隆我心® 注射剂
Lanoxin® Digoxin Injection 0.5mg B.P.

【成分名（中文名）】Digoxin（長葉毛地黃苷）

【劑型、含暈】注射剤：每毫升含Digoxin 0.25mg

【臨床藥理】
1. Digoxin於治療劑量下可產生以下兩種主要作用：
   (1) 心肌收縮力和速度的增加：一般認為，這種增加是由于心肌細胞內鈣的流入和離鈣離子之釋出的增加，使得心肌收縮肌細胞的活性增加所致。
   (2) 心肌組織之電生理學特性提高：一般認為，這種作用是由于鈣離子與三磷酸腺苷酸（Adenosine Triphosphatase）結合而使鈣離子通過心肌細胞膜之移位受抑制所致。房室及室內節律傳導速度減低，並使心室敏感度增加，此外，也由於Digoxin之直接及間接作用所致。

2. Digoxin之治療與中毒血清濃度如下：

<table>
<thead>
<tr>
<th>藥物</th>
<th>血清濃度 (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>治療</td>
<td>0.5-2.5</td>
</tr>
<tr>
<td>中毒</td>
<td>&gt;2.5</td>
</tr>
</tbody>
</table>

3. 給予Digoxin之治療劑量（Loading Dose）之前，必須確定病人在2-3星期前是否曾使用任何Digitalis製剤，由於殘餘效應，須減低劑量以避免產生毒性。

4. Digoxin之治療量應依照體重之基礎計算。

5. 推薦劑量僅為平均值，各劑量應依個別病人需要調整。

6. 不整脈之電性轉變（Electrical Conversion of Atrrhythms）須調整Digoxin之劑量。Digoxin中毒之病人一般對Electric Counterblock較具敏感性。

7. 测定法對於Digoxin在體內迅速清除無效。

8. 由於Digoxin引致之嚴重及完全的心室傳導阻斷存在下，鈣之補充可能會有危險。

9. 腎功能不全、年老、使用電子心節律器或維護之病患於使用本藥時，則其它病患可以耐受之劑量或血清濃度下，可能出現毒性反應，因此其療程需小心加以標定。

10. Digoxin是對療法治療中樞神經系統的副作用處之一重要原因。

11. Digoxin用於治療肥溼性及中樞神經系統，為因這些疾病會引發發生於治療的治療，因為這些藥物會引起膜透透腦部的不整脈有其它副作用。

12. 中樞神經系統在5-10分鐘內可感禆到藥效，此作用在1-10分鐘達到高峰。

13. 正常腎功能病人，Digoxin末期排泄半衰期為30-40小時，腎功能障礙及限於排泄的病人，半衰期可能延長至100小時。

【適應症】
心衰竭、心房撓動、心房纖維性顫動、陣發性心室性心頸過速。

【用法用量】
本藥限由緊急使用。

緊急注射及靜脈滴注劑量：（對於前後二星期內未曾服用強心醣類之病人）注射量之計算應從500到1000μg（0.5至1.0mg），依年齡、體重及腎功能而定。負荷量應於分次給予，第一次約於劑量後兩小時內注入，其它剰量則依4至8小時的間隔分次注入，每給予一次靜脈注射皆應評估臨床反應，第一次剰量應於靜脈輸注10至20分鐘的速度。

第一次剰量應使用靜脈輸注10至20分鐘的速度。

維持剰量：負荷剰量應依下表投予：

<table>
<thead>
<tr>
<th></th>
<th>1.5-2.5公斤之未足月新生兒</th>
<th>30μg/kg/24小時內</th>
</tr>
</thead>
<tbody>
<tr>
<td>足月新生兒及2歲兒童</td>
<td>30μg/kg/24小時內</td>
<td></td>
</tr>
<tr>
<td>5-10歲兒童</td>
<td>35μg/kg/24小時內</td>
<td></td>
</tr>
</tbody>
</table>

負載剰量應分次投予，第一次約投於劑量後兩小時內注入，其它剰量依4至8小時的間隔分次注入，每給予一次靜脈剰量皆應評估臨床反應，第一次剰量應於靜脈輸注10至20分鐘的速度。

【監測】
Digoxin的血藥濃度可用μg/ml之Conventional Units或nmol/L之SI單位表示。μg/ml=1.28×nmol/L；Digoxin的血藥濃度可用mg/ml之Conventional Units或nmol/L之SI單位表示。mg/ml=1.28×nmol/L。Digoxin的血藥濃度可用放射免疫測定法測定。

