PHARMACY PRACTICE BULLETIN

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A Unit of Department of Pharmacy Practice

DEVAKI AMMA MEMORIAL COLLEGE OF PHARMACY, CHELEMBRA, MALAPPURAM, KERALA

In the remembrance of

Sri. K.V. Sankaranarayanan

(01.01.1948 - 12.07.2013)

Founder, Devaki Amma Memorial Institutions

With His Heavenly Blessings

The Destination for Excellence

ISSUE HIGHLIGHTS

I) New Drug Profile
II) Review on Anticholinergic burden
III) Drug Approved by DCGI in past three months

DEPT HIGHLIGHTS

I) Seminars and Conferences Attended
II) Publications
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I) New Drug Profile - Teriparatide

Available as: Inj. Forteo.

Content: Recombinant parathyroid hormone. It is formed by the 34 n-terminal amino acids (biologically active) of the 84 amino acid chain of the parathyroid hormone.

Dose: 20 mcg subcutaneous injection per day.

Dosage form: Available as prefilled disposable pen. The pen is filled with 2.4 ml of teriparatide. Each ml of teriparatide contains 250 mcg of teriparatide.

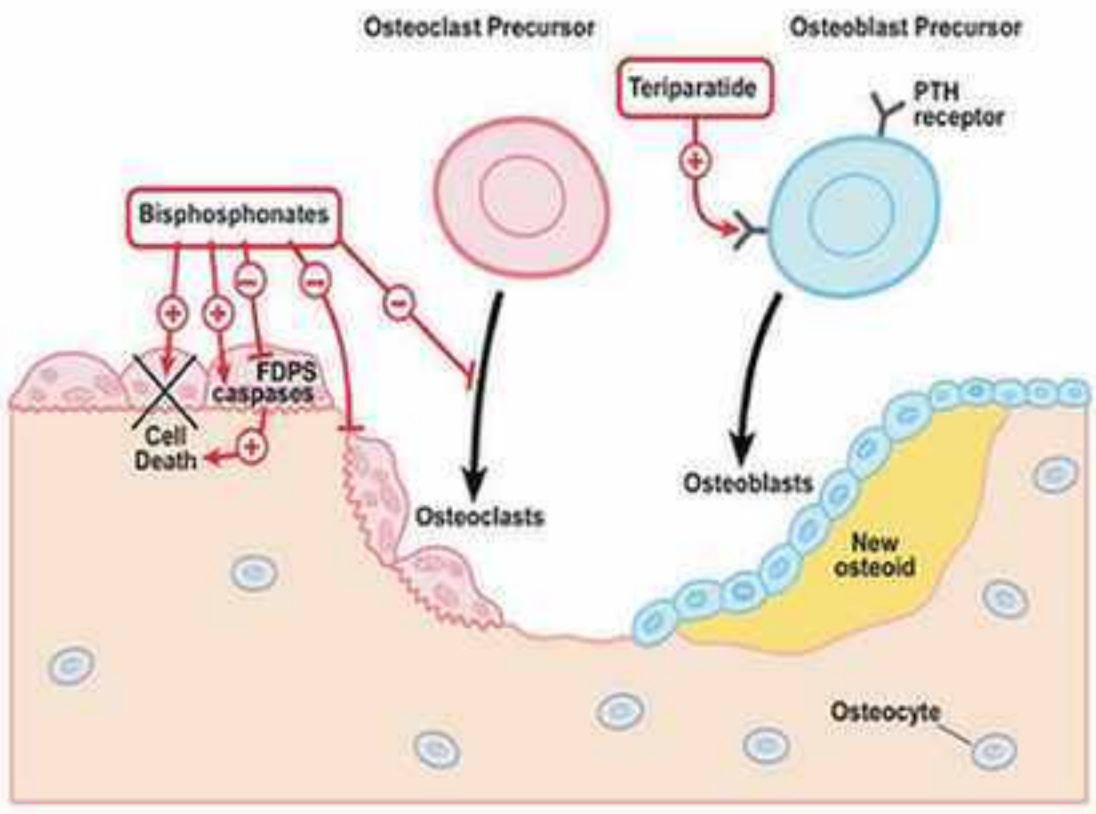
Storage: Should be stored in refrigerator at 2 - 90 C. Do not freeze.

