

**A REVIEW ARTICLE ON IMPLANTABLE DRUG DELIVERY SYSTEMS****DR.B.V. RAMANA. \* K. ESWAR KUMAR.**

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**ABSTRACT:**

The conventional routes of drug administration have limited control over drug release and maintaining constant plasma therapeutic drug concentrations for longer periods of time. To avoid these problems associated with utilization of traditional dosage forms, there was essential need for development of new dosage forms which would discharge drugs at controlled rate for local activity. This led to improvement of Novel Drug Delivery Systems (NDDS) that offers optimisation of therapeutic properties of drugs and makes them safer, productive and dependable over traditional ways of administration. Implantable drug delivery system (IDDS) forms a part of novel drug delivery system. This route of administering medications allows targeted distribution, location specificity, constant release rate, low amount of drug requirements, and minimisation of adverse effects with improved efficacy. It provides possibility of administering drugs once weekly to yearly which otherwise previously require frequent daily dosing. Different implantable technologies are currently in use for many therapeutic applications such as in dentistry, ophthalmology, contraception and oncology. However, the expensiveness of this newly improved drug delivery system is quite high which hinders its large-scale use. Moreover, the recently developed devices require further enhancement and hence thorough scientific trials are needed before wide implementation in populations.

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**Keywords:** Implantable drug delivery, implants, drug delivery system, implantable pump, modulated drug delivery, novel drug delivery system.

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**INTRODUCTION:**

Despite of progression and innovations in novel administration of drugs, regulation of constant uniform plasma therapeutic index of drugs is still a big concern. The potential harm of using periodic oral or IV drug administration comprises of elevated concentration of medication (peaks) which contribute to adverse effects or inadequate concentration of medication (troughs) which can lead to failure of therapy. The

old way to overcome the issue of the variable concentrations of medication includes constant intravenous infusion rate dependent on medication pharmacokinetic profile. In order to minimise these unwanted outcomes, there is a need of modern approach in achieving optimized rate of drug discharge. Implantable drug delivery systems have potential superiority in regional administration with better pharmacologic outcomes at minimum doses

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Due to which, they lower possible toxicities thereby improving likelihood for medication adherence. This kind of administration enables convenient delivering of medications that are ordinarily incompatible to be taken by oral way, escapes presystolic elimination as well as enzymatic destruction in abdomen, thus, remarkably enhancing bioavailability.

Implantable devices have ability to minimise the need of frequent drug intake as well as authorize medication needs with approachable way. At present, these devices are commonly employed in many therapeutic areas such as contraception, chemotherapy, dentistry etc. The expanding production and market availableness of implants are evident of immense growth in this sector.

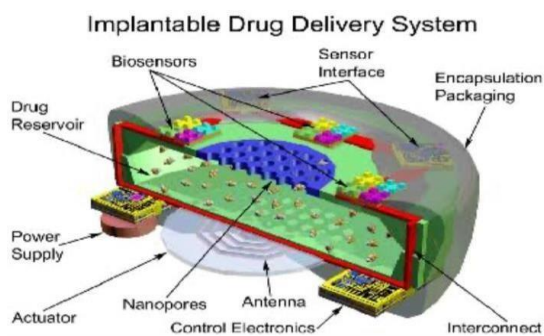


Fig 1: Implantable drug

delivery system.

The ideal requirements of an implantable device are:

- Exhibit zero order or modulated drug release kinetics

for constant delivery rate to minimise adverse effects.

- The dosing frequency shall be minimised for enhancing patient adherence and must fully discharge the medication during duration of therapy. Safe, stable and effective with good mechanical strength.
- Minimum dose is required.
- Reduced side effects

### DISADVANTAGES:

- Interaction b/w host and implant.
- Treatment cannot be abruptly stopped.
- Possibility of inadequate release of drug.
- Predicted danger of device failure.

### Limitations:

- Chances of toxicity.
- Painful.
- Dose tapering is not easy in case of need
- Need for surgery to insert the device

### Classification of implantable polymeric drug delivery device system.

Polymers are the key elements in implantable systems as they provide extended and optimised drug release. They act as rate-limiting membrane in implant system and the choice of which

must be done in keeping view of host biocompatibility and ease of sterilization.

