PHARMACIST'S OATH

- I swear by the code of Ethics of Pharmacy Council of India in relation to the community and shall act as an integral part of health care team.
- I shall uphold the laws and standards governing my profession.
- I shall strive to perfect and enlarge my knowledge to contribute to the advancement of pharmacy and the public health.
- I shall follow the system which I consider best for pharmaceutical care and counseling of patients.
- I shall Endeavour to discover and manufacture drugs of quality to alleviate sufferings of humanity.
- I shall hold in confidence the knowledge gained about the patients in connection with my professional practice and never divulge unless compelled to do so by the law.
- I shall associate with organizations having their objectives for betterment of the Profession of Pharmacy and make contribution to carry out the work of those organizations.
- While I continue to keep this oath unviolated, may it be granted to me to enjoy life and the practice of pharmacy respected by all, at all times!
- Should I trespass and violate this oath may the reverse be my lot!

The Old Year has gone. Let the dead past bury its own dead. The New Year has taken possession of the clock of time. All hail the duties and possibilities of the coming twelve months!

EDITOR: MRS. SAILI S. MASAL

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Maharashtra State Pharmacy Council's Drug Information Bulletin

January - March 2011

INSIDE THIS ISSUE:

MSPC's Drug Information Bulletin has been granted ASSOCIATE MEMBERSHIP of ISDB.

The International Society of Drug Bulletins (ISDB) is a world wide network of bulletins and journals on drugs and therapeutics that are financially and intellectually independent of pharmaceutical industry. It was founded in 1986, with the support of the WHO Regional Office for Europe. The overall aim of ISDB is to encourage and assist the development of independent drug bulletins in all countries and to facilitate co-operation amongst them.

MAHARASHTRA STATE PHARMACY COUNCIL
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From the Registrar's Desk:

Dear pharmacists,

Regards,

Saili S Masal

From Editorial Board Member

Creating new avenues & Improving status of Pharmacy Services in Indian Public Health Sector

Have you ever visited any State/Government hospital? Have you ever met any pharmacist working in government hospital? Have you ever asked him, what job he does or what job is assigned to him as a pharmacist in state health care system? Is his job a professional? Answer to all these questions will be frustrating and annoying for him. Basically because, jobs and nature of work a pharmacist doing in Indian Government run hospitals is no more than a "Drug handler, who is responsible for distributing medicines on the counter". In brief it is like this. Taking a stock from the headman in the morning, giving out to the patients as per the doctor's chit, and returning back the balanced stock to the headman in the evening. So simple!!!!!!! What is professional in that? Your second question would be-- Why it is so? Answer to this is very simple but disheartening and demoralizing. Firstly, only those pharmacists who don't get job anywhere, they join in government. So, that is last choice. But why this is a last choice? Because there is no much professional work to do, no future prospects, no challenges for work, and on the top of these upsetting issues, pharmacist in Indian state run hospitals is not given equal treatment with medical professionals, not equal even with the other Para-medicals like nursing, technicians etc.

I am working in public health care system since last three years as a Head of Pharmaceutical Services in the state of Maharashtra. I had also exposure to Central Government Public Health Care System. Presently, I am at the fag end of my carrier in Public health care service. Looking back from here, as far as my carrier growth is considered, what I see is utter disappointment. My fellow Medical colleagues, who had started with me, are now either Deans of Medical Colleges or Medical Superintendents or at least Heads of the Department. As against this, I got this single promotion to Class- I post, only after putting 30 years of my life. Here also, everyone is not that lucky to get this promotion, as this is the only single post available, only topmost post available to Pharmacy Profession in Public health care system in State of Maharashtra. Ironically, this promotional post is available only under Ministry of Medical Education. The condition of pharmacy services under Ministry of Health is still more pathetic and pitiable. In the Ministry of Health of State of Maharashtra, there is not even Class II promotional post available for Pharmacy Profession. Under directorate of Health Services, the pharmacist starts his/her carrier as Class III post and retires also as a Class III pharmacist. The condition of pharmacy services in other states of India is more or less similar and also disheartening.

On this background of unacceptable carrier prospects of pharmacy profession in Public health care system, one can very well anticipate that no pharmacist will like to enter in Government hospital services. Secondly, looking at the present appalling and terrible condition of hospital pharmacy in India,

I personally feel that though so many institutes are coming up and starting the hospital oriented pharmacy degrees like, PHARM- D., it is going to be a nightmare for the budding pharmacists who are opting for this course, hoping that they will have better prospects in public health care system or for that matter even in private / corporate hospitals. I am not against this new course, but some solid, firm, and positive efforts are needed to be made, at national and state level to create more graceful and acceptable opportunities for pharmacy profession in the Indian hospitals.

Every year more and more new colleges are opening; new budding pharmacists are coming out of these colleges with beautiful dreams in mind. But, at the same time, opportunities for them are shrinking with great speed, especially for those who cannot do the post-graduation, because of financial constraints. Therefore, the time has come now in India, that all those who are policy makers like Pharmacy Council of India, Heads of Educational Institutes, should come together and think seriously to open up widely the public health care system for the pharmacy profession, which had long been kept neglected and disregarded by our policy makers.

In view of getting recognition to Pharmacy Profession and Pharmacy services in state health services and in the society at large and in view of opening the Public Health Care System for the better pharmacy services in coming future, I am of the opinion that "Each Indian State should have a separate & independent Directorate of Pharmacy Services". Under this single umbrella of Pharmacy Directorate, then all Pharmacy Professional services can be brought together so that they will work together more efficiently and cohesively.

I am herewith proposing that this issue be taken up as a special, and common agenda for next decade by all the Pharmacy organizations, namely, I.P.A, I.H.P.A., A.P.T.I. and P.C.I. etc., & work towards it vigorously in the interest of pharmacy profession and in the interest of budding pharmacists.

Establishment of separate Directorate of Pharmacy at each State in the Country

The infrastructure of such a Directorate will open up not only new avenues to the upcoming pharmacist but also streamline the working of Pharmacy profession in a particular state under one roof & one control. Presently no such Directorate is in existence in any of the state of India. The detailed Organizational Chart such Directorate is as follows.

Proposed State level Organizational set up

State Government
Director General (Pharmacy Services)
↓

↓	↓	↓
Directorate of Pharmacy Pharmaceutical Education And Research	**Directorate of Regulation** and Legislation (F.D.A.)	**Directorate** of Hospital Services

Directorate of Pharmacy Education and Research
↓

↓	↓
Joint Director Pharmacy Education.	**Joint Director Pharmacy Research**
Responsible for - Education Regulation	Responsible for - Research in collaboration with - Pharmaceutical Industry

Directorate of Pharmaceutical Hospital Services.

↓

Joint Director Materials and Supplies Services

Joint Director Hospital Pharmacy

↓

Assistant Director
Tenders and Contracts

Assistant Director
Finance, Audit & Inventory Control

Assistant Director
Procurement &Warehousing

Joint Director Hospital Pharmacy Services

↓

Assistant Director
Hospital services
Services

Assistant Director
Clinical

↓

- **(**Responsible for Supervision over all the Superintendent of Pharmacies working in the State)

↓

Superintendents of District Pharmacies

-Responsible for procurement of Hospital supplies and monitoring of all procurement services in the district *(One post of Superintendent of Pharmacy at each district hospital and each teaching hospital)*

Superintendent of Pharmacy (Class- I)

↓

Head Pharmacist Store (HP)

Head Pharmacist Dispensary. (HP)

PIII PIII PIII

PIII PIII PIII

HP - Head Pharmacist Class II, PIII - Pharmacist Class III

Assistant Director
Clinical Services

Responsible for monitoring of all Clinical Pharmacy services throughout the State, Namely-

At National Level	**At National Level**
Study of Disease Pattern	Study on Drugs Price Structure
Selection of Essential Drugs (WHO)	Audits, Accounting and Inventory Controls

Formulation of National. Drugs .Policy Strict control over new drugs entry	Dissimulation of information on Drugs pricing.
At District Level Establishment of Drug Information Centre Poisons Information Centre.	**At District Level** Establishment of Drugs Utilization, Study Centre. Patient, Safety, Study Centre.

The above explained proposed organizational set up will open up new avenues in state hospital pharmacy services and will thus attract more and more pharmacists to join these services.

Secondly, this will uplift the general morale of hospital pharmacists who are already working in state health sector as they see the channels opening for their career development.

For those who are already working in state run hospitals

However, one thing should be noted here that, the pharmacist who is already working in state run health sector need to be provided with on- job/in-service opportunities to upgrade his qualifications, so that he will be eligible for promotions. In this regard a system already available for medical and nursing personnel to upgrade their on-job qualifications can be adopted for pharmacists also. By this way, the diploma holder will be allowed to join or deputed to take a part time course of degree, a degree holder shall be given to join a part time course to upgrade him to post graduation level and if one wishes he/she can upgrade himself/herself up to the level of doctorate.

Pharmacist in Alternate Medicine Faculty

Another area which can be explored is Sale of all Traditional medicines (Ayurvedic, Homeopathic ,Siddha etc.) to put under the supervision of " Registered Pharmacist " and licensing be issued to these "alternate medicine pharmacists" by pharmacy council of India. *However, before making such an amendment in Law, one subject imparting knowledge of these alternate/traditional medicines may be included in the syllabus of Diploma & Degree Pharmacy.*

Authored by- Dr. Suresh R. Sarvedekar, Asst. Director, Directorate of Medical Education & Health, Maharashtra.

संपादकीय.....

भारताच्या सार्वजनिक आरोग्य शाखेत औषध निर्माण व सेवा देणाऱ्या फार्मासिस्टच्या उन्नतीसाठी नवनवीन मार्गांचा विकास करणे आवश्यक आहे

आपण कधी राज्य किंवा केंद्र शासनाद्वारे चालविल्या जाणाऱ्या रूग्णालयात गेला आहात? सरकारी रूग्णालयात काम करणाऱ्या एखाद्या फार्मासिस्टला भेटला आहात का? त्याला कधी त्याच्या कामकाजाबाबत माहिती विचारली आहे का? सरकारी रूग्णालयातून फार्मासिस्टला जे काम दिले जाते ते त्याच्या पेशानुसार आहे काय? या सर्व प्रश्नांची उत्तरे मन उद्विग्न करणारी आहेत.भारतीय रूग्णालयातून फार्मासिस्टची ओळख म्हणजे फक्त औषधे हाताळणारी व वितरीत करणारी व्यक्ती - सकाळी साठा भांडारातून घ्यायचा , डॉक्टरांच्या चिटप्रमाणे रूग्णाना औषध वाटप करायचे आणि उरलेला साठा संध्याकाळी पुन्हा भांडारात जमा करायचा. यामध्ये व्यावसायिकता कोठे आढळते? या प्रश्नाचे उत्तर अतिशय निराशाजनक आहे. सर्वप्रथम म्हणजे ज्यांना बाहेर कोठेही काम मिळत नाही असे फार्मासिस्ट बहुतांश सरकारी रूग्णालयातून नोकरी करतात.म्हणजेच काम करण्यासाठी हा अगदी शेवटचा पर्याय असतो कारण याठिकाणी फार्मासिस्ट म्हणून करण्यासारखे काही कामच नसते, काही आव्हानच नसतात त्यामुळे व्यावसायिक उत्कर्ष होत नाही. सरकारी रूग्णालयातून वैद्यक पेशाइतके नाहीच पण इतर समांतर सेवा जसे नर्सिंग, टेक्निशिअन्स इतकाही दर्जा फार्मासिस्टला मिळत नाही.