Administration: Administered subcutaneously after taking it from the fridge. The prefilled disposable pen may release 20 mcg daily in a shot. It may be used for 28 days and then should be disposed even if it may have a little amount of drug left in it.

Indication: In post menopausal women with osteoporosis and has high risk of fracture; Men and women with glucocorticoids induced osteoporosis; and In men with primary hypogonadal osteoporosis at high risk of fracture.

Mechanism of action: The subcutaneous injection of teriparatide may show anabolic effects on the skeleton. It may increase the bone remodelling leading to thicker osteons. In normal cases, human parathyroid hormone in the body is released when the body is having low amount of calcium. The parathyroid may increase the dietary absorption as well as the bone resorption to increase the calcium levels in the body.

It is observed that at a sustained increase in parathyroid in the body it may accelerate both the resorption as well as the formation of the bones. The new bone formation may occur at the cortical as well as the trabecular bone in the body by enhancing the differentiation of osteoblasts from prosteoblasts.



Adverse drug reaction: Vomiting, Nausea, Itching at the site of injection, Orthostatic hypotension.

Duration of treatment: The studies have concluded use of teriparatide continuously to 2 years or 24 months.

Pharmacokinetics:

Absorption: The bioavailability is 95%; reaches the peak concentration at 30 min after injection and declines to non-quantifiable concentration within 3 hours.

Distribution: Half life is 1 hour.

Metabolism: Done by non-proteolytic enzyme (Kupffer cells).

Excretion: Through kidney.

Special population:

Pregnancy risk category: C; Animal studies have been performed and mild growth retardation and reduce motor activity in animal studies no controlled studies in human.

Renal impairment: No pharmacokinetic differences were observed in patients with mild to moderate renal impairment. But in case of severe impaired patients the AUC and t1/2 was increased by 73% and 77% but no increase in serum concentration of teriparatide was observed.

Hepatic impairment: No studies have yet been performed.

Prepared by,

Sruthy Maria Johns, Intern

II) Review on Anticholinergic burden

The neurotransmitter acetylcholine is widely distributed in the brain, occurring in all parts of the forebrain, midbrain and brain stem. It has mainly excitatory effects which are mediated by various subtypes of nicotinic or muscarinic receptors mediate the main cognitive effects attributed to cholinergic pathways namely effects on attention, learning and short term memory.

Anticholinergics are drugs that block acetylcholine receptors in central or peripheral tissues. Acetylcholine is a neurotransmitter that can innervate both muscarinic and nicotinic receptors. Anticholinergic drugs can block any one of the five muscarinic receptors by competitively binding to them. Muscarinic receptors are found in smooth muscles, motor neurons, heart and CNS.

Drugs with anticholinergic effects are commonly prescribed for the management of different conditions such as depression, psychosis, Parkinson's disease, muscle spasm, allergy, excessive gastric acid, nausea, vomiting, intestinal motility disorders, overactive bladder and chronic obstructive pulmonary disease.

While some drugs are well known to have anticholinergic properties (e.g., amitryptyline, doxepin, oxybutynin), numerous drugs have an unexpected anticholinergic activity that is not targeted for clinical effect (e.g., furosemide, digoxin).

The wide distribution of muscarinic acetyl choline receptor subtypes (M_1-M_5) in the central nervous system (CNS) and the rest of the body largely accounts for the variety of peripheral and CNS adverse effect associated with drugs with anticholinergic effects. Peripheral effects include: constipation, dry mouth, dry eyes, tachycardia and urinary retention. Whereas CNS effects include agitation, confusion, delirium, falls, hallucination and cognitive dysfunction.

