the recommended dose escalation for Lamotrigine. 4). Lamotrigine extended-release tablet (Lamictal XR) contains a modified-release eroding formulation as the core. The tablets are coated with a clear enteric coat and have an aperture drilled through the coats on both faces of the tablet (DiffCORE) to enable a controlled release of drug in the acidic environment of the stomach. 5). When Lamotrigine is prescribed with Carbamazepine, Phenytoin, Phenobarbital, Primidone or Valproate, the recommended dose for the treatment of seizure should be increased to 300 to 500 mg per day in two divided doses and doses for the treatment of bipolar disorder should be increased to 400 mg per day. 6). Nearly all cases of life-threatening rashes caused by Lamotrigine (Lamictal) have occurred within 2 to 8 weeks of treatment initiation.

Terminology:

Partial seizure	All seizures are caused by abnormal electrical disturbances in the brain. Partial (focal) seizures occur when this electrical activity remains in a limited area of the brain. The seizures may sometimes turn into generalized seizures, which affect the whole brain. This is called secondary generalization. Partial seizures can be further characterized as: 1. Simple - not affecting awareness or memory. 2. Complex - affecting awareness or memory of events before, during, and immediately after the seizure, and affecting behavior.
Diplopia	A disorder of vision in which two images of a single object are seen (as from unequal action of the eye muscles)—called also double vision.
Somnolence	The quality or state of being drowsy.
Ataxia	An inability to coordinate voluntary muscular movements that is symptomatic of some nervous disorders.
Hyponatremia	A low sodium serum concentration.
Simple and complex absence seizures	Simple absence seizure is defined as very brief clouding of the sensorium or loss of consciousness accompanied by certain generalized epileptic discharges without other detectable clinical signs. Complex absence is the term used when other signs are also present.
Diabetic Peripheral Neuropathy (DPN)	Diabetic neuropathy is nerve damage caused by diabetes. When it affects the arms, hands, legs and feet it is known as diabetic peripheral neuropathy. Diabetic peripheral neuropathy is different from peripheral arterial disease (poor circulation), which affects the blood vessels rather than the nerves.
Fibromyalgia	A chronic disorder characterized by widespread pain, tenderness, and stiffness of muscles and associated connective tissue structures that is typically accompanied by fatigue, headache, and sleep disturbances—called also fibromyalgia syndrome, fibromyositis.

14. ANTIDEPRESSANTS

(A) Tricyclic Antidepressants

Amoxapine	=	Asendin	Nortriptyline	=	Pamelor, Aventyl
Imipramine	=	Tofranil, Tofranil-PM	Amitriptyline	=	Elavil, Vanatrip
Doxepin	=	Sinequan, Silenor, Adapin, Prudoxin, Zonalon	Protriptyline	=	Vivactil
Clomipramine	=	Anafranil	Desipramine	=	Norpramin
Trimipramine	=	Surmontil			

(B) Tetracyclic Antidepressants

Maprotiline	=	Ludiomil
Mirtazapine	=	Remeron, Remeron SolTab

(C) Selective Serotonin Reuptake Inhibitors (SSRIs)

Fluoxetine	=	Prozac, Sarafem, Selfemra, Rapiflux, Prozac Weekly	Fluvoxamine	=	Luvox, Luvox CR
Paroxetine	=	Paxil, Paxil CR, Pexeva, Asimia	Citalopram	=	Celexa
Sertraline	=	Zoloft	Escitalopram	=	Lexapro

(D) Selective Serotonin-Norepinephrine Reuptake Inhibitors (SSNRIs)

Venlafaxine	=	Effexor, Effexor XR	Duloxetine	=	Cymbalta
Desvenlafaxine	=	Pristiq	Milnacipran	=	Savella

(E) MAO A Inhibitors

Isocarboxazid	=	Marplan
Phenelzine	=	Nardil
Tranylcypromine	=	Parnate

(F) MAO B Inhibitors

Selegiline	=	Zelapar, Emsam

(G) Phenylpiperazine Antidepressants

Nefazodone	=	Serzone
Trazodone	=	Desyrel, Oleptro

(H) Miscellaneous

Bupropion	=	Wellbutrin, Zyban, Budeprion, Aplenzin
Vilazodone	=	Viibryd
Lithium carbonate	=	Eskalith, Lithobid, Lithotabs

36. RHEUMATOID ARTHRITIS

A) NSAIDS and COX 2 Inhibitors

Please Refer to NSAIDs.

B). Corticosteroids

Methylprednisolone	=	Medrol, Depo-Medrol, Solu-Medrol
Triamcinolone	=	Aristocort, Kenalog
Dexamethasone	=	Decadron
Cortisone	=	Cortone
Prednisone	=	Deltasone

C). Interleukin Inhibitors

Tocilizumab	=	Actemra
Anakinra	=	Kineret
Rilonacept	=	Arcalyst
Canakinumab	=	Ilaris

D). Immunomodulatory Agents

Leflunomide	=	Arava
Rituximab	=	Rituxan
Abatacept	=	Orencia

E). TNF Alpha Blockers

Certolizumab	=	Cimzia
Etanercept	=	Enbrel
Adalimumab	=	Humira
Infliximab	=	Remicade
Golimumab	=	Simponi

F). Gold Compounds

Gold Sodium Thiomalate	=	Myochrysine, Aurolate
Auranofin	=	Ridaura

G). Miscellaneous

Azathioprine	=	Imuran, Azasan
Sulfasalazine	=	Azulfidine
Penicillamine	=	Depen
Cyclosporine	=	Gengraf, Neoral
Hydroxychloroquine	=	Plaquenil
Methotrexate	=	Rheumatrex
Sodium hyaluronate	=	Euflexxa, Hyalgan, Supartz
Hylan G-F 20	=	Synvisc, Synvisc One
Hyaluronan	=	Orthovisc
Flavocoxid	=	Limbrel

Definition: Rheumatoid arthritis is a chronic, systematic, inflammatory condition of joints, tendons and other organ structures.