मी स्वतः गेली तीन वर्षे महाराष्ट्र शासनाच्या सार्वजनिक आरोग्य सेवा विभागाच्या विभागप्रमुख म्हणून कार्यरत आहे. (Head of Pharmaceutical Services) केंद्र शासनाच्या आरोग्य विभागाचाही अनुभव मला आहे. आता मी सिंहावलोकन केले असता मन थोडे उदास होते. माझ्याबरोबरच वैद्यकीय सेवेत आलेले डॉक्टर्स आता विविध वैद्यकीय महाविद्यालयातून अधिष्ठाता या पदावर आहेत किंवा किमान अधीक्षक , विभाग प्रमुख म्हणून तरी आहेत. या माझ्या एकमेव वर्ग 1च्या पदावर पोहचण्याकरीता मला तीस वर्ष व्यतीत करावी लागली. फार्मसी विभागातील हे एकमेव सर्वोच्च पद महाराष्ट्र शासनाच्या सेवेत आहे. हे पद महाराष्ट्र शासनाच्या वैद्यकीय शिक्षण मंत्रालयाच्या अखत्यारीतील आहे. फार्मसी सेवा विभागाबाबतची मंत्रालयातील परिस्थिती अतिशय दयनीय आहे. फार्मसी सेवेत साधी दर्जा 2ची पदेही नाहीत. महाराष्ट्र शासनाच्या आरोग्य संचालनालयाच्या सेवेत वर्ग 3 मध्ये नोकरीस लागलेला फार्मासिस्ट वर्ग 3 मध्येच सेवानिवृत्त होतो. भारतातील इतर राज्यांतही विशेष वेगळी परिस्थिती नाही.

शासकीय सेवेत फार्मासिस्टबद्दल अशी अनास्था असल्यामुळेच शासकीय सेवेत येण्याची इच्छा होत नाही. तसेच सध्याची शासकीय रूग्णालयांची अनावस्था पाहता सध्या नव्याने सुरू होत असलेल्या फार्म-डी सारख्या शैक्षणिक अर्हता प्राप्त करणे हे दुःस्वप्न ठरण्याची शक्यता आहे. माझा यासारख्या नव्या शैक्षणिक अर्हता निर्माण करण्यास आक्षेप नाही परंतू त्याबरोबरच फार्मासिस्टच्या व्यावसायिक उन्नतीसाठी राज्य तसेच देशांतर्गत पातळीवर ठोस धोरण आणि प्रयत्न होण्याची गरज आहे. दरवर्षी नविन कॉलेजेस सुरू होत आहेत आणि विद्यार्थी शिकून बाहेर पडत आहेत. परंतू ज्याप्रमाणात फार्मसीचे विद्यार्थी शिकून बाहेर पडत आहेत त्याप्रमाणात त्यांच्याकरीता संधी उपलब्ध नाहीत. पदव्युत्तर शिक्षण ही आता नोकरी मिळण्यासाठी किमान पात्रता झाली आहे त्यामुळे ज्यांना हे काही कारणाने जमत नाही त्यांच्यासमोर मोठ्या समस्या आहेत. त्यामुळे फार्मसी कौन्सील ऑफ इंडीया, शैक्षणिक संस्थांचे प्रमुख यासारख्या धोरणात्मक निर्णय घेणाऱ्या संस्थांनी विचारपूर्वक फार्मासिस्टचा विकास साधण्यासाठी धोरण ठरविणे, त्यांच्याकरीता शासकीय सेवेत नोकरीच्या संधी निर्माण करण्यासाठी प्रयत्न करणे अत्यावश्यक आहे.

फार्मासिस्टची उन्नती आणि सार्वजनिक आरोग्य सेवेच्या माध्यमातून समाजाला चांगली फार्मसी सेवा मिळण्याकरीता मला असे वाटते की "भारतातील प्रत्येक राज्यात फार्मसी करीता वेगळे संचालनालय असावे व त्याखाली फार्मसीच्या सर्व उपशाखांचे काम व्हावे म्हणजे त्यामध्ये सुसूत्रता राहील व परिणामकारकता साधता येईल."

I.P.A., I.H.P.A., A.P.T.I. आणि P.C.I. यासारख्या फार्मसी क्षेत्रात काम करणाऱ्या संस्थांनी फार्मसीस्टच्या उन्नतीसाठी हा मुद्दा लावून धरावा असे वाटते.

<u>प्रत्येक राज्यात फार्मसीच्या स्वतंत्र संचालनालयाच्या निर्मितीबाबत</u>

प्रत्येक राज्यात फार्मसीकरीता स्वतंत्र संचालनालयाची निर्मिती केल्याने फक्त नविन मार्गच तयार होणार आहेत असे नसून फार्मसीच्या सर्व शाखांचे नियमन एकछत्री झाल्याने त्यांमध्ये सुसूत्रता निर्माण होईल व त्यायोगे फार्मसी शिक्षण आणि व्यवसाय यांचा विकास होईल. त्याची मांडणी खालीलप्रमाणे असावे असे वाटते.

राज्य पातळीवर फार्मसी संचालनालयाची निर्मिती करण्याकरीता प्रस्तावित उभारणी :-

(संदर्भ पृष्ठ क्र. 7 व 8)

पृष्ठ क्र 7 व 8वर वर्णन केलेल्या सेट-अपमध्ये राज्य शासनाच्या रूग्णालयांतून मोठ्याप्रमाणावर नोकऱ्या निर्माण होतील आणि विकासाच्या संधी असल्याने या नोकऱ्यांकडे तरुण वर्ग आकर्षित होईल. तसेच सध्या कार्यरत असलेल्या फार्मासिस्टमध्येही चैतन्य निर्माण होईल.

जे सध्या राज्य शासनाच्या रूग्णालयांतून काम करत आहेत त्यांना त्यांचे ज्ञान वृध्दींगत करण्यासाठी प्रशिक्षणाची किंवा उच्च शिक्षण घेण्याची संधी दिली पाहिजे. त्यामुळे नोकरीत बढती मिळू शकेल. अशाप्रकारच्या संधी वैद्यकीय आणि नर्सिंग क्षेत्रात यापूर्वीच उपलब्ध करण्यात आल्या आहेत. तसे झाल्यास पदविका धारक पदवीचा तर पदवीधर पदव्युत्तर अभ्यासक्रम पूर्ण करू शकतील.

इतर औषधी शाखांमध्ये फार्मासिस्टला संधी -

आयुर्वेदिक , युनानी आणि होमिओपॅथिक औषधांच्या विक्रीकरीता पंजीकृत औषध व्यवसायी हजर असणे सक्तीचे केल्यास त्यांना संधी उपलब्ध होतील. असा व्यवसाय करणाऱ्या फार्मासिस्टला अल्टरनेट मेडिसीन फार्मासिस्ट

म्हणून संबोधवे व हे काम फार्मसी कौन्सील ऑफ इंडियाकडून व्हावयास हवे. त्याकरीता कायद्यात व नियमात योग्य त्या सुधारणा करून घ्याव्या लागतील व अभ्यासक्रमात या विषयांचा समावेश करावा लागेल.

डॉ. सुरेश आर्. सर्वदेकर,
सहाय्यक संचालक,डायरेक्टोरेट ऑफ मेडिकल एज्युकेशन ॲण्ड हेल्थ, महाराष्ट्र.

Wish you all Happy & Healthy New Year!!!!!!!!!!

Healthy living handbook for 2011

- Live with the 3 E's -- Energy, Enthusiasm and Empathy
- Sleep well. Sleep for at least 7 hours every night, preferably 8 hours. Sleep for 1 hour in the afternoon as feasible.
- Exercise regularly. Walk for at least 45 minutes every day in fresh air (morning or evening), at least 5 days a week. It is preferable to walk briskly.
- While exercising, sense the limitations of your body. Adjust speed accordingly. You will be able to walk faster and longer after a few months. Aerobic activity like daily walks also detoxifies the body.
- Eat breakfast like a king, lunch like a prince and dinner like a beggar.
- Eat plenty of fresh fruit including citrus fruits like orange, sweet lime and vegetables.
- Skimmed milk and low fat dairy products should be consumed.
- Eat nuts (almonds, figs etc) and seeds, roasted snacks. Have a diet rich in whole grains like oats, barley, brown rice and whole wheat. Consume cold-pressed oils.
- Do not eat acidic foods. Avoid eating oily food, ghee, butter, fried items, avoid eating fast food. Eat in moderation bread, cake, chocolates, peanuts etc.
- Drink plenty of water during the day, at least 10 glasses each of 200 ml. The water removes the toxins and acidity.
- Do not take aerated/carbonated drinks like coca cola. Aerated drinks have an extremely high acidifying effect on the cells of the body, which is harmful to health.
- Keep your weight under control. A ready rule for ladies is that your maximum weight in kg should be 10% lower than your height in inches. E.g., if height is 5'3" (63"), the maximum weight is 57 kg & for men, maximum weight in kg should be equal to your height in inches. E.g., if height is 5'9" (69”), the maximum weight should not exceed 69 kg.
- Remain cheerful throughout, irrespective of any work, tension, responsibilities etc.
- Spend a time with your family, friends or loved ones.
- Sensitize your mind to what is happening within your body. Do not over-exert. Pay attention to any pains/aches etc.

QUERY OF THE QUARTER……

Acetaminophen toxicity

Que: Acetaminophen is considered to be toxic at higher dose and may cause hepatotoxicity. Which of the enzyme would most likely be deficient & which metabolic intermediate is accumulated? Management of acetaminophen overdose/ poisoning.

Acetaminophen is the most commonly used drug. Acetaminophen is rapidly and almost completely absorbed from the G.I. tract following oral administration. Acetaminophen has a half life of 1.25- 3 hours. Plasma half life of acetaminophen may be prolonged following toxic doses or in patients with liver damage. Hepatotoxicity with acetaminophen is likely to occur with oral ingestion of 140 mg/kg in adults. A single acute dose of 10-15 g of the drug is potentially fatal. The risk of toxicity increases in chronic alcoholics and patients taking isoniazid, rifampicin or both because of induction of liver microsomal enzymes.

The drug is metabolized by sulfate and glucuronide conjugation. **The parent compound and its metabolites are not toxic, but a small fraction of drug is metabolized by cytochrome P-450 dependant pathway which forms a toxic metabolite, called as N-acetyl-p-benzoquinoeimine (NAPQI).** NAPQI in normal dosage detoxified by glutathione and eliminated in urine or bile. In overdose, increased formation of NAPQI depletes hepatic stores of glutathione leading to hepatic necrosis/ toxicity.

Acetaminophen toxicity usually involves 4 phases:

1. Anorexia, nausea, vomiting, malaise & diaphoresis which may prompt you to take additional acetaminophen, but it is inappropriate.
2. Resolution of phase -1 complaints & replacement with abdomen pain & tenderness, liver enlargement, elevated bilirubin & hepatic enzyme concentrations, prolongation of prothrombin time & occasionally oliguria.
3. Anorexia, nausea, vomiting, malaise may occur after 3-5 days of initial symptom onset & signs of hepatic failure e.g. jaundice, hypoglycemia may occur.
4. Recovery or progression to fatal complete liver failure.

The level of alanine aminotransferase is found to be elevated in paracetamol overdose and considered as specific marker because aspartate aminotransferase is also found in cardiac and skeletal muscle and red blood cells.

Reported or ingested quantity of acetaminophen ingestion often is inaccurate and is not reliable guide to the therapeutic management of overdose; the preferred method to assess the risk is measurement of plasma or serum concentrations.

Management:

Pre-hospital:

1. Lay patient on left side to prevent aspiration
2. Administer activated charcoal

Hospital:

1. Provide oxygenation and ventilator support if required.

2. Control spontaneous vomiting by Metoclopramide.
3. Perform gastric lavage preferably within 4 hrs. post ingestion, however it has been found to be effective up to 6 hrs. post ingestion.
4. Administer activated charcoal, IV fluids & manage metabolic acidosis with sodium bicarbonate.
5. Haemoperfusion, though effective, is generally not indicated.
6. Massive hepatic failure may necessitate liver transplantation.
7. N-Acetylcysteine is the specific antidote. If plasma or serum acetaminophen concentrations cannot be obtained, it should be assumed that the over dosage is potentially toxic and acetylcysteine therapy should be initiated.