Anticholinergic burden

The cumulative exposure to multiple drugs with anticholinergic properties is widely referred to as anticholinergic burden. Numerous studies have reported anticholinergic burden to be an important predictor of cognitive and physical impairment in older populations. A higher anticholinergic burden is associated with greater risks of morbidity and mortality, a longer length of hospital stay, institutionalization and functional and cognitive decline in older people. Reducing the anticholinergic burden can cause significant improvements in short term memory, delirium, behavior, daily living and quality of life.

Anticholinergic burden in elderly

Older adults have a relatively high probability of being exposed to drugs with anticholinergic effects due to their

high medical comorbidity and the number of prescribed and OTC medications. Recent evidence has also demonstrated that drugs with anticholinergic effects may impair cognitive performance as well as physical performance in older adults. For instance, normal age related decline in memory could increase with susceptibility to the potential cognitive side effects of drugs with anticholinergic effects. Comorbid conditions in older adults, including Parkinson's disease and type 2 diabetes can also predispose to a decline in cognition and amplify the effects of drugs with anticholinergic effects on cognitive function. Age related changes in pharmacokinetics and pharmacodynamics lightly contribute to the high incidence of adverse outcomes in older people. For example the greater propensity of anticholinergic medications to cross the blood brain barrier, the greater risk of central side effects. Factors that are thought to increase the anticholinergic side effects in older people include a reduction in M_1 muscarinic receptors (the most abundant cholinergic receptor subtype in the CNS), an increase in blood brain barrier permeability, greater burden of multi morbidity, slower metabolism and drug elimination. Reducing the use of drugs with anticholinergic properties is one predictable way of modifying the risk of this morbidity in elderly people. The frequency of adverse drug reaction reports in older adults (>65 yrs) is seven fold higher than in younger adults. Epidemiological studies have reported that 20-50% of the older populations are routinely exposed to drugs with anticholinergic activity. Current estimate show that one-third to more than one-half of the commonly prescribed drugs for elderly people have potential anticholinergic effects. Moreover, older persons often take several medications simultaneously to treat different comorbidities (so called polypharmacy) of which more than one may have anticholinergic effects. It has been postulated that normal ageing is accompanied by a relative deterioration of the central cholinergic system. This central cholinergic deficit may contribute to the cognitive decline that occurs with normal ageing. It may also explain the increased sensitivity of elderly subjects to drugs which block central muscarinic receptors. Also, common medical problems existing elderly (such as angina, congestive heart failure, diabetes mellitus, urinary dysfunction, constipation, glaucoma, sleep disturbance and dementia) may be worsened by the use of drugs with anticholinergic properties.

Prepared by:

Ajith S., Pharm. D. Intern

III) Drug Approved by DCGI in past three months

1. Fingolimod Capsule 0.5 mg and Fingolimod Hydrochloride Bulk

Indication: For relapsing forms of multiple sclerosis (MS) in patients 10 years of age and older.