Dose	Special Notes
NSAIDS and COX- 2 Inhibitors	1). Some of the first medications available, NSAIDs are usually given as pills and have been used for decades to treat pain and inflammation of all different causes. These medications, such as aspirin, ibuprofen or naproxen, are often given as initial treatment to relieve rheumatoid arthritis symptoms.

	Dose	Special Notes
Corticosteroids		1). Steroids can reduce inflammation from rheumatoid arthritis but have limited ability to reduce the joint damage caused by rheumatoid arthritis. Steroids may be injected directly into a joint to relieve severe pain, but can also be taken as pills to help relieve overall symptoms. Prednisone is a common steroid used to treat rheumatoid arthritis.
C). Interleukin Inhibitors		
Tocilizumab (Injection)	1. Arthritis: 4 to 8 mg/kg given once every 4 weeks as a 60 minute single IV drip infusion. 2. Juvenile arthritis: 8 to 12 mg/kg given once every 2 weeks as a 60 minute single IV drip infusion.	1). Tocilizumab (Actemra) binds specifically to Interleukin (IL)-6 receptors, and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 is a pro-inflammatory cytokine produced by a variety of cell types including T- and B-cells, lymphocytes, monocytes and fibroblasts. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis. 2). Tocilizumab (Actemra) is indicated for the following: a). Moderate to severe active rheumatoid arthritis b). Systemic Juvenile Idiopathic Arthritis (patients 2 years of age and older) 3). Tocilizumab (Actemra) may be used as monotherapy or concomitantly with Methotrexate or other DMARDs. 4). Patients treated with Tocilizumab (Actemra) are at increased risk for developing serious infections that may lead to hospitalization or even death. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Tocilizumab (Actemra), including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. 5). G.I. perforation, infusion site reactions, anaphylaxis and severe infections are reported side effects of Tocilizumab (Actemra). 6). Live vaccines should NOT BE given concurrently with Tocilizumab (Actemra).
Anakinra (Injection)	1. Arthritis: 100 mg subcutaneously (SC) daily.	1). Anakinra (Kineret) is a recombinant, nonglycosylated form of the human interleukin-1 receptor antagonist (IL-1Ra). It blocks the biologic activity of IL-1 by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL 1RI). IL-1 production is induced in response to inflammatory stimuli and mediates various physiologic responses including inflammatory and immunological responses.

	Dose	Special Notes
Anakinra (Injection)		2). Anakinra (Kineret) is indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis (RA), in patients 18 years of age or older. It can be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents. 3). Physicians should consider a dose of 100 mg every other day for RA patients who have severe renal insufficiency or end stage renal disease. 4). Serious infection, neutropenia particularly when used in combination with TNF blocking agents, injection site reactions and hypersensitivity reactions are reported side effects of Anakinra (Kineret).
Rilonacept (Injection)	1. FCAS and MWS: 320 mg (loading dose) SC on day 1 followed by 160 mg SC once a week.	1). Rilonacept (Arcalyst) blocks IL-1β signaling by acting as a soluble decoy receptor that binds IL-1β and prevents its interaction with cell surface receptors. 2). Rilonacept (Arcalyst) is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older. 3). Mycobacterium intracellulare infection; gastrointestinal bleeding and colitis; sinusitis and bronchitis; Streptococcus pneumoniae meningitis, and injection site reactions are reported side effects of Rilonacept (Arcalyst).
Canakinumab (Injection)	1. FCAS and MWS: 150 mg given every eight weeks as a single dose via SC injection.	1). Canakinumab (Ilaris) binds to human IL-1β and neutralizes its activity by blocking its interaction with IL-1 receptors. 2). Canakinumab (Ilaris) is an interleukin-1β blocker indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS). 3). Vertigo, nasopharyngitis, diarrhea, influenza, headache, nausea and injection site reactions are reported side effects of Canakinumab (Ilaris).

D). Immunomodulatory Agents

	Dose	Special Notes
Leflunomide (Tablet)	1. Arthritis: 100 mg per day for 3 days followed by 20 mg daily.	1). Leflunomide (Arava) is an immunomodulatory agent which inhibits dihydroorotate dehydrogenase (an enzyme involved in de novo pyrimidine synthesis) and has antiproliferative activity. 2). Leflunomide (Arava) is indicated in adults for the treatment of active rheumatoid arthritis (RA): a. to reduce signs and symptoms b. to inhibit structural damage as evidenced by X-ray erosions and joint space narrowing c. to improve physical function. 4). Pregnancy must be excluded before the start of treatment with Leflunomide (Arava). It is contraindicated in pregnant women, or women of childbearing potential who are not using reliable contraception. 5). Severe liver injury, including fatal liver failure, has been reported in some patients treated with Leflunomide (Arava). Patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (ALT) > 2xULN (Upper Limit of Normal) before initiating treatment, should not be treated with Leflunomide (Arava). 6). Monitoring of ALT levels is recommended at least monthly for six months after starting Leflunomide (Arava), and thereafter every 6-8 weeks. If ALT elevation > 3 fold ULN occurs, a physician should interrupt Leflunomide (Arava) therapy. 7). Diarrhea, elevated liver enzymes (ALT and AST), alopecia and rash are also reported with the therapy.
Rituximab (Injection)	1. Arthritis: Administer two-1000 mg IV infusions separated by 2 weeks. Subsequent courses should be given every 24 weeks or based on clinical evaluation, but not sooner than every 16 weeks.	1). Rituximab (Rituxan) is indicated for the following: a. Non-Hodgkin's Lymphoma b. Chronic Lymphocytic Leukemia c. Rheumatoid Arthritis (in combination with Methotrexate) 2). Rituximab (Rituxan) should NOT be administered as an intravenous push or bolus. 3). 100 mg Methylprednisolone or its equivalent via IV prior to each infusion is recommended to reduce the incidence and severity of infusion reactions. Patients should also be premedicated with acetaminophen and an antihistamine.