Reference:

1. Gupta Sk., "Emergency Toxicology- Management of common poisons"; Narosa publishing house; pp.3-5

2. AHFS drug information 2004; pp. 2085-87

3. Clinical Evidence, 4 issue, BMJ publishing house, pp. 775-79

4. http://www.pharmweb.net/pwmirror/pwy/paracetamol/pharmwebpicc.html

5. http://www.patient.co.uk

तिमाहीतील प्रश्न.....

ॲसिटामीनोफेन विषबाधा

प्रश्न: ॲसिटामीनोफेनचा (पॅरासिटामोल) डोस जास्त झाल्यास विषसमान ठरून यकृतावर परिणाम करते का ? त्यामुळे कोणत्या पाचकरसाची कमतरता निर्माण होते आणि कोणत्या घटकाचा संचय होतो? ॲसिटामीनोफेनचे व्यवस्थापन कसे करावे?

ॲसिटामीनोफेनचा वापर मोठ्या प्रमाणावर केला जातो. ॲसिटामीनोफेनचे जठर आणि आतड्यांत दिड दोन तासात पूर्ण शोषण होते. अतिरिक्त प्रमाणात ॲसिटामीनोफेनचे सेवन झाल्यास किंवा यकृतास इजा झालेली असल्यास या प्रक्रियेस वेळ लागू शकतो. मोठ्या माणसांकरीता 140 मिलीग्रॅम प्रति किलो या प्रमाणापेक्षा अधिक घेतले गेल्यास यकृतावर दुष्परिणाम होऊ शकतात. 10 ते 15 ग्रॅम इतक्या प्रमाणात घेतले गेल्यास प्राणघातक ठरू शकते. मद्यपान करणाऱ्या व्यक्ती किंवा आयसोनिआझीड, रिफॅम्पीसीन ही औषधे घेणाऱ्या व्यक्ती यांना बाधा लवकर होऊ शकते कारण यकृतातून स्त्रवणाऱ्या पाचक रसांचे प्रमाण कमी असते.

या औषधाचे चयापचय सल्फेट आणि ग्लुकुरोनाईड यांच्या अभिक्रियेतून होते. मूळ रसायन आणि त्याचा बराचसा भाग हा दुष्परिणाम करणारा नसतो. परंतू त्यातील काही भागाचे पचन सायटोक्रोम P-450मुळे होते. त्यामुळे तयार होणाऱ्या हानीकारक घटकास N-acetyl-p-benzoquinoeimine (NAPQI) संबोधले जाते. NAPQI सामान्य प्रमाणात असल्यास ग्लुटोथिऑनद्वारे शुध्दी होते व मूत्र आणि यकृताच्या स्त्रावांतून उत्सर्जन होते. NAPQI चे प्रमाण जास्त वाढल्यास यकृताचा ऱ्हास होतो.

ॲसिटामीनोफेनचे दुष्परिणाम सर्वसाधारणपणे 4 टप्प्यांत होते -

1. भूक न लागणे , मळमळ, वांत्या, अस्वस्थ वाटणे आणि घाम येणे यामुळे ॲसिटामीनोफेन परत घेण्याची इच्छा होईल परंतू ते स्विकारार्ह नाही.

2. पहिली पातळी पार पडल्यावर ओटीपोटात दुखणे आणि संवेदनशीलता निर्माण होते, यकृताचा आकार मोठा होतो, बिलीरुबीनचे प्रमाण प्रचंड वाढणे आणि यकृतातील इतर पाचक रसांची तीव्रता वाढते , प्रोथ्रोंबिनचे प्रमाण वाढणे आणि लघवी जास्त होणे.

3. कावीळीसारखा आजार झाल्यावर भूक न लागणे , मळमळ, वांत्या, अस्वस्थ वाटणे अशी लक्षणे 3/4 दिवसांनी दिसू शकतात तसेच रक्तशर्करेचे प्रमाण वाढू शकते.

4. संपूर्णपणे यकृताचा ऱ्हास

अलानीन अमायनोट्रान्सफेरसची पातळी पॅरासिटामोल जास्त प्रमाणात घेतले गेल्यास वाढते, यास ॲसिटामीनोफेन ओव्हरडोसचा स्पेसिफीक मार्कर मानले जाते. कारण अस्पारटेट अमायनोट्रान्सफेरस ही हृदयाच्या आणि हाडांच्या स्नायूत व लाल रक्तपेशीत आढळते.

ॲसिटामीनोफेनचे प्रमाण सर्वसाधारणपणे स्थिर नसल्याने त्याचे अतिसेवन झाल्याचे निष्पन्न त्वरित होऊ शकत नाही. त्यामुळे रक्तरसाच्या चाचण्याची आवश्यकता असते.

व्यवस्थापन

रूग्णालयात जाण्यापूर्वी -

1. रूग्णास डाव्या कुशीवर झोपवावे म्हणजे कोणतेही द्रव आत खेचले जाणार नाहीत.
2. ॲक्टीवेटेड चारकोलचा वापर करावा.

रूग्णालयातील उपचार -

1. ऑक्सीजन आणि व्हेंटीलेटरचा वापर करावा.
2. मेटोक्लोप्रामीड देऊन उलटी थांबवावी.
3. आतडी स्वच्छ करण्यासाठी चार तासात उपाययोजना करावी कारण ॲसिटामीनोफेनचा परिणाम सहा तासांपर्यन्त राहतो.
4. ॲक्टीवेटेड चारकोल , IV फ्लुईडस्चा वापर करून सोडीयम बायकार्बोनेटमुळे चयापचयातून निर्माण होणाऱ्या ॲसिडोसीसचा परिणाम कमी होतो
5. लाल रक्त पसरवणे हे परिणामकारक असते परंतू तसे सहसा आढळत नाही.
6. यकृताची झालेली गंभीर हानी विचारात घेता कदाचित यकृत रोपण शस्त्रक्रिया करावी लागते.
7. N-Acetylcysteine हा यावरील प्रभावी उपाय आहे. रक्तरसातील ॲसिटामीनोफेनची तीव्रता न समजल्यास ॲसिटामीनोफेनमुळे दुष्परिणाम होणार आहेत असे गृहीत धरून याचा वापर करावा लागतो.

Drugs approved for marketing in India by CDSCO during the year 2010

PRODUCT NAME	INDICATION
Ferrous ascorbate 100mg + Folic acid 1.1 mg tablet and Omega-3-fatty acid 200mg capsules combikit	For iron, folic acid & omega-3-fatty acid deficiency
Sphaeranthus Indicus Extract Tablets 700mg	For the management of psoriasis.
Febuxostat 40mg Additional Strength	Same As approved
Dexamethasone Intravitreal Implant 0.7mg (in solid polymer drug delivery system)	For the treatment of macular edema following branch retinal vein occlusion (CRVO)
Buclizine Hcl 25mg Tablet (Additional Indication)	For the Symptomatic treatment of various allergic conditions (rhinitis, conjunctivitis and urticaria) and for prevention and treatment of motion sickness
Pemetrexed Disodium 500mg/100mg Powder for Injection (additional indication)	Indicated as a monotherapy for the maintenance treatment of locally advanced or metastatic Non Small Cell Lung Cancer (NSCLC) other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy. First line treatment should be a platinum doublet with gemcitabine, paclitaxel or docetaxel.
Levobetaxolol HCl Opthalmic Suspension 0.5%	For lowering of intraoccular pressure in patients with chronic open-angle glaucoma or occular hypertension.

Sarpogrelate Hydrochloride film coated Tablets 100mg	For the improvement of ischemic symptoms including ulcer, associated with chronic arterial occlusion.
Propanol 1-ol 18gm + Ethanol 100% 45gm/100ml solution	For hygenic and surgical hand disinfection
Aliskiren 150/160mg + Valsartan 300/320mg tablets	For the treatment of hypertension
Piroxicam 20mg tab& Paracetamol 500mg tab combikit	For treatment of fever and pain associated with acute upper respiratory tract inflammation, acute musculoskeletal disorders, pain after operative intervetion and following trauma, chronic condition like rheumatoid arthritis, osteoarthritis etc for short term management of acute painful episodes.
Soybean oil 60gm + Triglycerides (medium chain) 50gm + olive oil purified fish oil 30gm + dl-alpha-tocopherol 163-225mg + glycerol (anhydrous) 25gm + Egg lecithin 12gm + sodium hydroxide (to approx pH 8) + sodium pleate 0.3mg emulsion for infusion in 100ml.	Total parenteral nutrition following major abdominal, major thoracic or major urological surgery
Raltegravir (as Potassium) film coated Tablets 400mg	In combination with other anti retroviral agents for the treatment of human immunodeficiency virus (HIV-1) infection in treatment experienced patients with evidence of HIV-1 replication despite ongoing retroviral therapy.
Deflazacort Tablet 18mg (Additional Strength)	Same as approved
Pregabalin SR Tablet 75mg (Additional Strength)	Same as approved
Rivaroxaban film coated Tablets 10mg	For the prevention of venous thromboembolism in patients (VTE) in adult patients undergoing hip or knee replacement surgery.
Cinnarizine 20mg + Dimenhydrinate 40mg tablets	For the treatment of vertigo
Lipid Based Amphotericin-B Gel 0.1%	Indicated in the treatment of cutaneous and mucocutaneous mycotic infections caused by candida (Monilia) species.
Sodium Hyaluronate Injectable Gel 14mg/ml, 18mg/ml, 25.5mg/ml (Additional Strength)	Same as approved
Milnacipran Hcl 12.5mg (Addl. Strength)	Same as approved
Ropinirole 6mg ER Tablets (Addl. Strength)	Same as approved
Coseal Surgical Sealent 2/4/8ml (Addl. Indication)	(1) Enforcement of suture and staple lines in lung resection procedures. (2)Patients undergoing cardiac surgery to prevent or reduce the incidence, severity and extend of post surgical adhesion formation. (3)Patients undergoing laparotomy or laproscopic abdomino-pelvic surgery as an adjunct to good surgical technique intended to reduce the incidence, severity and extent of post surgical adhesion formation.
Pregabalin SR 75/150/300mg + Methylcobalamin 1500mcg tablets	For the treatment of adult patients with peripheral neuropathy
Ivabradine Hcl Tablets 5/7.5mg (Additional Indication)	For Symptomatic Treatment of chronic stable angina pectoris in coronary artery disease patients with normal sinus rhythm, indicated in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is >60bpm.
Paracetamol Solution for Infusion (10mg/ml) in 50ml (Additional Packsize)	Same as approved
Ketorolac Tromethamine Ophthalmic Solution 0.45%	Indicated for the treatment of pain and inflammation following cataract surgery.
Cytarabine Injection 100mg Additional Packsize (20ml)	In combination with other approved anticancer drugs is indicated for remission induction in acute non-lymphocytic leukemia of adults and children. It has also been found useful in the treatment of acute lymphocytic leukemia and the blast phase of chronic myelocytic leukemia. Intrathecal administration of cytarabine is indicated in the prophylaxis and treatment of meningal leukemia.
Olopatadine Hcl Nasal Spray 0.6% w/w (Additional Indication)	For the relief of the symptoms of seasonal allergic rhinitis in patients 6 years of age and older.
Sodium chloride 6.80gm + Potassium chloride 0.30 gm + Calcium chloride dihydrate 0.37gm + Magnesium chloride hexahydrate 0.20gm + Sodium acetate trihydrate 3.27gm + L-malic acid 0.67gm in	Replacement of extracellular fluid losses in case of isotonic dehydration, especially if acidosis is being imminent or present