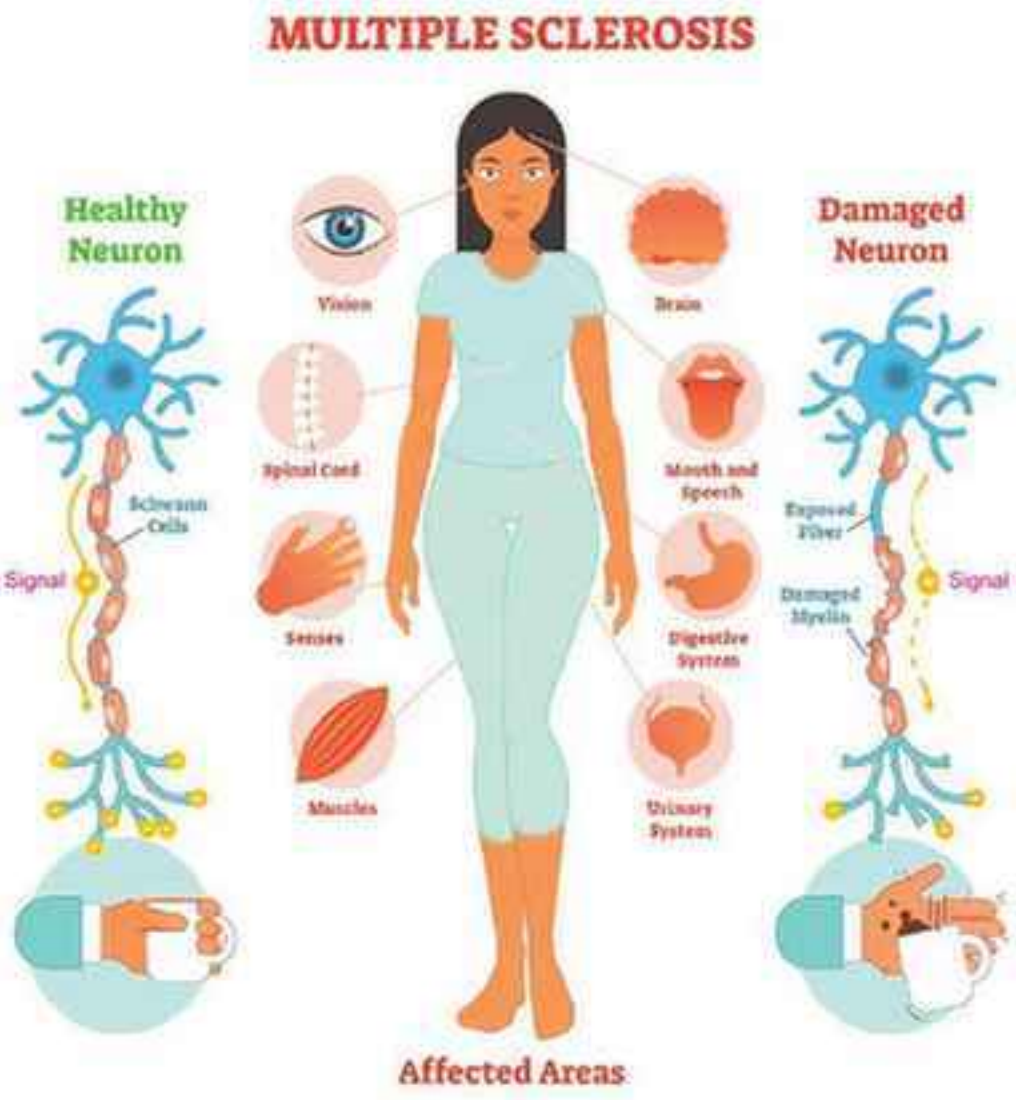
Mechanism of action: Fingolimod is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate. Fingolimod-phosphate is a sphingosine 1-phosphate receptor modulator, and binds with high affinity to sphingosine 1-phosphate receptors 1, 3, 4, and 5. Fingolimod-phosphate blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which fingolimod exerts therapeutic effects in multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

ADRs: Headache, liver transaminase elevation, diarrhea, cough, influenza, sinusitis, back pain, abdominal pain, and pain in extremity.

Pharmacokinetics:

Absorption: The Tmax of fingolimod is 12-16 hours. The apparent absolute oral bioavailability is 93%. Food intake does not alter Cmax or (AUC) of fingolimod or fingolimod-phosphate. Steady-state blood concentrations are reached within 1 to 2 months following once-daily administration and steady-state levels are approximately 10-fold greater than with the initial dose.

Distribution: Fingolimod highly (86%) distributes in red blood cells. Fingolimod-phosphate has a smaller uptake in blood cells of < 17%. Fingolimod and fingolimod-phosphate are > 99.7% protein bound. Fingolimod and fingolimod-phosphate protein binding is not altered by renal or hepatic impairment.