	Dose	Special Notes
Rituximab (Injection)		4). Rituximab (Rituxan) administration can result in serious, including fatal infusion reactions. Deaths within 24 hours of Rituximab (Rituxan) infusion have occurred. Approximately 80% of fatal infusion reactions occurred in association with the first infusion. 5). Acute renal failure requiring dialysis with instances of fatal outcome can occur in the setting of Tumor Lysis Syndrome (TLS) following treatment of non-Hodgkin's lymphoma (NHL) with Rituximab (Rituxan) monotherapy. 6). JC virus infection resulting in Progressive Multifocal Leukoencephalopathy (PML) and death can occur in patients receiving Rituximab (Rituxan). 7). Severe mucocutaneous reactions, neutropenia, cardiac arrhythmia, renal toxicity and bowel obstruction and perforation are also reported with the therapy.
Abatacept (Injection)	1. Arthritis: 500 to 1000 mg Administered as a 30 minute IV infusion. Following initial infusion, it should be given at 2nd and 4th week after the 1st infusion and every 4 weeks thereafter.	1). Abatacept (Orencia) is indicated for: a. Adult Rheumatoid Arthritis b. Juvenile Idiopathic Arthritis 2). Abatacept (Orencia) may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists. 3). Headache, upper respiratory tract infections, infusion site reactions, nasopharyngitis, and nausea are most commonly reported side effects of Abatacept (Orencia). 4). Concurrent administration of a TNF antagonist with Abatacept (Orencia) has been associated with an increased risk of serious infections. Concurrent administration of TNF antagonists is not recommended.
E). TNF Alpha Blockers		
Certolizumab (Injection)	1. Arthritis: a. Initial: 400 mg SC initially and at weeks 2 and 4, followed by 200 mg every other week.	1). Certolizumab (Cimzia) is a TNF blocker. TNFα is a key pro-inflammatory cytokine with a central role in inflammatory processes. 2). Certolizumab (Cimzia) is indicated for: a. Crohn's Disease b. Rheumatoid arthritis

	Dose	Special Notes
Certolizumab (Injection)	b. Maintenance: 400 mg SC every 4 weeks.	3). It is administered by subcutaneous injection. Injection sites should be rotated and injections should not be given into areas where the skin is tender, bruised, red or hard. 4). Patients treated with Certolizumab (Cimzia) are at increased risk for developing serious infections that may lead to hospitalization or even death. Most patients who developed these infections were taking concomitant immunosuppressants such as Methotrexate or corticosteroids. 5). Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Certolizumab (Cimzia), including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. 6). Serious infections, rash, heart failure, and malignancies are reported side effects of Certolizumab (Cimzia). Live vaccines should NOT BE given concurrently with Certolizumab (Cimzia). Certolizumab (Cimzia) must be refrigerated at 2°C to 8°C.
Etanercept (Injection)	1. RA, AS, JIA and PsA: 50 mg SC weekly. 2. PsO: 50 mg SC twice weekly for 3 months followed by 50 mg SC once weekly.	1). TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. It plays an important role in the inflammatory processes of rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) and the resulting joint pathology. Etanercept (Enbrel) is a TNF blocker. 2). Etanercept (Enbrel) is indicated for the following: a. Rheumatoid arthritis (RA) (monotherapy or with Methotrexate) b. Juvenile idiopathic arthritis (JIA) (patients ages 2 and older) c. Psoriatic arthritis (PsA) d. Ankylosing spondylitis (AS) e. Plaque psoriasis (PsO) 3). Patients treated with Etanercept (Enbrel) are at increased risk for developing serious infections that may lead to hospitalization or even death. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Etanercept (Enbrel), including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. 4). Infections, injection site reactions, diarrhea, rash, pruritus and hypersensitivity reactions are also reported with the therapy. Etanercept (Enbrel) must be refrigerated at 2°C to 8°C.

	Dose	Special Notes
Adalimumab (Injection)	1. RA, AS and PsA: 40 mg SC every other week. 2. JIA: 20 to 40 mg SC every other week. 3. PsO: Initially 80 mg SC, followed by 40 mg given every other week starting one week after the initial dose. 4. Crohn's disease: 160 mg initially on Day 1, followed by 80 mg two weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg every other week.	1). TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Elevated levels of TNF are found in the synovial fluid of rheumatoid arthritis, including juvenile idiopathic arthritis, psoriatic arthritis, and ankylosing spondylitis patients and play an important role in both the pathologic inflammation and the joint destruction that are hallmarks of these diseases. Increased levels of TNF are also found in psoriasis plaques. Adalimumab (Humira) binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF receptors. 2). Adalimumab (Humira) is indicated for the following: a. Rheumatoid arthritis (RA) (monotherapy or with Methotrexate) b. Juvenile idiopathic arthritis (JIA) (patients ages 4 and older) c. Psoriatic arthritis (PsA) d. Ankylosing spondylitis (AS) e. Plaque psoriasis (PsO) f. Crohn's disease 3). Patients treated with Adalimumab (Humira) are at increased risk for developing serious infections that may lead to hospitalization or even death. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Adalimumab (Humira), including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. 4). Injection site reactions, infections, rash and liver enzyme elevations are reported with Adalimumab (Humira). Live vaccines should not be given concurrently with Adalimumab (Humira). 5). Adalimumab (Humira) must be refrigerated between 2° and 8° C. The prefilled syringes should be protected from exposure to light.
Infliximab (Injection)	1. Arthritis: 3 mg/kg given as an IV induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks thereafter.	1). Infliximab (Remicade) is a TNF blocker. It is indicated for the following: a. Rheumatoid arthritis (RA) (in combination with Methotrexate) b. Ulcerative colitis c. Psoriatic arthritis (PsA) d. Ankylosing spondylitis (AS) e. Plaque psoriasis (PsO) f. Crohn's disease 2). Prior to infusion with Infliximab (Remicade), premedication may be administered at the physician's discretion. Premedication could include antihistamines (anti-H_1 +/- anti-H_2), acetaminophen and/or corticosteroids.