1000ml solution for infusion	
Chemically Modified Sodium Hyaluronate and Caboxymethylcellulose Absorbable Adhesion Barrier.	As an adjunct in abdominal or pelvic surgery for reducing the incidence, extent and severity of postoperative adhesions at the site of placement.
Lornoxicam 4mg/4mg + Thiocolchicoside 4mg/8mg tablets	For the treatment of patients with acute painful musculoskeletal conditions
Cefixime 100mg/200mg + Cloxacillin 500mg/500mg tablets	For the treatment of adult patients with upper & lower respiratory tract infections, skin and soft tissue infections
Celecoxib Mouth Dissolving Tablet 50/100/200 mg	For the Treatment of Osteoarthritis and Rheumatoid Arthritis
Propofol 2% w/v Injection (additionalStrength)	Same as Approved
Spironolactone 25mg + Furosemide 20mg tablets	For treatment of resistant oedema associated with secondary hyperaldosteronism; resistant hypertension, chronic cardic failure and hepatic cirrhosis
Olopatadine5mg + Ambroxol30mg tablets	For the management of cough in adult patients only
Methylcobalamin750mcg + Pregabalin75/150mg + Vitamin B61.5mg + Folic acid0.75mg + Benfothiamine7.5mg capsules	For the treaetment of painful diabetic neuropathy in adults only
Calcium acetate 435mg + Magnesium carbonate 235mg tablets	For the management of hyperphosphatemia in adults patients with renal failure being treated with dialysis (hemodialysis or peritoneal dialysis
Dicyclomine2.5mg + Dried Aluminimum Hydroxide200mg + Light Magnesium Oxide100mg + Simethicone 20mg per 5ml suspension.	For the treatment of the symptoms of functional gastrointestinal disorders like irratible bowel syndrome, functional dyspepsia, peptic ulcers., GERD which includes smooth muscle spasm, flatulence, abdominal distension, hyperacdity, gastric distress, bloting etc.
Sertaconazole 2% w/v+ Zinc Pyrithione 1% w/v Shampoo	For the treatment in adults patients with dandruff/seborrheic dermatitis of the scalp
Faropenam Sodium Extended Release Tablet 225/300/450 mg	For the Treatment of respiratory tract infections, urinary tract infection, skin and skin structure infections and gynaecological infections
Amlodipine5mg + Ramipril10mg/5mg Tablets (additional strength)	For the treatment of hypertension only
Doxofylline MR Tablet 650 mg	For the treatment of Bronchial Asthma and COPD in Adults
Lidocaine7.5mg + Prilocaine2.5mg per acutation spray	For the treatment of adult male patients with premature ejaculation
Pramipexole Di HCl monohydrate ER Tablet 0.375/0.75/1.5/3/4.5 mg	For the treatment of the sign and symptoms of idiopathic parkinsons disease
Drosperinone 3mg + Ethinyl Estradiol0.02mg tablets	For the treatment of symptoms of premenstrual dysphoric disorders (PMDD) in women (additional indication)
Miglitol 25 mg + Metformin 500mg tablets	Additional Strength
Propranolol 40mg (SR Pellets) + Fluarizine 5mg/10mg capsules	For the prophylaxis of migraine
Citicholine 500mg + Piracetam 400mg Tablets	For the treatment of acute stroke
Diclofenac 50mg + Chlorzoxazone500mg Tablets	For the treatment of acute inflammation conditions associated with spasm in adults only
Mecobalamin 750 mcg + Pyridoxine 1.5mg + Nicotinamide 45 mg + Benfotiamine 150mg Tablets	For the treatment of diabetic neuropathy in adults
Etoricoxib 1%+ Menthol 5% Spray	For the topical treatment of acute musculoskeletal pain
Pantoprazole 40mg + Cinitapride (ER) 3mg Capsules	For the treatment of patients suffering from non-ulcer dyspepsia (NUD) or gasteroesophageal reflux disease (GERD)
Atorvastatin 20mg + Ramipril 2.5mg/5mg Capsules	Additional higher strength
Lamotrigine Orodispersible Tablet 12.5 mg(additional strength)	Same as Approved
Trabectedin powder for Conc. solution for infusion (Additional Indication)	In combination with pegylated liposomal doxorubicin, it is indicated for the treatment of patients with relapsed platinum- sensitive ovarian cancer
Lornoxicam 8mg/8mg + Thiocolchicoside 4mg/8mg Tablets	Additional higher strength

Diclofenac sodium SR Tablet 150 mg	For the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondilytis,gout,painful post perative pain following dental surgery etc.
Magnesium Valproate CR Tablet 200/ 300/400/ 500 mg (additonal strength)	Same as Approved
Lidocaine 2.5% w/w+Prilocaine 2.5% w/w Gel	Additional higher Strength
Nicotinic Acid and Laropiprant Modified Release Tablets: Nicotinic Acid.....1000 mg aropiprant.....20mg L	1. For the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia (characterised by elevated levels of LDL-cholesterol and triglycerides and low HDl-cholesterol) and in patients with primary hypercholesterolemia (heterozygous familial and non-familial). 2. In combination with HMG-CoA reductase inhibitors (statins), when cholesterol lowering effect of HMG-CoA reductase inhibitor monotherapy is inadequate. It can be used as monotherapy only in patients in whom HMG-CoA reductase inhibitors are considered inappropriate or not tolerated. Diet or other non-pharmacological treatments (e.g. exercise, weight reduction) should be continued during therapy.
Pantoprazole Mouth Dissolving Tablet 20/40 mg	For the treatment of gastric ulcer, duodenal ulcer & gastroesophageal reflux disease (GERD).
Praziquntel 175mg + Pyrantel 504mg + Febental 525mg Tablets	For the treatment of mixed infections with roundworms and tapeworms in dogs
Difluprednate Opthalmic Emulsion 0.05% w/v	For the treatment of inflammation and pain associated with ocular surgery.
Tolperisone Hcl SR 450mg Tablets	For the relief of painful muscle spasms of the skeletal muscualture.
S(-)Metoprolol 25mg/50mg (ER) + Atorvastatin (IR)10mg tablets	For the treatment of patients with both essential hypertension and hypercholesterolemia
Atorvastatin10mg + Ramipril 5mg + Aspirin (EC pellets) 75mg/150mg + Metoprolol (ER tablets) 25mg Capsules	For secondary prophylaxis of ischemic heart disease in patients where use of such combinations in appropriate
Lamotrigine 25mg Modified Release Tablet (Addl. Strength)	Same as Approved
Imatinib Mesylate 100/400mg Tablets (Addl. Indication)	Adjuvant treatment of adult patients following resection of gastro-intestinal stromal tumours (GIST)
Azithromycin SR Granules for Oral Suspension 1gm (Addl. Strength)	Same as Approved
Gemfibrozil Capsule USP & Gemfibrozil Tablet USP 200mg/600mg (Addl. Indication)	For the treatment of other dyslipidemias: (a) Fredrickson Types III and V.(b) Associated with diabetes.(C) Associated with xanthomata.
Ibuprofen 400mg + Chlorzoxazone 500mg Tablets	For the short term treatment of musculoskeletal pain associated with inflammation and spasm in adults only
Doxophylline (SR) 400mg/800mg + Montelukast 10mg/10mg Tablets	For the treatment of bronchial asthma in adults
Dronedarone(as Hydrochloride) film coated tablet .... 400 mg.	To reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation (AF) or atrial flutter (AFL), with a recent episode of AF/AFL and associated cardiovascular risk factors (i.e., age > 70, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter > 50mm or left ventricular ejection fraction [LVEF] < 40%), who are in sinus rhythm or who will be cardioverted.
Dosulepin Hcl Tablet 25mg/75mg (Additional Indication)	For the treatment of chronic pain.
Prasugrel (as Hydrochloride) film coated tablet ....5 mg / 10mg.	To reduce the rate of thrombotic cardiovascular (CV) events (including stent thrombosis) in patients with acute coronary syndrome (ACS) who are to be managed with percutaneous coronary intervention (PCI) as follows: 1. Patients with unstable angina (UA) or non-ST-elevation myocardial infarction (NSTEMI). 2. Patients with ST-elevation myocardial infarction (STEMI) when managed with primary or delayed PCI.
Tofisopam uncoated tablet JP... 50/100mg	For the treatment of anxiety and depression.
Zotepine tablet 25/50/100mg	For the treatment of schizophrenia
Armodafinil uncoated tablet ..50/150/250mg	To improve wakefulness in patients with excessive sleepiness associated with treated obstructive sleep apnea (OSA), shift work sleep disorder (SWD) or narcolepsy.

Indacaterol (as Maleate) Inhalation Powder Hard Capsules ….. ...150/300mcg	For maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD).
Ranolazine ER Tablets 750mg (Additional Strength)	Same as Approved
Tacrolimus Capsules 3mg (Additional Strength)	Same as approved
Cefixime 100mg/200mg + Ofloxacin 100mg/200mg Tablets	For the treatment of patients with typhoid fever and urinary tract infection in adults
Liquid paraffin 6% + White soft paraffin 15%w/v Cream	For symptomatic relief of dermatological condition associated with dry skin including atopic dermatitis, eczema, pruritus, ichthyosis, xerosis, psoriasis
Levosimendan Injection 2.5mg / ml	For the short term treatment of acutely decompensated chronic heart failure (ADHF) in situations where conventional therapy is not sufficient and in cases where ionotropic support is considered appropriate.
Thiocholchicoside SR Tablet 16 mg	As an adjuvant treatment in painful spasms associated with degenerative vertebral disorders and vertebral static problems, torticollis dorsal pain, low back pain, traumatological and neurological disorders.
Telmisartan 40/80 mg+ Indapamide SR 1.5/1.5 mg tablet	For the treatment essential hypertension
one strip of 3 uncoated tablets of artesunate 150mg & one strip of 2 uncoated tablets of FDC of Sulphadoxine IP 500mg + Pyrimethamine IP 25mg	Additional strength
Lapatinib Ditosylate Tablets 250mg (addl. Indication)	In combination with letrozole for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated.
Pentosan polysulfate Sodium Cpasules 100mg	For the relief of bladder pain or discomfort associated with interstitial cystitis.
Indapamide (SR) 1.5mg/1.5mg +Nebivolol 2.5mg/5mg tablet	For the treatment of hypertension not controlled with monotherapy
Cinitapride (ER) 3mg + Omeprazole (EC) 20mg Capsules	For the treatment of gastirc ulcer,gastroesophageal reflux disease(GERD) & Dyspepsia not responding to omeprazole alone
Timolol Maleate Long Acting Ophthalamic Solution 5mg/ml	For the treatment of elevated intraocular pressure in patient with ocular hypertension or open angle glaucoma.
Telmisartan tablet 20/40/80 mg(Additional indication)	For the prevention of cardiovascular morbidity and mortality in patient 55 years older at high risk of cardiovascular disease
Dexketoprofen Trometamol 25mg + Thiocolchicoside 4mg tablets	For the treatment of acute low back pain and other musculoskeletal painful & inflammatory conditions in adult patients
Troxipide film coated Tablets 50mg /100mg	For the treatment of Gastric ulcers and for amelioration of gastric mucosal lesions (erosion, hemorrhage, redness and edema) in the diseases such as acute gastritis, acute exacerbation stage of chronic gastritis.
Ambrisentan film coated Tablets 5 mg / 10mg	For the treatment of pulmonary arterial hypertension (WHO Group I) in patients with WHO class II or III symptoms to improve exercise capacity and delay clinical worsening.
Rosuvastatin Calcium Tablet(Additional Indication)	Risk reduction of MI stroke and arterial evascularisation procedure in patients without clinically evident CHD but with multiple risk factor
Paracetamol SR 1000mg Bilayered tablet	For symptomatic treatment of pain and fever
Tacrolimus PR Caps 0.5/1/5 mg	For Prophylaxis of transplant rejection in adult kidney or liver allograft rejection
Rizatriptan Benzoate orally disintegrating tablet 10 mg(Additional Dosage Form)	Same as Already approved
Ramipril 1.25/ 2.5/5/10 mg(Additional Indication)	For the treatment ofnon-diabetic overt glomerular or incipient nephropathy
Exenatide Inj. (Additional Indication)	Use in patients with type-2 diabetes mellitus who are using a thiazolidinedione alone or in combination with metformibn but have not achieved adequate glycemic control
Temozolomide lyophilised powder 100mg / vial	For the treatment of "Adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment." Children from the age of three years, adolescents and Adult patients with malignant giloma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy.