Metabolism: The biotransformation of fingolimod in humans occurs by 3 main pathways: by reversible stereoselective phosphorylation to the pharmacologically active (S)-enantiomer of fingolimod-phosphate, by oxidative biotransformation catalyzed mainly by the cytochrome P450 4F2 (CYP4F2) and possibly other CYP4F isoenzymes with subsequent fatty acid-like degradation to inactive metabolites, and by formation of pharmacologically inactive non-polar ceramide analogs of fingolimod.

Inhibitors or inducers of CYP4F2 and possibly other CYP4F isozymes might alter the exposure of fingolimod or fingolimod-phosphate. In vitro studies in hepatocytes indicated that CYP3A4 may contribute to fingolimod metabolism in the case of strong induction of CYP3A4.

Following single oral administration of [14C] fingolimod, the major fingolimod-related components in blood, as judged from their contribution to the AUC up to 816 hours post-dose of total radiolabeled components, are fingolimod itself (23.3%), fingolimod-phosphate (10.3%), and inactive metabolites [M3 carboxylic acid metabolite (8.3%), M29 ceramide metabolite (8.9%), and M30 ceramide metabolite (7.3%)].

Elimination: Fingolimod blood clearance is 2.3 L/h, and the average apparent terminal half-life (t1/2) is 6 to 9 days. Blood levels of fingolimod-phosphate decline in parallel with those of fingolimod in the terminal phase, yielding similar half-lives for both. After oral administration, about 81% of the dose is slowly excreted in the urine as inactive metabolites. Fingolimod and fingolimod-phosphate are not excreted intact in urine but are the major components in the feces with amounts of each representing less than 2.5% of the dose.

2. Menotropin Injection 600 IU/ml- 1 ml and 2 ml multidose vial

Indication: This medication is used to treat certain fertility problems in women. It provides follicle stimulating hormone (FSH) and luteinizing hormone (LH) that help stimulate healthy ovaries to make eggs. This medication is usually used in combination with another hormone (human chorionic gonadotropin-hCG) to help you become pregnant by bringing about the growth and release of a mature egg (ovulation).

This medication is not recommended for women whose ovaries no longer make eggs properly (primary ovarian failure).

Mechanism of action: Menotropin, administered for 7 to 20 days, produces ovarian follicular growth and maturation in women who do not have primary ovarian failure. In order to produce final follicular maturation and ovulation in the absence of an endogenous LH surge, hCG must be administered following treatment, at a time when patient monitoring indicates sufficient follicular development has occurred.

Pharmacokinetics:

Absorption: The SC route of administration trends toward greater bioavailability than the IM route for single and multiple doses of Menotropin.

Distribution: Human tissue or organ distribution of FSH and LH has not been studied for Menotropin.

Metabolism: Metabolism of FSH and LH has not been studied in humans.

Elimination: The elimination half-lives for FSH in the multiple-dose phase were the same at 13 hours for Menotropin SC and Menotropin IM.