The polymers in implants are mainly categorised into two major groups – passive polymeric implants:

They are simple, singular and uniform devices, mainly contains simple drug loaded in biocompatible matrix. They do not have any mobile part or technique and depend on passive diffusion for release of drug load. Passive devices can be subcategorized as nonbiodegradable and biodegradable

## 2.Active or dynamic polymeric implants:

This kind of Implantable use definite propulsion in regulating discharge of medicine across the aid. Thus, it offers advanced standard in drug discharging. They use some sorts of energy dependent methods for positive impulse to regulate discharge. The power origin can range different from osmotic pressure gradient to electromechanical forces.

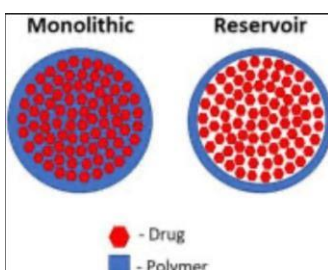


Fig 2 : monolithic and reservovir.

## Implant pumps :

Various drugs need exterior source to control amount and expulsion which is

not achieved by biodegradable or nonbiodegradable systems except in magnetically modulated devices. The presence of sophisticated microsystems has made easy in designing pumps as little adequate that it can be implanted hypo dermally to deliver drugs.

Pumps discharge medications via pressure difference which is obtained by pressing the reserve either osmotically or mechanically resulting in flow of drug at optimised way. The pumps should possess desirable properties like noninflammatory, non-thrombogenic, nonantigenic, noncarcinogenic, convenience, long reserve and battery life, easily organisable, and can be inserted using local anaesthesia. It should also be simple to check the condition and working of the system. Hence, pump systems deliver drugs with ideal precision.

Presently five groups of implant pumps are present. These pumps are infusion, osmotic, peristaltic, positive displacement and modulated discharge microsystems.

## Types of implants pumps:

### Infusion pump:

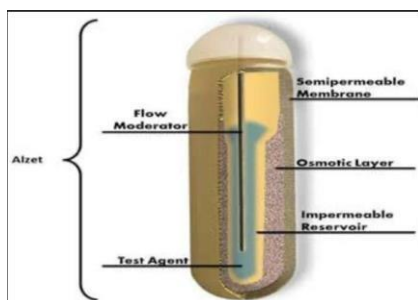
Infusion pumps distribute the stored medicament inside the body with the help of a fluorinated hydrocarbon as energy source. They were earlier used in delivering insulin to diabetic people who

need more than one dose in a day. This results in plasma peaks and troughs of insulin which may lead to diabetes induced complications.

The pump contains disc-like container constructed by lightweight bio composite titanium that comprises of foldaway that divides the container interiorly in two isolated compartments. The former compartment comprises of the energy source while the latter stores insulin. A gas forces the stored drug to expel via sif and course controller which gives optimised drug delivery at a mentioned temperature. It does not require external source of energy to drive the pump. A load of stored dose is released across a silicone rubber membrane that itself seals then moved across a Teflon layer when pump stock is refilled. The device is recharged by the force of the delivery drive that pressurises the device. Apart from application in insulin delivery, it is found useful in field of anticoagulation and chemotherapy.

**Osmotic pump:**

Fig3: osmotic pump

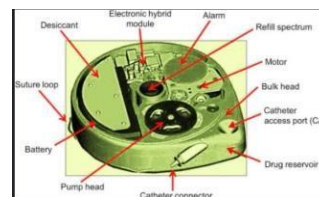


Osmotic pumps are extensively prevalent of all implant types. These devices involve medication confined in a selectively permeable membrane that permits an inward movement of aqueous fluids in the device by simple osmosis. The built hydrostatic pressure forces invariable expulsion of medication

through an orifice in membrane of system and whose swiftness in discharge can be altered by modifying the structure of semi-permeable membrane. However, the pace of discharge remains persistent or zero order till stored load is been exhausted

**Peristaltic pumps:**

Fig 4 peristaltic pumps



Peristaltic pumps work by external source of power mainly by batteries and consist of cylindrically rotating apparatus. An exterior source modulates the flow of drug from it. This class of pumps are made of a rubber membrane of silicone and their duration of use is dependent on the battery as energy source used. These systems are quite expensive to be used in standard practice in market.