Fluticasone Propionate 50mcg/125mcg/250mcg + Salmeterol xinafoate 25mcg/25mcg/25mcg Powder for inhalation	For the maintenance treatment of asthma and for the treatment of COPD associated with chronic bronchitis
Cross linked Hyaluronic Acid 24mg + Lidocaine 3mg Pre-filled syrings	For filling any medium sized depression of the skin via mid dermis injection as well as for lip definition. The presence of lidocaine is meant to reduce the patients pain during the treatment
Aceclofenac 1% w/w + Menthol 5% Spray	For the treatment of acute painful inflammatory conditions in adults only
Metformin SR 500mg/500mg + GliclazideSR 60mg/30mg + Pioglitazone 15mg/15mg tablets	As 3rd line treatment of type II diabetes mellitus when diet, exercise and the single agents and the second line therapy with two drugs do not result in adequate glycemic control
3 tablets of artesunate 100mg + 3 tablets of Artesuante 50mg & 2 tablets of FDC of Pyrimethamine 25mg + Sulphadoxine 500mg combipack	Additional strength
Calcium carbonate 600mg +Simethicone 80mg Chewable tablet	To relive the uncomfortable symptoms of acid indigestion, heart burn, gas or sour stomach
Activated Dimethicone 50mg + Magnesium Hydroxide 250mg+ Dried Aluminium Hydroxide250 mg + Sorbitol (70%)1.25 gm /5ml Solution	For treatment of symptoms of hyperacidity (e.g. heartburn, epigastric discomfort, or their equivalents) that are often associated with dyspepsia, peptic ulcers, gastritis, peptic esophagitis and indicated for relief of flatulence
Aspirin 75mg + Simvastatin 10mg/20mg + Lisinopril 5mg/10mg + Atenolol 25mg/50mg Tablets	For secondary prevention of coronory heart disease/stroke in patients where use of such combination is appropriate
Irsogladine Maleate Tablet 2mg /4mg	For gastric ulcers, improvement of gastric mucosal lesion (erosion, hemorrhage, redness and edema) caused by acute gastritis and acute exacerbation stage of chronic gastritis.
Lacosamide film coated tablet 50mg /100mg /150mg /200mg	As an adjunctive treatment of partial onset seizures in patients > 17 years of age.
Carmustine for inj. 100 mg	Indicated as palliative therapy as a single agent or in established combination therapy with other approved chemotherapeutic agents in the following: 1.Brain tumors—glioblastoma, brainstem glioma, medulloblastoma, astrocytoma, ependymoma, and metastatic brain tumors. 2.Multiple myeloma—in combination with prednisone.3.Hodgkin's Disease—as secondary therapy in combination with other approved drugs in patients who relapse while being treated with primary therapy, or who fail to respond to primary therapy. 4.Non-Hodgkin's lymphomas—as secondary therapy in combination with other approved drugs for patients who relapse while being treated with primary therapy, or who fail to respond to primary therapy.
Monteleukast Sodium Tablet 10mg; Monteleukast Sodium 4/5mg Chewable Tablet; Monteleukast Sodium Oral granule(Additional Indication)	For the relief of symptoms of seasonal allergic rhinitis in adults and pediatric patients 2 years of age and older.
Ramosetron Dispersible Tablet 0.1 mg	For the prevention and treatment of gastrointestinal symptoms(nausea and vomitting) associated with ematogenic cancer chemotherapy
Amitraz 2%w/v pour on solution	For the control of ticks on cattle and ostriches
Flupirtine Maleate Capsules 100mg	For treatment of acute and chronic pain ,i.e, for painful increased muscle tone of the posture and motor muscles, primary headache, tumor pain, dysmenorrhea and pain after traumatologic / orthopaedic operations and injuries.
Lidocaine Patch 350mg (Additional Pack Size)	For the relief of pain associated with post-herpetic neuralgia. It should be applied only to intact skin.
Oseltamivir Phosphate (Additional indication)	In the treatment of children 6 to 12 months of age during a pandemic influenza outbreak.
Methylcobalamin 1500mcg +Folic acid 0.7mg +Niacinamide 12mg injection	For the treatment of diabetic neuropathy in adults
Methylcobalamin 1500mcg +Pyridoxine 100mg +Nicotinamide 100mg injection	For the treatment of diabetic neuropathy in adults
1 tablet of Tenofovir disoproxil 300mg + Lamivudine 300mg & 2 tablet of Nevirapine 200mg combipack	For the treatment of HIV infection in adults

Vitamin A (oily form) as palmiate 2000IU + Vitamin B1 1mg + Vitamin B2 1mg + Vitamin B6 1.34mg + Vitamin B12 1mcg + Ascorbic acid 33.3mg + Vitamin D3 200IU + Folic acid 0.3mg + Calcium pantothenate 1mg + Niacinamide 15mg + Dibasic calcium phosphate 100mg + Phosphorus 77mg+ Ferrous fumarate 50mg + Copper 0.01mg+ Potassium iodide 0.0015mg + Heavy magnesium oxide 1mg + Manganse sulphate 0.01mg + Potassium sulphate 1mg + Zinc sulphate 0.15mg Capsule	For the treatment of vitamin deficiency states in adults
Ramipril MR Capsules 2.5/5 mg (Additional Strength)	Same As Approved
Sitagliptin Phosphate 25/50/100 mg Tablet (Additional Indication)	(i) Use of Sitagliptin Phosphate in combination with Metformin and a PPARγ agonist as an adjunct to diet & exercise in adult patients with type-2 Diabetes mellitus who are inadequately controlled on combination therapy with Metformin and a PPARγ agonist. (ii) Use of Sitagliptin Phosphate in combination with insulin, alone or in combination with Metformin.
Erlotinib HCl 25/100 mg Tablet (Additional Indication)	As monotherapy for maintenance treatment in patients with locally advanced or metastatic non-small cell lung cancer with stable disease after 4 cycles of standard platinum based first line chemotherapy.
Gemcitabine HCl injection 2gm/vial (Additional Strength)	Same as Approved
Etizolam 0.25 mg tablet (Additional Strength)	Same As Approved
Dexketoprofen1.25% w/w +Linseed Oil 3.0%w/w +Menthol 5%w/w +Methyl Salicylate 10%w/w (12.5mg)	For the topical treatment of acute musculoskeletal pain
Cefuroxime Sodium 750/1500mg +Sulbactam Sodium 375/750mg	For the treatment of mild to moderate lower respiratory tract infection
HPMC 0.3% +Dextran 0.1% + Glycerin 0.2%	For the temporary relief of burning and irritation due to dryness of the eye and for use as a protection against further irritation. For the temporary relief of discomfort due to minorirritations of the eyes or to exposure to wind or sun
Cyanocobalamin 15mcg+Chromium Picolinate USP 250mcg+Folic Acid USP 1500 mcg+Nicotinamlide IP100 mg+Pyridoxine 3mg +Selenius Acid USP 100mcg+Zinc Sulfate Monohydrate USP 61.8 mg eq. to 22.5 mg	For Mineral & Vitamins deficiency states in adult patients
Methylparaben 0.15%w/w +Propyl paraben 0.05%w/w+Glycerin 20%w/w +CMC 1.74%w/w +Allantoin 0.5%w/w +Benzyl alcohol 0.5%w/w.	For short term treatment of chronic wounds including stage III & IV pressure sores, leg ulcers
Clonazepam IR 0.5mg/0.5mg+ Paroxetine CR 12.5/25mg	For the treatment of patients with co-morbid depression and axiety
Nilotinib Capsules 200mg	For the treatment of chronic and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia (CML) in adult patients resistant to or intolerant to prior therapy that included imatinib.
Imipenem 50mg + Clistatin 50mg	Treatment of infection caused by susceptible bacteria for the following indication as in neonates and infants (below 3 months of age) 1. Lower respiratory tract infections 2. Urinary tract infections 3. Intra-abdominal infections 4. Bacterial septicemia 5. bone and joint infections 6. Skin and Skin structure infections 7. Bacterial endocarditis
Lidocaine Lozenges 100mg (Additional Strength)	Same as Approved
Metoprolol succinate ER 25/50 mg+Telmisartan 20/40mg	For the treatment of essential hypertension
Etodolac 300/300mg +Thiocolchicoside 4/8mg	For the treatment of patients with acute painful musculoskeletal conditions
Celecoxib 100/200mg +Diacerein 50/50mg	For the treatment of adult patients with osteoarthritis of knee and/or hip joints
Metoprolol succinate ER 25mg+50mg + Olmesartan 20/20mg	For the treatment of essential hypertension

1 tablet of Atazanavir 300mg & 1 tablet of ritonavir Ritonavir 100mg & FDC of Tenofovir Disoproxil fumarate 300mg + Lamivudine 300mg (Each Co-pack contains :- 1 capsule of Atazanavir 300mg & 1 Tablet of Ritonavir 100mg & 1 Tablet of FDC of Tenofovir Disoproxil Fumarate 300mg + Lamivudine 300mg)	For the treatment of HIV infections in adults
Gliclazide 40/80mg+Metformin 500mg+Pioglitazone15mg	Additional strength
Lidocaine HCl Ophthalmic Sterile Gel 35 mg/ml	Indicated for ocular surface anaesthesia during ophthalmologic procedures.
Naftopidil Tablets 25/50/75mg	For the treatment of dysuria associated with benign prostratic hyperplasia.
Metformin 500/850/1000mg+Sitagliptin Phosphate 50/50/50mg (Additional Indication)	A) FDC is indicated as triple combination therapy with a PPARy agonist (i.e a thiazolidinedione) as an adjunct to diet and exercise in patients inadequtely controlled on their maximal tolerated dose of metfomin and a PPARy agonist. B) FDC is also indicated as add-on to insulin(i.e triple combination therapy) as an adjucnjt to diet and exercise to improve glycemic contrl in patients when stable dosage of insulin and metformin alone do not provide adequte control.
Bimatoprost Eye Drps 0.1mg/ml	for the treatment of hypotrichosis of the eye-lashes by increasing their growth including length, thickness & darkness.
S(+) Etodolac 5/10%w/w + Camphor 4%w/w + Menthol 10%w/w + Methyl salicylate 5%w/w + Linseed oil 3%w/w	For the painful & inflammatory conditions associated with joint, tendons, ligaments and muscles
Cefpodoxime 100/200mg+Dicloxacillin ER 500/500mg	For the treatment of lower RI, Skin and soft tissue, bone and joint infections and ENT infections in adult patients prone to antibiotic induced diarrhoea
Voglibose0.3 + Metformin (SR) 500mg	Additional higher strength
Amoxycillin Oral Suspension 200/400 mg per 5ml	in the treatment of infections due to susceptible strains of the designated micro-organisms in the condition of E.N.T infection, skin & skin structure infection, lower respiratory tract infection, genito-urinary tract infection, gonorrhea, acute uncomplicated (anogenital & urethral) infections.
Olmesartan 40mg + Amlodipine 5mg (Additional Strength)	Additional indication: 1. For the treatmenmt of hypertension alone or with other antihypertensive agents 2. To use as initial therapy in patients who are likely to need multiple antihypertensive agents to achieve their blood pressure goals
Doripenem 500 mg powder for injection (Additional Indication)	Complicated intra-abdominal infections and complicated urinary tract infections, including complicated and uncomplicated pyelonephritis and cases with concurrent bacteremia
Nadolol tablet USP 20/40/80 mg	in the treatment of angina-pectoris, cardiac arrythmias & essential hypertension.
Fluconazole For Oral suspension 50/200 mg per 5ml (Pack Size : 35ml)	for the treatment of systemic candidiasis, mucosal candidiasis, prevention of fungal infections in patients with malignancy.
Metformin 500/500mg + Repaglinide 1/2mg	Indicated as an adjunct to diet and excersice to improve glycemic control in adults with type 2 diabetes mellitus who are already treated with a meglitinide & metformin or who have inadequte glycemic control on a meglotinide alone or metformin
Hydroxyzine Hydrochloride SR Tablets 25/50/75mg	For management of pruritus due to allergic conditions such as chronic urticaria and atopic contact dermatoses, and in histamine - mediated pruritus.
Rosuvastatin 5/10/20mg+Fenofibrate 67/145/160mg	For the treatment of combined hyperlipidemia in patients with normal hepatic and renal function
Fexofenadine 120mg + Montelukast 10mg	For treatment of allergic rhinitis in adults only

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Drug of the quarter……..