	Dose	Special Notes
Infliximab (Injection)	2. Crohn's disease, ulcerative colitis, PsA and PsO: 5 mg/kg given as an IV induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter. 3. Ankylosing spondylitis: 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks thereafter.	3). Patients treated with Infliximab (Remicade) are at increased risk for developing serious infections that may lead to hospitalization or even death. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Infliximab (Remicade), including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. 4). The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNFα, IL-1, IL-6, IL-10, IFN) during chronic inflammation. Therefore, it is expected that for a molecule that antagonizes cytokine activity, such as Infliximab (Remicade), the formation of CYP450 enzymes could be normalized. Upon initiation or discontinuation of Infliximab (Remicade) in patients being treated with CYP450 substrates with a narrow therapeutic index, monitoring of the effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) is recommended and the individual dose of the drug product may be adjusted as needed. 5). Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including Infliximab (Remicade). 6). Infections, infusion site reactions (e.g., dyspnea, flushing, headache and rash), liver toxicity, lupus-like syndrome and myalgia are reported with Infliximab (Remicade) therapy. Infliximab (Remicade) must be refrigerated at 2°C to 8°C.
Golimumab (Injection)	1. RA, PsA and AS: 50 mg SC given every month.	1). Golimumab (Simponi) is a human monoclonal antibody that binds to both the soluble and transmembrane bioactive forms of human TNFα. It is a TNF blocker. It is indicated for the following: a. Rheumatoid arthritis (RA) (in combination with Methotrexate) b. Psoriatic arthritis (PsA) c. Ankylosing spondylitis (AS) 2). Patients treated with Golimumab (Simponi) are at increased risk for developing serious infections that may lead to hospitalization or even death. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Golimumab (Simponi), including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. 3). Golimumab (Simponi) must be refrigerated between 2° and 8° C.

	Dose	Special Notes
Golimumab (Injection)		4). Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including Golimumab (Simponi). 5). Serious infections, liver enzyme elevations and injection site reactions are reported side effects of Golimumab (Simponi).
F). Gold Compounds		
Gold Sodium Thiomalate (Injection)	1. Arthritis: a. 1st Week: 10 mg b. 2nd Week: 25 mg c. 3rd and subsequent injections, 25 to 50 mg until there is toxicity or major clinical improvement, or, in the absence of either of these, the cumulative dose of Gold Sodium Thiomalate reaches one gram. 2. JIA: 10 mg initially followed by 1 mg/kg weekly (not to exceed 50 mg for a single injection).	1). The predominant action of Gold Sodium Thiomalate (Myochrysine) appears to be a suppressive effect on the synovitis of active rheumatoid disease. It is indicated for the following: a. Rheumatoid arthritis (RA) b. Juvenile idiopathic arthritis (JIA) 2). Gold Sodium Thiomalate (Myochrysine) should be administered only by intramuscular injection, preferably intragluteally. It should be given with the patient lying down. He should remain recumbent for approximately 10 minutes after the injection. 3). Gold Sodium Thiomalate (Myochrysine) is continued until the cumulative dose reaches one gram unless toxicity or major clinical improvement occurs. If significant clinical improvement occurs before a cumulative dose of one gram has been administered, the dose may be decreased or the interval between injections increased as with maintenance therapy. 4). Gold salts should NOT be used concomitantly with Penicillamine. 5). Leukopenia, thrombocytopenia, aplastic anemia, angioedema, glossitis, stomatitis, proteinuria, renal toxicity, rash, and glossitis are reported side effects of gold compounds. For serious renal, hematologic, pulmonary, and enterocolitic complications, high doses of systemic corticosteroids (prednisone 40 to 100 mg daily in divided doses) are recommended.
Auranofin (Capsule)	1. Arthritis: 6 mg once daily or 3 mg PO BID.	1). Auranofin (Ridaura) is indicated for the treatment of arthritis. 2). Anemia, leukopenia, granulocytopenia, thrombocytopenia, proteinuria, hematuria, pruritus, rash, stomatitis and persistent diarrhea are commonly reported side effects of Auranofin (Ridaura).