**Mechanism of drug discharge from implant devices.**

There are primarily four ways of medication discharge through the implant devices – polymer disintegration, optimized expansion, osmosis and simple diffusion. Implants acting by optimized expansion, water absorption in device controls drug discharge which is generally inadequate over normal dispersion and thus contributes to a steady proportion of release. The

disintegration of expanded matrix allows diffusion of drug mainly and improving the disintegrating capacity of the matrix significantly enhances the efficiency of the implant.

Osmosis mediated release and free diffusion techniques of drug release are appropriate for delivering drugs linearly where the quantity of liberated drug relies proportionally to square root of discharge duration. Osmosis is simple passage of aqueous molecules from an area of low concentration to a greater concentration via a semipermeable membrane which creates a pressure gradient. Diffusion works by process in which solute moves voluntarily in all areas to saturate chemical composition. The mobile substances are called diffusants and a membrane through which diffusants travels is known as diffusional barrier. The concentration gradient is the impulsion for the release of medicament from system. However the discharge profile of drugs depends upon contents of delivery system which in turn relies on factors like imbibition, osmotic pressure, and passive diffusion, and molecules stability, diffusion coefficient in polymer, drug content, and disintegration rate of polymer in vivo.

**Methods of implant manufacture.**

The important methods of preparation of implants are described below:

**Hot melt extrusion:**

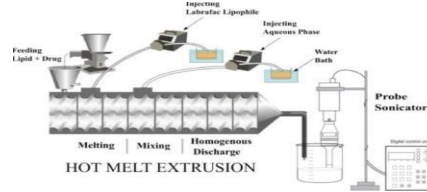


Fig 5: hot melt extrusion.

The drug is made to dissolve in an appropriate solvent to make a solution mixture. Then polymer is slowly incorporated and allowed to soak for 15-20 minutes. The swollen product is mixed thoroughly till it forms like dough and moved into ejection cylinder and elongated rod-like structure is obtained with use of showerhead. The product is made to dry overnight at ambient temperature and trimmed into required dimensions.

**compaction.**

The drug with polymer are diffused to make a suspension and subjected to lyophilisation to produce a cake. It is further exposed to compaction to derive an implant by Carver hydraulic machine with a force of a metric ton. It offers advantage of no usage of heating and solvents thus ideally compatible for designing implants that embody thermo labile matter notably proteinaceous content. These implantable show a quick release profile which necessitates optimisation by layering them. Additionally, implants produced have asymmetrical appearance having numerous cavities that can further

contribute in unsteady discharge.

### **Moulding.**

The polymeric material is subjected to heating then incorporated in form of a mould followed by solidification. A decrease occurs in relative molecular mass of the polymers due to high heat applied. Molecular mass as well as dispersability may be lowered using different ways and is furthermore amplified by this method. Due to which, these types of implantables disintegrated earlier as compared to factory-made mistreatment injections moulding

### **3D Printing:**

It is an inexpensive, consistent and versatile procedure and can be useful in

$$\text{swelling index} = \frac{w_2 - w_1}{w_1} \times 100$$

future especially in quick manufacture of standard units for investigatory purposes. However, it is not used in mass production but its suitability progressed in 2015 when FDA approved one such material. This technique is mainly applied in creating prostheses and implants used in dentistry and orthopaedics.

### **Evaluation parameters of implants:**

Various parameters are implemented in the evaluation of implants after manufacture by any appropriate method. These are as follows :

**Shape and size:** The size of an implant is verified using Vernier Callipers under light

**Uniform Thickness:** The individual thickness of separate implants as well as the variations among them is determined by using Vernier Callipers. At least three specimens must be determined and average value is found out

**Uniform Weight:** The aim of this test is to calculate the uniform weight of each implant. The test is performed by random selection of twenty implants and weighing them separately. Mean weight is obtained. From the results, two implants must not weigh more than the mean weight and none of them must have twofold value of mean.