Tocilizumab

Tocilizumab has been approved by the USFDA for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor inhibitor therapies (i.e., infliximab). It has been approved for a number of inflammatory disease states, including RA in Japan (2005) and the European Union (2009). Tocilizumab has not been studied and its use should be avoided in combination with biological disease-modifying antirheumatic drugs (DMARDs) such as tumor-necrosis-factor antagonists, interleukin-1 receptor (IL-1R) antagonists, anti-CD20 monoclonal antibodies and selective co-stimulation modulators because of the possibility of increased immunosuppression and increased risk of infection

Studies on tocilizumab:

1. Chugai Humanized Anti-Human Recombinant Interleukin-6 Monoclonal Antibody (CHARISMA) trial:

It was a multicenter, randomized, double-blind, placebo-controlled trial with 354 participants. It was found that Tocilizumab monotherapy or tocilizumab in combination with methotrexate was superior to methotrexate alone for the treatment of rheumatoid arthritis (RA) inadequately responding to methotrexate or other disease-modifying antirheumatic drugs.

2. According to a randomized, double-blind, double-dummy, parallel study, it was found that adults successfully treated with methotrexate or biological agents for active rheumatoid arthritis, tocilizumab monotherapy resulted in significantly more patients achieving an American College of Rheumatology criteria improvement of 20 percent (ACR20 response) at week 24, compared with methotrexate monotherapy. The numbers of participants in the study were 570.

There were significant improvements in tocilizumab-treated patients compared with methotrexate in the reduction in the mean number of swollen joints and the mean number of tender. The mean CRP level normalized in the tocilizumab-treated group, but not in the methotrexate group. Comparing tocilizumab with methotrexate-treated patients increases in ALT of more than 3 times the ULN to 5 times the ULN occurred in 2.5% and 1% of patients and increases of 5 times the ULN or greater occurred in 1.1% vs 0.7%, respectively. Neutropenia occurred more frequently in the tocilizumab group compared with methotrexate, grade 1, grade 2, and grade 3. Serious infections and infestations occurred in 1.4% of tocilizumab-treated patients and in 0.7% of methotrexate-treated patients.

Adverse Reactions:

Tocilizumab administration may cause rash, upper abdominal pain, increase in SGOT, SGPT level, dizziness, headache.

Some serious adverse reaction such as Decreased platelet count, gastrointestinal perforation, anaphylaxis reaction may occur following tocilizumab administration.

Drug Interactions:

Tocilizumab can interact with CYP450 substrates with a narrow therapeutic index such as alfentanil, carbamazepine, theophylline, warfarin, cisapride, Aminophylline. This interaction is moderate in severity and results in altered plasma concentration of CYP450 substrates with a narrow therapeutic index.

The mechanism behind this interaction is as follows:

In states of chronic inflammation, the formation of CYP450 enzymes is suppressed by increased levels of cytokines such as interleukin-6 (IL-6). Upon administration of an IL-6 receptor inhibitor, such as tocilizumab, the formation of CYP450 enzymes could be normalized. In patients receiving CYP450 substrates with a narrow therapeutic index concomitantly with tocilizumab, such normalization may have a clinically relevant effect on CYP450 substrates levels through an increase in CYP450-mediated quinidine metabolism.

Clinical management: If tocilizumab therapy is initiated in a patient being treated with a CYP450 substrate with a narrow therapeutic index, monitor for therapeutic effect and adjust dose of previous as needed.

Dosage:

For the treatment of moderately to severely active rheumatoid arthritis in patients who have had an inadequate response to 1 or more tumor-necrosis-factor antagonist therapies, the recommended starting dose when used in combination with (non-biologic) disease-modifying antirheumatic drugs (DMARDs) or as monotherapy is **4 milligrams/kilogram** (mg/kg) administered once every 4 weeks as a 60-minute intravenous infusion. Based on clinical response, the dose may be increased to **8 mg/kg every 4 weeks**. **Doses exceeding 800 mg per infusion are not recommended.**

Tocilizumab should not be initiated in patients who have alanine transaminase (ALT) or aspartate aminotransferase (AST) elevations 1.5 times upper limit of normal and no dosage adjustment is required in renal impairment.

Tocilizumab should not be initiated in patients with an absolute neutrophil count (ANC) below 2000 per cubic milliliter (mm (3)) or platelet count below 100,000/mm.

Patient counselling:

1. Consult your doctor before taking any flu shots as they may not work well for you when you are using Tocilizumab

2. Avoid being near people who are sick or have infections, Wash your hands often, Stay away from rough sports or other situations where you could be bruised, cut, or injured, Brush and floss your teeth gently, Be careful when using sharp objects, including razors and fingernail clippers as this medicine lowers the number of some types of blood cells in your body. Because of this, you may bleed or get infections more easily.

Reference:

1. http://www.medscape.com/viewarticle/731720_6
2. Actemra (tocilizumab) package insert. South San Francisco, CA: Genentech, Inc; January 2010.
3. Genovese MC, McKay JD, Nasonov EL, et al. Interleukin-6 receptor inhibition with tocilizumab reduces disease activity in rheumatoid arthritis with inadequate response to disease-modifying antirheumatic drugs: the TOWARD study. Arthritis Rheum . 2008; 58:2968-2980.
4. MICROMEDEX(R) Healthcare Series Vol. 146.

तिमाहीतील औषध.....

टोसीलीझुमॅब

अमेरीकन अन्न व औषध प्रशासनाने टोसीलीझुमॅब या औषधास मोठ्या वयाच्या व्यक्तींना होणाऱ्या संधीवातावर ज्यांच्याकडून एक किंवा अधिक अर्बुदांमुळे पेशीसमूह नष्ट होणा-या आजारावर उपचारांना प्रतिसाद दिला जात आहे (उदा. इनफ्लिक्सीमॅब) अशा रूग्णांकरीता मान्यता दिली आहे. या औषधास □पानमध्ये 2005 साली तर युरोपीय देशांत 2009 साली मान्यता दिली आहे. टोसीलीझुमॅबच्या परिणामांचा अभ्यास अद्याप संधीवातावरील इतर औषधांबरोबर जसे टयुमर नेक्रोसीस फॅक्टर अँटागॉनीस्ट , इंटरल्युकीन-1 रिसेप्टर अँटागॉनीस्ट , अँटी सीडी20 मोनोक्लोनल अँटीबॉडीज आणि सिलेक्टीव्ह कोस्टीम्युलेशन मॉड्युलेटर्स झालेला नाही कारण शरीरात बाहेरून घेऊन रोपण केलेल्या अवयवांना सामावून घेण्याच्या प्रक्रियेस विरोध निर्माण झाल्याने संसर्ग होण्या□ शक्यता आहे.

टोसीलीझुमॅबवरील अभ्यास -

1. च्युगाई ह्युमनाईझ्ड ॲन्टी-ह्युमन रिकॉम्बीनंट इंटरल्युकीन-6 मोनोक्लोनल ॲन्टीबॉडी (CHARISMA) ट्रायल :

354 व्यक्तींवर विविध पैलूतून निष्क्रीय पदार्थांचा वापर करून परिक्षण करण्यात आले. संधीवातावर केवळ मेथोट्रॅक्झेटच्या वापराने होणाऱ्या परिणामांपेक्षा नुसत्या टोसीलीझुमॅबचा किंवा मेथोट्रॅक्झेट बरोबर टोसीलीझुमॅबचा परिणाम अधिक चांगला दिसून येतो.

2. अमेरिकन कॉलेज ऑफ ऱ्हुमॅटोलॉजी येथे 570 रूग्णांचे टोसीलीझुमॅबच्या उपचारांची तुलना मेथोट्रक्झेटच्या उपचारांशी केली असता 20 टक्क्यांनी फरक आढळला.

टोसीलीझुमॅबचे उपचार सुरू असलेल्या रूग्णांमध्ये सांधे आणि सांध्यांच्या टोकांवर येणारी सूज कमी झाली असल्याचे आढळले. टोसीलीझुमॅब घेणाऱ्या रूग्णांमध्ये प्रथिनांची पातळी सामान्य झाल्याचे आढळले. मेथोट्रॅक्झेट गटाशी तुलना करता टोसीलीझुमॅब घेणाऱ्या रूग्णांमध्ये रक्तातील न्युट्रोफील्सचे प्रमाण कमी झाल्याचे आढळते. त्यामुळे 1.4% रूग्णांना संसर्ग झाल्याचे आढळते तर मेथोट्रॅक्झेटचे उपचार झालेल्यांमध्ये हे प्रमाण 0.7% इतके आहे.

विरुध्द प्रतिसाद -

टोसीलीझुमॅबमुळे पुरळ येणे, ओटीपोटात दुखणे, SGOT, SGPT पातळ्यांत वाढ होणे, चक्कर येणे, डोकेदुखी हे परिणाम दिसू शकतात.

टोसीलीझुमॅबमुळे होणारे गंभीर परिणाम म्हणजे प्लेटलेट्सची संख्या कमी होणे, मोठ्या आतड्याला भोक पडणे किंवा रूग्ण अतिसंवेदनशील होणे.

औषधांच्या क्रिया-प्रक्रिया -

टोसीलीझुमॅबच्या अल्फेन्टानील, कार्बामाझेपीन, थीओफायलीन, वारफारीन, सीसाप्राईड, अमिनोफायलीन या CYP450 गटातील औषधांशी क्रिया-प्रक्रिया होतात. ही नियंत्रित स्वरूपाची असते. रक्तरसातील CYP450□ तीव्रता वा□ते. ती पुढीलप्रमाणे घडते -

दीर्घकाल होणाऱ्या दाहामुळे इंटरल्युकीन-6 सारख्या वाढलेल्या सायटोकीन्सच्या पातळीमुळे CYP450च्या प्रथिनांची निर्मिती कमी होते. टोसीलीझुमॅबच्या वापरामुळे CYP450च्या पातळीत वाढ होण्यास मदत होते.

वैद्यकीय उपचार व्यवस्थापन - CYP450चा उपचार घेत असलेल्या रूग्णास टोसीलीझुमॅबचाही उपचार देण्याची गरज निर्माण झाल्यास डोस प्रमाणित करण्यात यावा.

मात्रा (Dosage) - ॲक्टीव्ह ऱ्हुमॅटॉईड अथ्रायटीसच्या रूग्णांकरीता वापर करताना ज्यांचा 1 किंवा अधिक टयुमर नेक्रोसीस फॅक्टर अँटागॉनीस्ट थेरपीस पुरेसा प्रतिसाद मिळत नाही अशा रूग्णांकरीता 4मिलीग्रॅम/किलो चार आठवड्यातून एकदा शीरेतून देण्यात यावे. ही मात्रा 8मिलीग्रॅम/किलो पर्यन्त वाढू शकते परंतू 800 मिलीग्रॅमपेक्षा अधिक देऊ नये. ज्या रूग्णांना अलानाईन ट्रान्समीनेस (ALT) किंवा ॲस्पारटेट

अमायनोट्रान्सफेज (AST) ची पातळी सामान्य प्रमाणाच्या 1.5पट असल्यास हे औषध देऊ नये. मूत्रपिंड विकारात डोस बदलण्याची आवश्यकता नाही.
2000प्रति घनमिलीलीटर पेक्षा कमी न्यूट्रोफील्सचे किंवा 100000 प्रति मिलीमीटरपेक्षा कमी मापन येत असल्यास टोसीलीझुमॅब देऊ नये.