G). Miscellaneous

	Dose	Special Notes
Azathioprine (Tablet)	1. Arthritis: 50 to 100 mg given as a single or on a twice daily schedule. 2. Renal Transplant: Initial Dose: 3 to 5 mg/kg daily beginning at the time of transplant. Maintenance Dose: 1 to 3 mg/kg daily.	1). Azathioprine (Imuran, Azasan) is a purine-antagonist anti-metabolite that primarily is used as an immunosuppressant. Azathioprine is metabolized to 6-mercaptopurine (6-MP). Via hypoxanthine-guanine phosphoribosyltransferase (HGPRT) and a series of multi-enzymatic processes involving kinases, 6-MP is converted to form 6-thioguanine nucleotides (6-TGNs) as major metabolites. The cytotoxicity of Azathioprine (Imuran, Azasan) is due, in part, to the incorporation of 6-TGN into DNA. 2). Azathioprine (Imuran, Azasan) is indicated for the following: a). For the prevention of rejection in renal homotransplantation b). For the treatment of active rheumatoid arthritis (RA) to reduce signs and symptoms 3). Thiopurine S-methyltransferase (TPMT) genotyping or phenotyping can be used to identify patients with absent or reduced TPMT activity. Patients with low or absent TPMT activity are at an increased risk of developing severe, life-threatening myelotoxicity from Azathioprine if conventional doses are given. Physicians may consider alternative therapies for patients who have low or absent TPMT activity. 4). One of the pathways for inactivation of Azathioprine (Imuran, Azasan) is inhibited by Allopurinol. Patients receiving Azathioprine and Allopurinol concomitantly should have a dose reduction of Azathioprine, to approximately 1/3 to 1/4 the usual dose. It is recommended that a further dose reduction or alternative therapies be considered for patients with low or absent TPMT activity receiving Azathioprine and Allopurinol because both TPMT and xanthine oxidase (XO) inactivation pathways are affected. 5). The use of Ribavirin for hepatitis C in patients receiving Azathioprine has been reported to induce severe pancytopenia and may increase the risk of azathioprine-related myelotoxicity. Inosine monophosphate dehydrogenase (IMDH) is required for one of the metabolic pathways of azathioprine. Ribavirin is known to inhibit IMDH, thereby leading to accumulation of an Azathioprine metabolite, 6-methylthioionosine monophosphate (6MTITP), which is associated with myelotoxicity (neutropenia, thrombocytopenia, and anemia). Patients receiving Azathioprine with Ribavirin should have complete blood counts, including platelet counts, monitored weekly for the first month, twice monthly for the second and third months of treatment, then monthly or more frequently if dosage or other therapy changes are necessary.

	Dose	Special Notes
Azathioprine (Tablet)		6). Nausea, vomiting, leukopenia, thrombocytopenia, fever and arthralgia are reported with Azathioprine (Imuran, Azasan) therapy.
Sulfasalazine (Tablet, DR-EC) DR: Delayed Release EC: Enteric Coating	1. Arthritis: 2 grams per day in two divided doses. 2. JRA: 30 to 50 mg/kg per day in two divided doses. 3. UC: 3 to 4 grams per day in three equally divided doses, preferably after meals.	1). Sulfasalazine (Azulfidine EN) is metabolized by intestinal bacteria to sulfapyridine and 5-aminosalicylic acid. The mode of action of Sulfasalazine (Azulfidine EN) may be related to antiinflammatory and/or immunomodulatory properties of these two metabolites. 2). Sulfasalazine (Azulfidine EN) is indicated for the following: a. Rheumatoid arthritis b. Juvenile rheumatoid arthritis (JRA) c. Ulcerative colitis (UC) 3). Azulfidine EN is particularly indicated in patients who cannot take uncoated sulfasalazine tablets because of gastrointestinal intolerance (e.g., anorexia, nausea). If symptoms of gastric intolerance (anorexia, nausea, vomiting, etc.) occur after the first few doses of Azulfidine EN-tabs, they are probably due to increased serum levels of total Sulfapyridine, and may be alleviated by halving the daily dose of Azulfidine EN-tabs and subsequently increasing it gradually over several days. If gastric intolerance continues, the drug should be stopped for 5 to 7 days; then reintroduced at a lower daily dose. 4). Anorexia, headache, nausea, vomiting, gastric distress, blood dyscrasias, hypersensitivity reactions, skin rash, urine discoloration and skin discoloration are reported with the therapy. 5). Patients with glucose-6-phosphate dehydrogenase deficiency should be observed closely for signs of hemolytic anemia. This reaction is frequently dose related. If toxic or hypersensitivity reactions occur, Sulfasalazine (Azulfidine EN) should be discontinued immediately. 6). Sulfasalazine (Azulfidine EN) should be carefully prescribed to patients hypersensitive to sulfonamides and/or salicylate.
Penicillamine (Capsule)	1. Wilson's disease: 0.75 to 1.5 gram per day depending on copper serum concentration.	1). Penicillamine (Cuprimine) is a chelating agent indicated: a). For the removal of excess copper in patients with Wilson's disease. b). For reducing excess cystine excretion in cystinuria. c). For the treatment of rheumatoid arthritis 2). Because Penicillamine (Cuprimine) can cause severe adverse reactions, its use in rheumatoid arthritis should be restricted to patients who have severe, active disease and who have failed to respond to an adequate trial of conventional therapy.