**Swelling Index:** A specimen is placed in swelling solution of phosphate buffer pH

7 for an hour and the weight is estimated. The remaining solution is cautiously removed by gently cleaning with dry sheet. The magnitude of swelling for every unit at any instant is determined by given formula:

Where,  $W_2$  and  $W_1$  represent the specimen's mass at specified instant and in dried form, correspondingly.

**E In-vitro dissolution profile:** In-vitro dissolution profile of the implant is crucial in estimation of release and the stability of drug. Dissolution medium is taken in a container while optimal conditions and RPM are fixed. The implant is placed in the vessel and the



paddle is rotated. The samples are taken out after specific time intervals. The samples are thereafter examined by UV visible spectrophotometry at a particular wavelength. The procedure is repeated for at least three observations and the average value is noted.

**F Stability testing:** This test is done to detect disparities in standard of drug accompanied by time and storage characteristics like temperature, moisture, light, shelf life, etc.

**G.Interaction analysis between polymer and drug:**

Implant containing drug is analysed using FTIR for finding suitability of drug with other formulation components and possibility of such interactions.

Ideal properties of implantable drug delivery systems:

- Environmentally stable
- toxic and non-carcinogenic
- Biocompatible  
Biostable.

**Classification: Mechanism of drug release from implantable**

**therapeutic system: 1.Diffusion**

**Controlled System.**

- Polymer membrane permeation controlled implantable delivery system
- Polymer matrix diffusion controlled

implantable delivery system

- Membrane-matrix hybrid type implantable delivery system
- Micro reservoir partition controlled implantable delivery system
  - Hydrophilic reservoir/Lipophilic matrix
  - Lipophilic reservoir/hydrophilic matrix

**2.Activation Controlled System.**

- Osmotic pressure activated drug delivery system
- Vapor pressure activated drug delivery system
- Magnetically activated drug delivery system
- Hydration Activated drug delivery system
- Hydrolysis activated drug delivery system

**Classification based on Route of Administration:**

Subcutaneous  
Implants-Grafted  
beneath skin for  
prolong  
drugtherapy.ex.  
Norplant  
subdermal



implant

Intraocular Implants/Inserts- implanted/inserted in eyeex- Ocuserts

Intravaginal Implants- inserted in vagina

Intrauterine Implants- inserted in uterus ex. Copper-T

**polymembrane permeation controlled implantable delivery system.**

Drug reservoir is totally encapsulated within a capsule shaped or spherical compartment with a rate controlling polymeric membrane.

The encapsulation of the drug reservoir system inside the polymeric membrane can be done by the encapsulation, microencapsulation, molding, extrusion etc.

Example: Norplant subdermal implant-implantation of 6 units of Norplant subdermal implant in the subcutaneous tissue of human's arm.

**Polymer matrix diffusion controlled implantable drug delivery system.** This type of implants are formed by dispersion of the solid particles throughout a polymer matrix, They are of following types :

- Hydrophilic swellable polymers
- Lipophilic polymers non swellable polymers

- Porous polymers

It can also be prepared by :Taking drug polymer dispersions are then molded or extruded to form drug delivery devices of various shapes or dissolving the drug and polymer in an organic solvent followed by conservation or solid evaporation at an elevated temperature under a vacuum to form microsphere.

**Example:** Compudose implant. - It is a cylindrically-shape implant in which estradiol crystals are dispersed in a viscous silicone elastomer and coated in rigid (drug-free) silicone rod by extrusion that improves growth rate

**Membrane-matrix hybrid type implantable drug delivery system.**

This delivery system is a hybrid form of polymer membrane permeation controlled delivery system and the polymer matrix permeation controlled drug delivery system.

It shows the constant drug release kinetics just like the polymer membrane permeation controlled drug delivery system.

These are also prepared by the homogeneous dispersion of the drug solid particles throughout

a. this reservoir polymer matrix is encapsulated within a rate controlling polymeric membrane. This is actually a sandwich type implantable device.