रूग्ण समुपदेशन :-

1. लस घेण्यापूर्वी डॉक्टरांचा सल्ला घ्यावा.
2. आजारी व्यक्तींजवळ जाऊ नये ,नियमितपणे हात धुवावे. सुरक्षित ठिकाणी असावे. दांत स्वच्छ धुवावे. धारदार वस्तू वापरताना काळजीपूर्वक वापर करावा. अन्यथा इजा व संसर्ग होण्याची शक्यता वाढते.

News from USFDA: Safety Announcement for dronedarone

The U.S. Food and Drug Administration (FDA) is alerting healthcare professionals and patients about cases of rare, but severe liver injury, including two cases of acute liver failure leading to liver transplant in patients treated with the heart medication dronedarone.

Dronedarone is a drug used to treat abnormal heart rhythm in patients who have had an abnormal heart rhythm (atrial fibrillation or atrial flutter) during the past 6 months. Dronedarone can reduce the risk of being hospitalized for these heart problems. Dronedarone was approved with a Risk Evaluation and Mitigation Strategy (REMS) with a goal of preventing its use in patients with severe heart failure or who have recently been in the hospital for heart failure. In a study of patients with these conditions, patients given dronedarone had a greater than two-fold increase in risk of death.

Additional Information for Patients

- Contact your healthcare professional if you develop itching, yellow eyes or skin, dark urine, loss of appetite, or light-colored stools. These may be signs of liver injury.
- Talk to your healthcare professional about any concerns you have with this medication.
- Do not stop taking dronedarone unless told to do so by your healthcare professional.

Additional Information for HCPs

- Advice patients to contact a healthcare professional immediately if they experience signs and symptoms of hepatic injury or toxicity (anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching) while taking dronedarone.
- Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment. However, it is not known whether routine periodic monitoring of serum liver enzymes (ALT, AST, and alkaline phosphatase) and bilirubin in patients taking dronedarone will prevent the development of severe liver injury.
- If hepatic injury is suspected, dronedarone should be promptly discontinued and testing of serum liver enzymes and bilirubin should be performed. If hepatic injury is found, appropriate treatment should be initiated.
- Dronedarone should not be restarted in patients who experience hepatic injury without another explanation for the observed liver injury.

Ref: http://www.fda.gov/Drugs/DrugSafety/ucm240011.htm

Alert for ***Crimean Congo Hemorrhagic Fever***

Dear readers……..

After an outbreak of swine flu, a new flu called as ***Crimean-Congo hemorrhagic fever is arrived on the doors of Maharashtra,*** *so with the help of this bulletin* ***MSPC's DIC*** *appeal to all of you to read & understand the details of CCHF and aware others about the same. We hope this information will surely help to create awareness amongst all.*

 **What is Crimean-Congo hemorrhagic fever (CCHF)?**

Crimean-Congo hemorrhagic fever is caused by Crimean-Congo hemorrhagic fever virus (CCHFV). This virus is a member of the genus *Nairovirus* in the family Bunyaviridae. It belongs to the CCHF serogroup. The disease is endemic in many countries in Africa, Europe and Asia, and during 2001, cases or outbreaks have been recorded in Kosovo, Albania, Iran, Pakistan, and South Africa.

 **Who is at risk of developing CCHF?**

- Animal herders, cattle workers, and slaughter houses in endemic areas are at risk of CCHF.
- Healthcare workers in endemic areas are at risk of infection through unprotected contact with infectious blood and body fluids.
- Individuals and international travelers with contact to cattle in endemic regions may also be exposed.

 **How is CCHF spread and how do humans become infected?**

The CCHF virus may infect a wide range of domestic and wild animals. A number of tick genera are capable of becoming infected with CCHF virus, but the most efficient and common vectors for CCHF appear to be members of the Hyalomma genus. The most important source for acquisition of the virus by ticks is believed to be infected small vertebrates on which immature Hyalomma ticks feed. Once infected, the tick remains infected through its developmental stages, and the mature tick may transmit the infection to large vertebrates, such as livestock. Domestic ruminant animals, such as cattle, sheep and goats, are viraemic (virus circulating in the bloodstream) for around one week after becoming infected.

In humans, the majority of cases have occurred in those involved with the livestock industry, such as agricultural workers, slaughterhouse workers and veterinarians.

Humans become infected through the skin and by ingestion. Sources are:

- being bitten by a tick,
- crushing an infected tick with bare skin,
- contacting animal blood or tissues and
- Drinking unpasteurized milk.

The following figure shows how transmission of CCHF virus occurs:

Human-to-human transmission occurs, mainly when skin or mucous membranes are exposed to blood during hemorrhages or tissues during surgery.

Possible horizontal transmission has been reported from a mother to her child.

What is the incubation period?

The incubation period is influenced by the route of exposure. Infections acquired via tick bites usually become apparent after 1 to 3 days; the longest incubation period reported by this route is nine days.

Exposure to blood or tissues usually results in a longer incubation period. Current estimates suggest that these infections become apparent, on average, after 5 to 6 days, but incubation periods up to 13 days are known.

What are the symptoms of Crimean-Congo hemorrhagic fever?

The onset of CCHF is sudden.

General	Fever, aching muscles, dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light).
G.I symptoms	Nausea, vomiting and sore throat early on, which may be accompanied by diarrhoea and generalized abdominal pain.
Over the next few days	Sharp mood swings, and may become confused and aggressive. After two to four days, the agitation may be replaced by sleepiness, depression and lassitude, and the abdominal pain may localize to the right upper quadrant, with detectable liver enlargement.
Other clinical signs	Fast heart rate, enlarged lymph nodes, and a rash caused by bleeding into the skin, both on internal mucosal surfaces, such as in the mouth and throat, and on the skin.
Haemorrhagic	Bleeding from the upper bowel, passed as altered blood in the faeces, blood in the urine, nosebleeds and bleeding from the gums.
Evidence of	Hepatitis. The severely ill may develop hepatorenal (i.e., liver and kidney) and pulmonary failure after the fifth day of illness.

How to Diagnose CCHF?

- Diagnosis of suspected CCHF is performed in specially-equipped, high biosafety level laboratories.

- IgG and IgM antibodies may be detected in serum by enzyme-linked immunoassay (the "ELISA" or "EIA" methods) from about day six of illness. IgM remains detectable for up to four months, and IgG levels decline but remain detectable for up to five years.
- Patients with fatal disease do not usually develop a measurable antibody response and in these individuals, as well as in patients in the first few days of illness, diagnosis is achieved by virus detection in blood or tissue samples. There are several methods for doing this. The virus may be isolated from blood or tissue specimens in the first five days of illness, and grown in cell culture. Viral antigens may sometimes be shown in tissue samples using immunofluorescence or EIA.
- More recently, the polymerase chain reaction (PCR), a molecular method for detecting the viral genome, has been successfully applied in diagnosis.

What is the treatment available for CCHF?

According to the WHO, CCHF can be treated but recovery is slow.

- General supportive therapy is the mainstay of patient management in CCHF. Intensive monitoring to guide volume and blood component replacement is required.
- Antiviral drug ribavirin has been used in treatment of established CCHF infection with apparent benefit.
- Although an inactivated, mouse brain-derived vaccine against CCHF has been developed and used on a small scale in Eastern Europe, there is no safe and effective vaccine widely available for human use.

Prevention and control:

1. Avoid area where tick vectors are abundant & active i.e. spring and fall.	2. Use of insect repellants containing DEET (N, N-diethyl-m-toluamide) on the skin & premetharin on clothing.
3. Do not rotate the tick during removal.	Healthcare workers who have had contact with tissue or blood from patients with suspected or confirmed CCHF should be followed up with daily temperature and symptom monitoring for at least 14 days after the putative exposure.
4. Regular examination of clothing & skin for ticks & their removal. Avoid direct contact with infected person.	5. Wearing gloves or other protective clothing to prevent skin contact with infected tissue or blood.

References:

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4. Pitches DW. Removal of ticks: a review of the literature. Euro Surveill. 2006;11(33):pii=3027. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3027

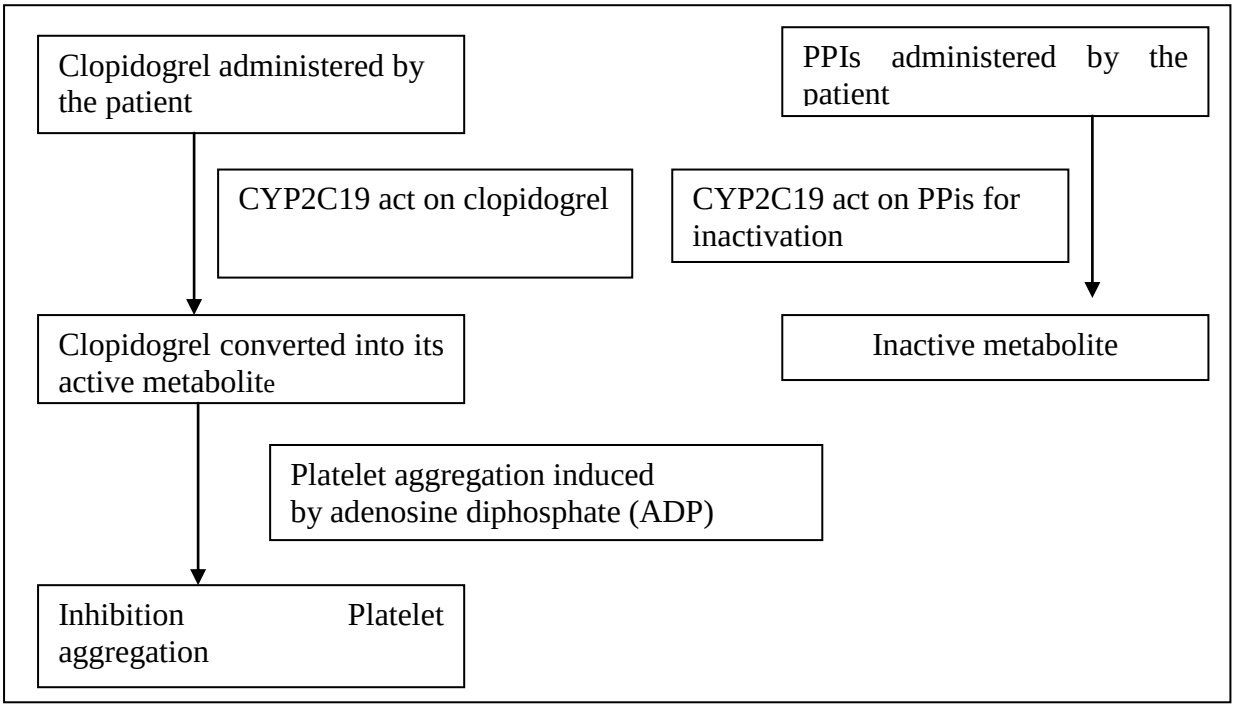
Potential Interaction between Clopidogrel and Proton Pump Inhibitors: A review

Clopidogrel is widely used in patients with acute coronary syndromes and following percutaneous coronary intervention with stent implantation. The antiplatelet action of clopidogrel is felt to be of critical importance for the reduction of abrupt thrombotic occlusion of stents, particularly with drug-eluting devices. Proton-pump inhibitors (PPIs) and clopidogrel are frequently co prescribed, although the benefits and harms of their concurrent use are unclear. Although the current evidence remains controversial, the potential for increased risk of thrombotic complications warrants cautious use of this drug combination until further research can determine the extent of this interaction and whether it is a drug-class effect. **This article will review the mechanism behind interaction of clopidogrel and PPis:**