	Dose	Special Notes
Penicillamine (Capsule)	2. Cystinuria: 1 to 4 gram per day divided into four doses. 3. Arthritis: 125 to 1500 mg per day.	3). The principal rule of treatment with Penicillamine (Cuprimine) in rheumatoid arthritis is patience. The onset of therapeutic response is typically delayed. Two or three months may be required before the first evidence of a clinical response is noted. 4). Penicillamine (Cuprimine) should NOT be used in patients who are receiving gold therapy, antimalarial or cytotoxic drugs, oxyphenbutazone, or phenylbutazone. Other measures, such as salicylates, other non-steroidal anti-inflammatory drugs, or systemic corticosteroids, may be continued when penicillamine is initiated. 5). Anorexia, nausea, generalized pruritus, early and late rashes, lupus-like syndrome, urticaria and exfoliative dermatitis, severe bone marrow suppression, proteinuria, tinnitus, optic neuritis and peripheral sensory and motor neuropathies are reported with Penicillamine (Cuprimine) therapy.
Cyclosporine (Capsule) (Oral solution) (Injection)	1. Arthritis and Psoriasis: 2.5 to 4 mg/kg/day divided into two doses. 2. Organ Transplant: Initial Dose: 10 to 15mg/kg 4 to 12 hours prior transplant. Maintenance Dose: 5-10 mg/kg/day.	1). The effectiveness of Cyclosporine (Gengraf, Neoral) results from specific and reversible inhibition of immunocompetent lymphocytes in the G0- and G1-phase of the cell cycle. T-lymphocytes are preferentially inhibited. The T-helper cell is the main target, although the T-suppressor cell may also be suppressed. Cyclosporine (Gengraf, Neoral) also inhibits lymphokine production and release including interleukin-2. It is indicated for the following: a. For the prophylaxis of organ rejection in kidney, liver, and heart allogeneic transplants (Sandimmune, Neoral and Gengraf) b. Rheumatoid arthritis (Neoral and Gengraf only) c. Severe recalcitrant psoriasis (Neoral and Gengraf only) 2). Gengraf capsule has increased bioavailability in comparison to Sandimmune capsule. Gengraf and Sandimmune are not bioequivalent and cannot be used interchangeably without physician supervision. For a given trough concentration, Cyclosporine exposure will be greater with Gengraf than with Sandimmune. If a patient who is receiving exceptionally high doses of Sandimmune is converted to Gengraf, particular caution should be exercised. Similarly, Neoral capsules and oral solution have increased bioavailability in comparison to Sandimmune capsules and Sandimmune oral solution. Neoral and Sandimmune are not bioequivalent and cannot be used interchangeably without physician supervision. 3). Psoriasis patients previously treated with PUVA and to a lesser extent, methotrexate or other immunosuppressive agents, UVB, coal tar, or radiation therapy, are at an increased risk of developing skin malignancies when taking Cyclosporine (Gengraf, Neoral).

Dose	Special Notes
Cyclosporine (Capsule) (Oral solution) (Injection)	4). Cyclosporine (Gengraf, Neoral) in recommended dosages, can cause systemic hypertension and nephrotoxicity. The risk increases with increasing dose and duration of cyclosporine therapy. Renal dysfunction, including structural kidney damage, is a potential consequence of cyclosporine, and therefore, renal function must be monitored during therapy. 5). A 25 to 50 % dose reduction can be made at any time to control adverse events, e.g., hypertension elevations in serum creatinine (30% above patient's pretreatment level) or clinically significant laboratory abnormalities. Renal dysfunction, tremor, hirsutism, hypertension and gum hyperplasia are reported side effects of Cyclosporine (Gengraf, Neoral). 6). Compounds that decrease Cyclosporine absorption such as Orlistat should be avoided. Cyclosporine is extensively metabolized by cytochrome P-450 III-A. Substances that inhibit this enzyme could decrease metabolism and increase Cyclosporine concentrations. Substances that are inducers of cytochrome P-450 activity could increase metabolism and decrease Cyclosporine concentrations. Monitoring of circulating Cyclosporine concentrations and appropriate dosage adjustment of Cyclosporine are essential when these drugs are used concomitantly. 7). Cyclosporine should not be used with potassium sparing diuretics because hyperkalemia can occur. Caution is also required when cyclosporine is coadministered with potassium sparing drugs (e.g. angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists), potassium containing drugs as well as in patients on a potassium rich diet. Control of potassium levels in these situations is advisable. 8). There have been reports of a serious drug interaction between Cyclosporine and the herbal dietary supplement, St. John's Wort. This interaction has been reported to produce a marked reduction in the blood concentrations of cyclosporine, resulting in subtherapeutic levels, rejection of transplanted organs, and graft loss. 9). Grapefruit and grapefruit juice affect metabolism, increasing blood concentrations of Cyclosporine, thus should be avoided. 10). Simultaneous coadministration of Cyclosporine significantly increases blood levels of Sirolimus. To minimize increases in Sirolimus blood concentrations and its toxicities, it is recommended that Sirolimus be given 4 hours after Cyclosporine administration.

	Dose	Special Notes
Hydroxychloroquine (Tablet)	1. Arthritis: Initial Dose: 400 to 600 mg daily with a meal or glass of milk for 4 to 12 weeks. Maintenance: 200 to 400 mg daily with a meal or glass of milk. 2. Lupus disorder: 400 to 800 mg daily for 4 to 12 weeks followed by 200 to 400 mg daily maintenance dose.	1). Hydroxychloroquine (Plaquenil) is indicated for the following: a). Malaria b). Discoid and systemic lupus erythematosus c). Arthritis 2). Retinopathy is the major side effect of Hydroxychloroquine (Plaquenil). The most common visual symptoms attributed to the retinopathy are: reading and seeing difficulties (words, letters, or parts of objects missing), photophobia, blurred distance vision, missing or blacked out areas in the central or peripheral visual field, light flashes and streaks. Retinopathy appears to be dose related and has occurred within several months (rarely) to several years of daily therapy; a small number of cases have been reported several years after antimalarial drug therapy was discontinued. 3). Anorexia, nausea, vomiting, diarrhea, abdominal cramps, aplastic anemia, agranulocytosis, leukopenia, anemia, thrombocytopenia (hemolysis in individuals with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency) are also reported with the therapy.
Methotrexate (Tablet) (Injection)	1. Arthritis: 7.5 mg once weekly OR 2.5 mg every 12 hours for 3 doses given as a course once weekly. 2. JRA: 10 mg/m^2 once weekly. 3. Psoriasis: 10 to 25 mg per week until adequate response is achieved.	1). Methotrexate inhibits an enzyme called dihydrofolic acid reductase. Dihydrofolates must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Therefore, Methotrexate interferes with DNA synthesis, repair, and cellular replication. Actively proliferating tissues such as malignant cells, bone marrow, fetal cells, buccal and intestinal mucosa, and cells of the urinary bladder are in general more sensitive to this effect of Methotrexate. When cellular proliferation in malignant tissues is greater than in most normal tissues, Methotrexate may impair malignant growth without irreversible damage to normal tissues. 2). Methotrexate is indicated for the following: a. Neoplastic diseases b. Psoriasis c. Rheumatoid Arthritis d. Polyarticular-Course Juvenile Rheumatoid Arthritis 3). Methotrexate has been reported to cause fetal death and/or congenital anomalies. Therefore, it is not recommended for women of childbearing potential. Pregnant women with psoriasis or rheumatoid arthritis should not receive Methotrexate.