**Example:** Norplant II subdermal implant.

**Microreservoir Partition Controlled Implantable Delivery System:**

- In this device the drug reservoir is a suspension of drug crystals in an aqueous solution of water miscible polymer & it also forms a homogeneous dispersion.
- Microdispersion is obtained by the high energy dispersion technique. size and shapes of drug delivery devices can vary further coated with a layer of biocompatible polymer to modify the mechanism & the rate of drug release.
- It is fabricated by dispersing the drug reservoir, which is a suspension of norgestomet in anaqueous solution of PEG 400, in a viscous mixture of silicone elastomer.

**Example:** Syncromate implant. Ex. Syncromate –

### Osmotic Pressure Activated Drug Delivery System:

- Osmotic pressure is the main source of energy in this case to activate and modulate the delivery of drug. The drug reservoir is either solution or semi solid formulation which is contains with semipermeable compartment with

controlled water permeability.

Example alzet osmotic pump.

### Vapour Pressure Activated Drug Delivery System:

- In this device the vapor pressure is mainly used as the power source to activate the controlled delivery of drugs.
- The drug reservoir contains a solution. The reservoir stays inside an infusate chamber
- Infusate chamber is physically separated from the vapour pressure chamber by freely movable bellows.
- Vapour pressure chamber contains a vaporizable fluid viz. Fluorocarbon.
- Fluorocarbon vaporizes at body temperature and & creates the vapour pressure which will forcefully move the bellow in upwards direction.
- Therefore the drug solution enters into the cannula at a constant flow rate and we can calculate the flow rate with the help of the equation.

### Magnetically Activated Drug Delivery System:

- Electromagnetic energy is used as the activation source to trigger the drug delivery.
- It contains a homogeneous

dispersion of a drug with low polymer permeability at a rather high drug-polymer ratio to form hemispherical pellet.

- The external surface of the hemispherical pellet is totally covered with a pure polymer, viz. Ethylene vinyl acetate copolymer.
- By applying an external magnetic field the drugs are activated by the electromagnetic energy to release from the pellet at a much higher rate of delivery.
- **Example:** Bovin serum albumin (BSA) is generally given by the help of this device.

### Hydration Activated Drug Delivery System:

In this type of device drug molecules are released upon activation by hydration of the drug delivery device by tissue fluid at the implantation site.

- This device is generally prepared from the hydrophilic polymer.
- Drug molecules are released by the diffusion through the water saturated pore channels in the swollen polymer matrix.
- **Example:** Norgestomet releasing hydron implant for estrus synchronization in heifers.
- This subdermal implant is

extremely small in size and can be easily implanted into the animal's ear flap (dorsal side).

- The drug release is activated by the hydrolysis.
- This hydrolysis is generally happened on the polymer base by the application of the tissue fluid at the implantation site.
- the drug delivery device is fabricated by dispersing a loading dose of drugs in micronized form in biodegradable polymer and then it is molded into a pellet or beadshaped implant.

### Lupron Depot 3.75 Mg Intramuscular Syringe Kit :

This medication is given by injection into a muscle by a health care professional. It is given as directed by your doctor, usually once every month.

This product slowly releases the medication into your blood over a 1-month period.

If you are using this medication at home, learn all preparation and usage instructions from your healthcare professional and the product package. Learn how to store and discard medical supplies safely.

Wash your hands properly mix the medication. Before injecting each



dose, clean the injection site with rubbing alcohol. Change the injection site each time to lessen injury under the skin. Inject each dose within 2 hours of mixing. If more than 2 hours have passed since mixing.

The length of treatment is based on your medical condition, response to treatment, and lab tests. Use this medication regularly to get the most benefit from it. To help you remember, mark your calendar to keep track of when to receive the next dose. During the first few weeks of treatment, your hormone levels will actually go up before they go down. This is a normal response to this medication. Your symptoms may get worse for a few weeks. Tell your doctor if your condition does not get better or if it gets worse. It may take at least 3 months for your symptoms to get better.