The liver enzyme CYP2C19 converts clopidogrel prodrug to an active metabolite, and reduced CYP2C19 activity has been correlated with inhibition of platelet aggregation and increased cardiovascular events. All available PPIs are s a moderately strong CYP2C19 inhibitor. **The basic mechanism of this interaction is described in following diagrams:**

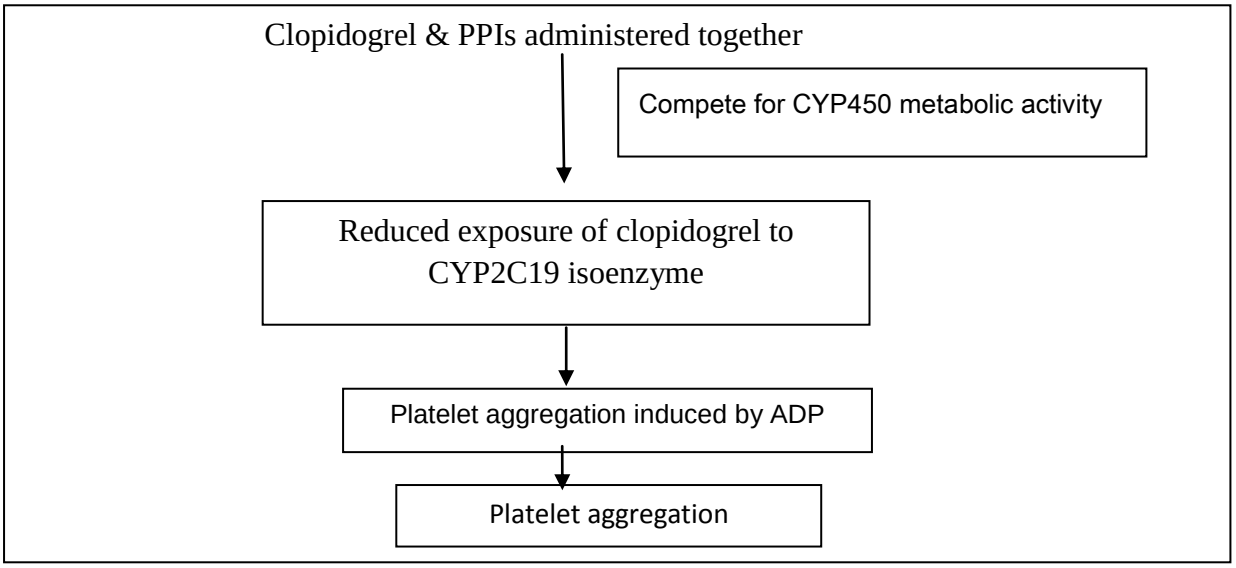
1. Role of CYP2C19 in clopidogrel and PPIs metabolism:
The biotransformation of clopidogrel to its active metabolite requires the hepatic cytochrome P450 2C19 isoenzyme.

Diagram 1 Role of CYP2C19 in clopidogrel and PPIs metabolism



2. Interaction of clopidogrel with PPis and resultant reduce efficacy of clopidogrel:
According to first step it is understood that Clopidogrel must be converted by cytochrome P450 (CYP) enzymes into its active metabolite, which then prevents platelet aggregation induced by adenosine diphosphate (ADP). The inactivation of omeprazole (Prilosec) by the same CYP enzyme system leads to competitive inhibition of this process and can decrease this level of inhibition.

Diagram 2 basic mechanisms behind interaction



Therefore, Patients treated with clopidogrel who carry CYP2C19 loss-of-function alleles have reduced levels of the active metabolite of clopidogrel, decreased inhibition of platelet aggregation, and increased risk for major cardiovascular disease. All currently available PPIs are CYP2C19 substrates, and some inhibit CYP2C19 metabolism. Omeprazole cotherapy in patients undergoing percutaneous coronary intervention with stenting resulted in decreased formation of the active metabolite of clopidogrel and in attenuated platelet inhibition. Concomitant use of clopidogrel and PPIs should be avoided due to the potential for reduced clopidogrel active metabolite concentrations and reduced platelet inhibition. While the clinical implications remain to be determined, the use of proton pump inhibitors with clopidogrel without clear indication should be avoided (. Until more research is conducted, consider using a histaminergic (H2) blocker (except cimetidine) or antacid in place of PPIs in patients who require acid-lowering therapy.

So, the USFDA provided advisory statements for all healthcare professionals & patients while prescribing clopidogrel and PPIs together.

Until more data are available, the FDA has issued the following general recommendations:

(i) Healthcare providers should continue to prescribe and patients should continue to take clopidogrel as directed because clopidogrel has demonstrated benefits in preventing blood clots that could lead to a heart attack or stroke;

(ii) Healthcare providers should re-evaluate the need for starting or continuing treatment with a PPI, including omeprazole OTC (over-the-counter) in patients taking clopidogrel; and

(iii) Patients taking clopidogrel should consult with their healthcare provider if they are currently taking or considering taking a PPI, including omeprazole OTC.

References:

1. Potential Interaction between Clopidogrel and Proton Pump Inhibitors From, *American Journal of Cardiovascular Drugs: Drugs, Devices, and Other Interventions*, November 2009 retrieved from medscape.com

2. Proton pump inhibitor side effects and drug interactions: Much ado about nothing? Cleveland clinic journal of medicine volume 7 8, number 1, January 2011

3, Wayne A. Ray, Katherine T. Murray, Marie R. Griffin, Cecilia P. Chung, Walter E. Smalley, Kathi Hall, et.al; Outcomes With Concurrent Use of Clopidogrel and Proton- Pump Inhibitors A Cohort Study, Annals of Internal Medicine Volume 152, Number 6.

4. MICROMEDEX(R) Healthcare Series Vol. 146

क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्समधील संभाव्य देवाण-घेवाण - आढावा

महारोहिणीच्या गंभीर आजाराची लक्षणे आढळल्यास आणि महारोहिणीस काही डाग असल्यास क्लॉपिडोग्रेल हे औषध मोठ्याप्रमाणात वापरले जात असल्याचे आढळते. क्लॉपिडोग्रेलची प्लेटलेटविरोधी कृती महत्त्वपूर्ण आहे त्यामुळे रक्ताच्या गुटळ्या होण्याची प्रक्रिया मंदावते. क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्स सर्वसाधारणपणे एकाच वेळी दिले जाते. परंतू त्यावर अधिक संशोधन अजून झालेले नाही त्यामुळे ही औषधे बऱ्याच कालावधीसाठी देत नाहीत.

या लेखामध्ये क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्स या औषधांतील क्रिया-प्रक्रियांचा आढावा घेतला आहे - यकृतातील प्रथिन CYP2C19 क्लॉपिडोग्रेलला चयापचय योग्य बनवते. या प्रथिनाचा संबंध प्लेटलेट निर्मिती आणि हृदयातील व रक्तवाहिन्यांतील घटनांशी असतो. सर्व प्रोटॉन पंप इनहिबिटर्स नियंत्रितरित्या CYP2C19 इनहिबिटर्स असतात.

खालील तक्त्यात क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्स यांच्यातील कार्याचे वर्णन दिसते :-

1. क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्सच्या चयापचयात CYP2C19 चा सहभाग -

क्लोपिडोग्रेलच्या जैवरुपांतरणासाठी यकृतातील P450 2C19 आयसोएन्झाईम या सायटोक्रोमची गरज असते.

Diagram 1 (संदर्भ पृष्ठ क्र. 29)

2. क्लोपिडोग्रेलची प्रोटॉन पंप इनहिबिटर्सशी आंतरक्रिया आणि क्लोपिडोग्रेलची घटलेली उपयुक्तता -

क्लोपिडोग्रेलचे सायटोक्रोम P450 2C19 या प्रथिनाद्वारे □यापचयाचा घटक म्हणून प्रथम रुपांतर होणे आवश्यक असते त्याच्याकडून अडेनोसाईन डायफॉस्फेटमुळे वाढणारे प्लेटलेटचे प्रमाण वाढण्यास प्रतिबंध होतो. याच CYP प्रथिनामुळे ओमेप्रॅझॉलची निष्क्रीयता वाढते त्यामुळे या प्रक्रियेत व्यत्यय येतो व प्रतिबंधाची पातळी खाली येते.

Diagram 2 (संदर्भ पृष्ठ क्र.30)

त्यामुळे क्लोपिडोग्रेलचे उपचार सुरू असलेल्या रूग्णात CYP2C19मुळे प्रक्रियेत बाधा येत असल्यास हृदयविकारांची शक्यता वाढते. सध्या उपलब्ध असलेली सर्व प्रोटॉन पंप इनहिबिटर्स ही CYP2C19 ची घटक आहेत काहीं मुळे CYP2C19च्या चयापचयास प्रतिबंध होतो. महारोहिणीवर स्टेन्टींग केलेल्या रूग्णांवर ओमेप्रेझॉलचा वापर केल्यामुळे क्लोपिडोग्रेलच्या चयापचयात फरक पडत असल्यामुळे प्लेटलेट निर्मितीवर प्रतिबंधात व्यत्यय येतो. त्यामुळे क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्सचा एकत्रित वापर दीर्घकाळ करणे धोक्याचे ठरू शकते. यावर अधिक संशोधन होणे आवश्यक असल्याने सध्या हिस्टामिनेर्जिक (H2) ब्लॉकर (सिमेटीडीन विरहित) किंवा ॲसिडीटी कमी करणारी ॲन्टासीड वापरणे योग्य ठरेल.

त्यामुळे क्लोपिडोग्रेल आणि प्रोटॉन पंप इनहिबिटर्सच्या वापराबाबत अमेरिकन अन्न व औषध प्रशासनाने सावधगिरीचा इशारा दिला आहे. तो खालीलप्रमाणे -

अ) क्लोपिडोग्रेलचा वापर हृदयरोग्यांनीडॉक्टरांच्या सल्ल्याने करावा. त्यामुळे रक्तात गुठळी होण्यास प्रतिबंध -ोतो.

□) डॉक्टरांनी ओमेप्रेझॉल आणि क्लोपिडोग्रेल बरोबर प्रोटीन पंप इनहिबिटर्सचा वापर करण्याची खरोखरच गरज आहे का हे पडताळून पहावे.

क) क्लोपिडोग्रेल घेणाऱ्या रूग्णांनी त्यांना ओमेप्रेझॉल बरोबर प्रोटीन पंप इनहिबिटर्स दिली जातात का हे पहावे.

MAHARASHTRA STATE PHARMACY COUNCIL'S DRUG INFORMATION CENTRE

NOTIFICATION OF SUSPECTED ADVERSE DRUG REACTION

Patients Name : ---------- Age : ---------- Sex : ----------

Address & Contact Number :----------

Prescriber :----------

Suspected drug (s) :----------

Date of drug Started :----------

Date of adverse reaction Started :----------

Brief description of the reaction :----------

Name of the reporting Community Pharmacist :---------- ---------

Address & Contact No.:----------

Signature :---------- Date :----------

Please return this filled form to MSPC's Drug Information Centre, E.S.I.S. Hospital Compound, L.B.S. Marg, Mulund (W), Mumbai-400 080 Tel:25930607 Telefax: 25684291

Do you want to Subscribe Council's DRUG INFORMATION BULLETIN?

If yes, send us following information

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Address.....

Phone..... Fax..... E-mail.....

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Send additional Rs.75/- so total of Rs.175/- to receive four more booklets viz.*Drug Interaction Manual, Drugs Harmful In Pregnancy, Essential Drug List for Children* & Drugs harmful in hepatic and renal impairment with bulletin.

Note:- Demand Draft should be sent in favor of " Maharashtra State Pharmacy Council-DIC", E.S.I.S Hospital Compound, L.B.S. Marg, Mulund (West), Mumbai-400 080, Maharashtra"*[Cheques are not acceptable] OfficeTime:10.30am to 3.00pm (Mon-Fri) 10.30am to 1pm (Sat)*

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