Dose	Special Notes
Methotrexate (Tablet) (Injection)	4). Methotrexate is available in a packaging system designated as the Rheumatrex Dose Pack for therapy with a weekly dosing schedule of 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg and 20 mg. 5). Methotrexate elimination is reduced in patients with impaired renal function. Such patients require especially careful monitoring for toxicity, and require dose reduction or, in some cases, discontinuation of Methotrexate administration. 6). Concomitant administration of some NSAIDs with high dose Methotrexate therapy has been reported to elevate and prolong serum methotrexate levels, resulting in deaths from severe hematologic and gastrointestinal toxicity. Penicillins may reduce the renal clearance of methotrexate; increased serum concentrations of methotrexate with concomitant hematologic and gastrointestinal toxicity have been observed with methotrexate. Use of methotrexate with penicillins should be carefully monitored. 7). Methotrexate causes hepatotoxicity, fibrosis and cirrhosis, but generally only after prolonged use. Persistent abnormalities in liver function tests may precede appearance of fibrosis or cirrhosis in the rheumatoid arthritis population. Therefore, liver function tests should be performed regularly. 8). Methotrexate-induced lung disease is a potentially dangerous lesion, which may occur acutely at any time during therapy and which has been reported at doses as low as 7.5 mg/week. It is not always fully reversible. Pulmonary symptoms (especially a dry, nonproductive cough) may require interruption of treatment and careful investigation. 9). Diarrhea and ulcerative stomatitis require interruption of therapy; otherwise, hemorrhagic enteritis and death from intestinal perforation may occur. 10). Severe, occasionally fatal, skin reactions have been reported following single or multiple doses of methotrexate. Reactions have occurred within days of oral, intramuscular, intravenous, or intrathecal methotrexate administration. Recovery has been reported with discontinuation of therapy.

	Dose	Special Notes
Methotrexate (Tablet) (Injection)		11). Potentially fatal opportunistic infections, especially Pneumocystis carinii pneumonia, may occur with methotrexate therapy. 12). Rash/pruritus/dermatitis, diarrhea, alopecia, leucopenia (WBC less than 3000/mm^3), pancytopenia, dizziness, nausea, vomiting and vasculitis are reported with the therapy. Certain side effects such as mouth sores may be reduced by folate supplementation with methotrexate.
Sodium hyaluronate (Injection)	1. Osteoarthritis: Injected directly into knee once a week, for a total of three to five injections.	1). Sodium hyaluronate (Euflexxa, Hyalgan, Supartz) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen). 2). Sodium hyaluronate (Euflexxa, Hyalgan, Supartz) is a gel-like, elastic, sterile product containing natural, highly purified hyaluronan. Hyaluronan is a natural substance found in the body. It is present in particularly high amounts in joint tissues and in the fluid that fills the joints. The body's own hyaluronan acts like a lubricant and a shock absorber in the joint. It is needed for the joint to function properly. 3). Mixing of quaternary ammonium salts such as benzalkonium chloride with hyaluronan solutions results in formation of a precipitate. Sodium hyaluronate (Euflexxa, Hyalgan, Supartz) should not be administered through a needle previously used with medical solutions containing benzalkonium chloride. A physician should not use disinfectants for skin preparation that contain quaternary ammonium salts. It should NOT be injected intravascularly because intravascular injection may cause systemic adverse events. 4). Arthralgia, joint swelling, joint effusion and injection site pain are reported side effects of sodium hyaluronate (Euflexxa, Hyalgan, Supartz).
Hylan G-F 20 (Injection)	1. Osteoarthritis: a. Synvisc Injected directly into a knee once a week, for a total of three injections.	1). Hylan G-F 20 (Synvisc, Synvisc One) is an elastoviscous high molecular weight fluid containing hylan A and hylan B polymers produced from chicken combs. Hylans are derivatives of hyaluronan (sodium hyaluronate). Hylan G-F 20 (Synvisc, Synvisc One) is unique in that the hyaluronan is chemically crosslinked. Hyaluronan is a long-chain polymer containing repeating disaccharide units of Na-glucuronate and N-acetylglucosamine. 2). Hylan G-F 20 (Synvisc, Synvisc One) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond to simple analgesics, e.g., acetaminophen.