## Side Effects

Hot flashes (flushing), increased sweating, night sweats, tiredness, headache, stomach upset, breast changes, acne, joint /muscle aches, trouble sleeping, reduced sexual interest, vaginal discomfort/dryness, swelling of the ankles /feet, dizziness or mild burning/pain/bruising at the injection site may occur. If any of these effects last or get worse, tell your doctor or pharmacist promptly.

When this medication is used regularly, your menstrual period should stop (or bleeding should get lighter). Menstrual periods usually return within 3 months after treatment is stopped. Tell your doctor promptly if regular periods continue during treatment with leuprolide

Remember that this medication has been prescribed because your doctor has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.

Tell your doctor right away if you have any serious side effects, including: mental/mood changes (such as depression, thoughts of suicide, mood swings, aggression), new/worsening bone pain, easily broken bones.

Get medical help right away if you have any very serious side effects, including: seizures

A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction including: rash, itching, swelling (especially of the face, tongue /throat), severe dizziness, trouble breathing

This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor or pharmacist. In the US - Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or at [www.fda.gov/medwatch](http://www.fda.gov/medwatch).



## Precautions

Before using leuprolide, tell your doctor or if you are allergic to it; or to similar drugs (such as histerrilin triptorelin); or if you have any other allergies This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist formore details.

Leuprolide may weaken your bones and increase your risk for bone loss (osteoporosis) if used for a long time. Before using this medication, tell your doctor or pharmacist if you have osteoporosis or if you have any of the following risk factors for osteoporosis: long-term alcohol use, smoking, family history of osteoporosis and broken bones, use of certain medication (for example, corticosteroids such as prednisone certain anti seizure drugs such as phenytoin).

This drug may make you dizzy. Alcohol or marijuna (cannabis) can make you more dizzy. Donot drive, use machinery, or do anything that needs alertness until you can do it safely. Limit alocholic beverages. Talk to your doctor if you are using marijuana (cannabis).

Drug interactions may change how your medication work or increase your risk for serious side effects. This document does not contain all possible

drug interactions. Keep a list of all the products you use (including prescription/nonprescription drugs and herbal products) and share it with your doctor and phramacist Do not start, stop, or change the dosage of any medicines without your doctor's approval.If someone has overdosed and has serious symptoms such as passing out or trobule breasting call 911. Otherwise, call a poison control center right away. US residents can call their local poison control center at 1-800-222-1222. Canada residents can call a provincial poison controlcenter.

## Notes :

Do not share this medication with others.

Lab and/or medical tests (such as hormone levels, bone tests, cholesterol/triglyceride levels) should be done while you are using this medication. Keep all medical and lab appointments. Consult your doctor for more details.

## Missed Dose:

It is important to get each dose of this medication as scheduled. If a dose is missed, ask the doctor or pharmacist right away for a new dosing schedule. Do not double the dose to catch up.

## Storage:

Store at room temperature away from



light and moisture. Do not store in the bathroom. Once mixed, use the medication right away. Keep all medication away from children and pets. Do not flush medications down the toilet or pour them into a drain unless instructed to do so. Properly discard this product when it is expired or no longer needed. Consult your pharmacist or local waste disposal company.

## **Zoladex Implant:**

This medication is an implant that slowly releases hormone into your body. It is placed by a health care professional by injection under the skin of the lower abdomen below the navel. The implant itself will be completely absorbed into the body over weeks or months.

Receive this medication as directed by your doctor. The 3.6-milligram syringe is usually injected every 4 weeks. The 10.8-milligram syringe is usually injected every 12 to 13 weeks. Follow the dosing schedule carefully to get the most benefit from it. To help you remember, mark your calendar to keep track of when to receive the next dose. Do not stop this medication without your doctor's approval.

The dosage is based on your medical

condition and response to treatment.

During the first few weeks of treatment, your hormone levels will actually increase before they decrease. This is a normal response by your body to this drug. This may cause new or worsening symptoms (such as increased pain, increased difficulty urinating in men) for the first few weeks. Tell your doctor right away about these symptoms. See also Side Effects section.

In women, menstrual periods should stop when this medication is used regularly. Tell your doctor promptly if regular periods continue after 2 months of treatment with goserelin.