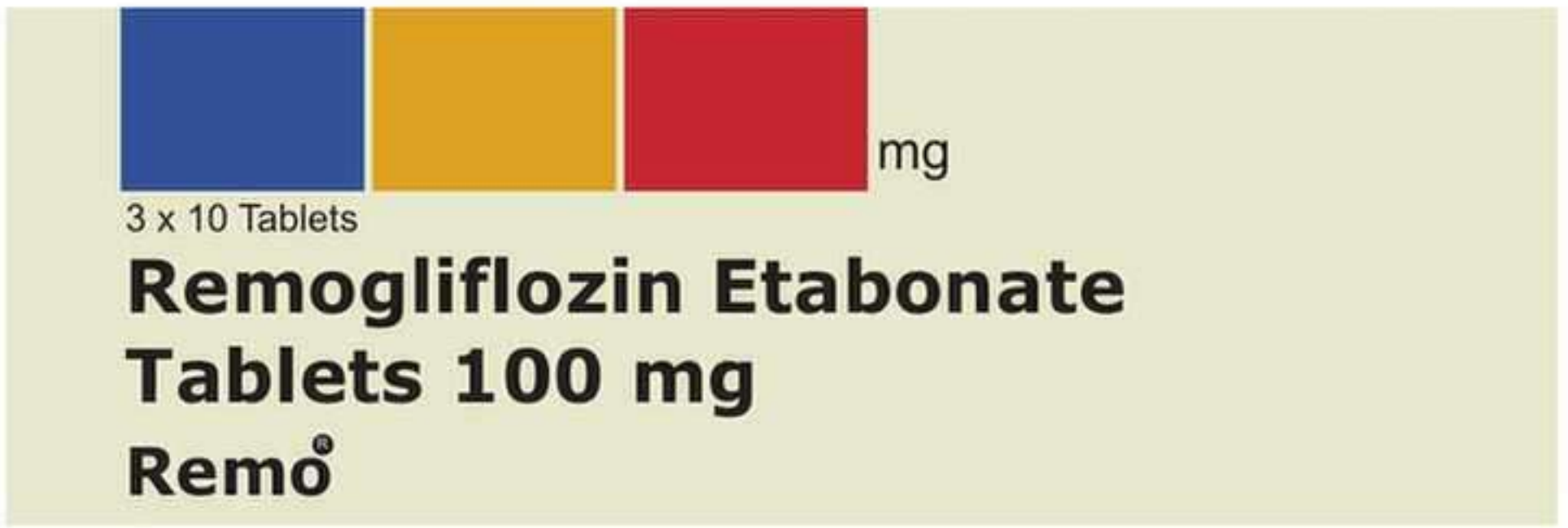
Administration: Dissolve the contents of one to six vials of Menotropin in 1 mL of sterile saline and administer subcutaneously immediately. The lower abdomen (alternating sides) should be used for subcutaneous administration.

3. Remogliflozin Etabonate Bulk and Remogliflozin Etabonate Film Coated Tablets 100 mg

Indication: Type 2 diabetes mellitus in adults aged 18 years and older with to improve glycemic control as-Monotherapy when diet and exercise alone do not provide adequate glyceamic control and add on therapy with metformin, together with diet and exercise, when these do not provide adequate glycemic control.

Mechanism of action: Inhibitor of sodium-glucose co-transporter type 2 (SGLT2). These drugs lower blood glucose by increasing urinary glucose excretion.

ADRs: The commonest adverse effects are genital mycotic infections, urinary tract infections, and dizziness.



Prepared by:
Ajith S., Pharm. D. Intern

DEPARTMENT ACTIVITIES

I) Seminars and Conferences Attended

Pharm. D Interns Mr. Irshad and Mr. Sharafudheen attended "Workshop on Basics of Research Methodology and Publications" on 26th May 2019 at HCG Cancer Hospital, Bangalore.

II) Publications

1. Shaimol T, Sriram Vijay, Raihana P. T., Renitha Thampi, Sanjay Sreekumar. Comparison on the efficacy of using piracetam with oral iron versus iron alone in children with breath holding spells in a tertiary care hospital in Calicut. Journal of Medical Pharmaceutical and Allied Sciences, May 2019; 8(3): 2223-2234.

2. Anilasree B.P., Sanjay Sreekumar, Nafla Nazeer, Husna P, Rabee Bin Abdul Azeez, Nehila Basheer. Drug utilization evaluation of antidiabetic therapy with type 2 diabetes mellitus of a tertiary care hospital in Calicut. Journal of Medical Pharmaceutical and Allied Sciences, May 2019; 8(3): 2235-2253.

III) Scholarship

Jayalakshmi P. J. (Pharm D., 2015 - 2021) received scholarship for academic year 2018-19 from SIR DORABJI TATA TRUST.

Courses Offered

	Ph.D.	
	Pharm. D.	
	M.Pharm.	M. Ed.
M. Arch.	B. Pharm.	B. Ed.
B. Arch.	D.Pharm.	D.Ed. (TTC)

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For Suggestion, Feedback and Interaction

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