	Dose	Special Notes
Hylan G-F 20 (Injection)	b. Synvisc-One Injected directly into a knee as a single injection dose.	3). Please note Synvisc-One is the same formulation as Synvisc. The only difference is that Synvisc-One is provided with one injection, compared to the three injections required for Synvisc. Both treatments can provide up to six months of osteoarthritis knee pain relief. 4). Arthralgia, joint swelling, joint effusion and injection site pain are reported side effects of Hylan GF-20 (Synvisc, Synvisc One).
Hyaluronan (Injection)	1. Osteoarthritis: a. Orthovisc Injected directly into the knee joint in a series of intra-articular injections one week apart for a total of three or four injections.	1). Orthovisc is the only NON-AVIAN sourced hyaluronic acid injection therapy which has up to six months of clinically proven efficacy with just 3 injections. Patients with known avian (derived from birds) allergies may be prescribed Orthovisc. Orthovisc is derived from bacterial cells. 2). Orthovisc is indicated in the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy and to simple analgesics, e.g., acetaminophen.
Flavocoxid (Capsule)	1. Osteoarthritis: 250 to 500 mg PO every 12 hours with or without food.	1). Flavocoxid (Limbrel) is the first prescription product developed and formulated specifically to safely meet the distinctive nutritional requirements of patients with osteoarthritis through dual inhibition (COX + LOX) of arachidonic acid metabolization and antioxidant action rather than COX-2 selective inhibition. It is intended for the clinical dietary management of the metabolic processes of osteoarthritis (OA). 2). Flavocoxid (Limbrel) consists of a proprietary blend of two types of flavonoids, Free-B-Ring flavonoids and flavans, from Scutellaria baicalensis and Acacia catechu, respectively. 3). Flavocoxid (Limbrel) is comprised primarily of the flavonoids such as baicalin and catechin. These or similar ingredients can be found in common foods such as soy, peanuts, cauliflower, kale, apples, apricots, cocoa and green tea. Flavocoxid (Limbrel) provides levels of these flavonoids needed to meet the distinctive nutritional requirements of people with osteoarthritis and cannot be obtained by simply changing the diet. 4). Hypertension, fluid accumulation in knee, psoriasis, nausea and fever are reported side effects of drug.

Terminology:

Familial cold autoinflammatory syndrome (FCAS)	Familial cold autoinflammatory syndrome is a condition that causes episodes of fever, skin rash, and joint pain after exposure to cold temperatures.
Muckle-Wells Syndrome (MWS)	Muckle-Wells syndrome is a disorder characterized by periodic episodes of skin rash, fever, and joint pain.
Tumor lysis syndrome	Tumor lysis syndrome (TLS) refers to the constellation of metabolic disturbances that may be seen after initiation of cancer treatment.
JC Virus Infection	The JC virus or John Cunningham virus (JCV) is a type of human polyomavirus (formerly known as papovavirus) and is genetically similar to BK virus and SV40. It was discovered in 1971 and named using the two initials of a patient with progressive multifocal leukoencephalopathy (PML).
Progressive multifocal leukoencephalopathy	Progressive multifocal leukoencephalopathy (PML), also known as progressive multifocal leukoencephalitis, is a rare and usually fatal viral disease that is characterized by progressive damage (-pathy) or inflammation of the white matter (leuko-) of the brain (-encephalo-) at multiple locations (multifocal).
Juvenile Idiopathic Arthritis	Juvenile rheumatoid arthritis (JRA) is a term used to describe a common type of arthritis in children. It is a long-term (chronic) disease resulting in joint pain and swelling.
Crohn's Disease	Crohn's disease is a form of inflammatory bowel disease (IBD). It usually affects the intestines, but may occur anywhere from the mouth to the end of the rectum (anus).
Psoriatic arthritis	Psoriatic arthritis is a type of arthritis that often occurs with psoriasis of the skin. The arthritis may be mild and involve only a few joints, particularly those at the end of the fingers or toes.
Ankylosing spondylitis	Ankylosing spondylitis is a long-term disease that causes inflammation of the joints between the spinal bones, and the joints between the spine and pelvis. It eventually causes the affected spinal bones to join together.
Plaque psoriasis	Plaque psoriasis is the most common type of psoriasis. The skin is red and covered with silvery scales and is inflamed. Patches of circular to oval shaped red plaques that itch or burn are typical of plaque psoriasis. The patches are usually found on the arms, legs, trunk, or scalp but may be found on any part of the skin. The most typical areas are the knees and elbows.

Wilson's disease	Wilson's disease is an inherited disorder in which there is too much copper in the body's tissues. The excess copper damages the liver and nervous system.
Cystinuria	Cystinuria is characterized by excessive urinary excretion of the dibasic amino acids, arginine, lysine, ornithine, and cystine, and the mixed disulfide of cysteine and homocysteine. Arginine, lysine, ornithine, and cysteine are soluble substances, readily excreted. Cystine, however, is so slightly soluble at the usual range of urinary pH that it is not excreted readily, and so crystallizes and forms stones in the urinary tract. Stone formation is the only known pathology in cystinuria. Normal daily output of cystine is 40 to 80 mg. In cystinuria, output is greatly increased and may exceed 1 g/day. At 500 to 600 mg/day, stone formation is almost certain. When it is more than 300 mg/day, treatment is indicated.
Discoid and systemic lupus erythematosus	Systemic lupus erythematosus (SLE) is an autoimmune disease, which means the body's immune system mistakenly attacks healthy tissue. This leads to long-term (chronic) inflammation. SLE is much more common in women than men. It may occur at any age, but appears most often in people between the ages of 10 and 50. African Americans and Asians are affected more often than people from other races. Discoid lupus erythematosus distinguishes itself from systemic lupus erythematosus (SLE) through the severity of rashes. In SLE, a malar rash in a butterfly pattern may appear across the nose and cheeks of patients or red rashes may develop in reaction to sunlight. But in discoid lupus, chronic inflammatory sores develop on the face, ears, scalp and on other body areas.
Vasculitis	A general term for a group of diseases that feature inflammation of the blood vessels.