Usually, this medication will not need to be removed because the implant will be slowly and completely absorbed by your body. However, in the unlikely event that you have serious side effects or other problems, your doctor may remove this medication.

Tell your doctor if your condition gets worse.

## **Side Effects**

Hot flushes (flushing), dizziness, headache, increased sweating, decreased sexual interest/ability, trouble sleeping, nausea, change in breast size, vaginal, or hair loss may occur. Pain, bruising, bleeding, redness, or swelling at the injection site may also occur. If any of these effects last or get



worse, tell your doctor or pharmacist promptly.

Remember that this medication has been prescribed because your doctor has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have any side effect.

Tell your doctor right away if you have any serious side effects, including: vaginal burning/pain, pain during sex (in women), breast pain tenderness, new/worsening bone pain, new broken bone, burning feeling in feet/toes, swelling of the ankles feet, unusual tiredness, signs of kidney problems (such as change in the amount of urine), stomach/abdominal or swelling, mental/mood changes (such as depression mood swings, hallucination).

This medication may rarely make your blood sugar rise, which can cause or worsen diabetes. Tell your doctor right away if you have symptoms of high blood sugar such as increased thirst/urination. If you already have diabetes, check your blood sugar regularly as directed and share the results with your doctor. Your doctor may need to adjust your diabetes medication, exercise program, or diet. In men using this medication for

prostate cancer rare but very serious urinary blockage problem or spinal cord problem (compression) can occur, especially during the first month of treatment. Tell your doctor right away if you have any of the following serious side effects: severe back pain, numbness/tingling/weakness of the arms/legs, inability to move, painful/difficult urination, blood cancer.

A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction including: rash, itching/swelling (especially of the face/tongue /throat), severe dizziness, trouble.

### **Precautions :**

Before using goserelin, tell your doctor or pharmacist if you are allergic to it; or to LHRH or

LHRH-like hormones (such as triptorelin); or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist for more details.

Before using this medication tell your doctor or pharmacist your medical history, especially of: unexplained abnormal vaginal bleeding, diabetes, long-term alcohol use, smoking, personal or family history of bone loss



(osteoporosis), heart disease (such as heart attack), high cholesterol triglyceride levels, stroke urinary blockage problem (in men), spinal cord problem (in men), mental/mood problems (such as depression).

If you have diabetes, this drug may make it harder to control your blood sugar. Check your blood sugar regularly as directed and share the results with your doctor. Tell your doctor right away if you have symptoms of high blood sugar (see Side Effects section). Your doctor may need to adjust your diabetes medication, exercise program, or diet.

Low levels of potassium or magnesium in the blood may also increase your risk of QT prolongation. This risk may increase if you use certain drugs (such as diuretics/"water pills ") or if you have conditions such as severe sweating, diarrhea, or vomiting. Talk to your doctor about using Gosselin safely.

### **Interactions**

Drug interactions may change how your medications work or increase your risk for serious side effects. This document does not contain all possible drug interactions. Keep a list of all the products you use (including prescription/nonprescription drugs and herbal products) and share it with your doctor and pharmacist. Do not start,

stop, or change the dosage of any medicines without your doctor's approval.

Does Zoladex

Implant interact with other drugs

you are taking?

Enter your

medication into the

WebMD interaction

checker

### **Overdose:**

This implant may be harmful if swallowed. If someone has swallowed it and has serious symptoms such as passing out or, call 911. Otherwise, call a poison control center right away.

US residents can call their local poison control center at 1-800-222-1222.

Canada residents can call a provincial poison control center.

### **Notes:**

Lab and/or medical tests (such as blood sugar ,hormone levels) should be done while you are using this medication.

Keep all medical and lab appointments.

Consult your doctor for more details.

### **Missed Dose :**

It is important to get each dose of this medication as scheduled. If you miss a dose, ask your doctor or pharmacist right away for a new dosing schedule.

Sudden/unusual vaginal bleeding (breakthrough bleeding) may occur if a dose is missed.

### **Storage:**

Different brands of this medication





have different storage needs. Check the product package for instructions on how to store your brand, or ask your pharmacist. Keep all medication away from children and pets.

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