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【注意事項】

【禁忌】
1. 禁用於體敏性完全心阻斷或二級房室阻斷，尤其是有Stokes-Adams發作病史之病人。

2. 禁用於因心肌醣體中毒引起之心律不整。

3. 禁用於營養不良或營養不良者之心理不整。例如：Norfolk-Parkinson-White症候群。除非能夠評估適當之副反應及Digoxin對該些症狀之處方，否則應限制使用。未有上中高心律不整者，使用時須小心使用。

4. 禁用於肥厚性阻塞性心肌病變，除非在同時有心房纖維顫動及心衰竭時，使用時須小心使用。

5. 禁用於對Digoxin或其它Digitalis製剤過敏之病人。
2. 孕婦及授乳婦女使用本品，尚無足夠報告有何副作用發生，但仍應就其危險與效益加以考慮。

FDA Pregnancy Category (懷孕冊級數)：C

3. 當下列醫療問題存在時，不可使用Digoxin：

(1) 腦中風、癲癇、肝機能異常
(2) 心室細編豎動
(3) 心肌梗塞

4. 當下列醫療問題存在，使用Digoxin須小心考慮：

肺功能不全、肝功能不全、糖尿病、心臟瓣膜病、心房黏液瘤、心房顫動、心絞痛

5. 使用Digoxin時，下列之檢測在病人之監視下特別重要：

血壓、心率、電圖(EGK)、血清電解質(特別是鈣和磷)

6. 病人須依照指示治療，除非在同一時間服用，否則不可無故逾時或間斷服用；若發生異常，應立刻通知醫師。

7. 許多人經常會將本藥物與其它外用藥物混淆不清，而造成嚴重意外。因此，為減少這種危險，處方開藥師應事を下列表現：

(1) 警告病人本藥的危險性
(2) 使用適當的見證於容器上，適當標示“心臟藥物”
(3) 相似類型之藥物使用不同大小或外觀之容器

8. 對於曾長期服用心臟配體相關藥物，應重新考慮其長期使用必要性，減少其類藥物使用。

9. 老年人或有其他疾病者使用Digoxin時，應重新考慮其使用必要性，其使用及維持用量皆應考慮減量，低血濃時會使心肌對強心配體作用特別敏銳，低血濃及血濃差異甚大時會增加心肌對強心配體的敏感性。

10. 靜脈注射或高血濃時可能引起血流凝固及產生高血壓及/或減少心搏血量，因此對於高血壓性血栓和急性心肌梗塞病人緩解靜脈注射十分必要。

11. 甲狀腺病患者使用時須小心，甲狀腺功能不全時應減少Digoxin初期及維持劑量。甲狀腺亢進病人具有可能Digoxin抗體故需增加劑量。在甲狀腺機能治療過程中，當甲狀腺機能亢進已控制時應減低劑量。接受抗血凝療程時或接受血塩療程時，病人可能需要較高劑量。由於血凝療程的療程對血塩療程的療程影響十分有限，因此對血塩療程的療程影響十分有限。

12. 適於在服用Digoxin前使用心電圖配體測試，應在電擊前暫停Digoxin 24小時。必要時，例如：心律不整，若無心電圖監測，應使用低濃度心電圖測試。對於治療期間達強心配體的作用時心律不整不能診斷，心律不整應延後24小時。

13. 肌肉注射有時會有肌肉痛，此現象通常不需特別治療。

14. 感到呼吸困難，可能會增加心肌對Digoxin之敏感性。

(對高齡者的給藥)

因對高齡者使用Digoxin中毒，應由少量開始投與，監測血中濃度 Marketable，應細心觀察並審慎投與。

(對孕婦及授乳婦女的給藥)

因對懷孕或授乳婦女使用Digoxin中毒，應由少量開始投與及監測血中濃度及電圖等，應細心觀察並審慎投與。

(適用症)

1. 一般使用Digoxin時，有時會造成出血傾向，有時會造成出血傾向，但大部分為輕微，偶爾會有嚴重出血傾向，偶爾會有嚴重出血傾向。

2. 對於心房顫動或心房顫動，已有藥物治療者，Digoxin能有效降低心房顫動及心房顫動，故應考慮使用Digoxin治療。

3. 对於心房顫動或心房顫動，已有藥物治療者，Digoxin能有效降低心房顫動及心房顫動，故應考慮使用Digoxin治療。

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8. Digoxin是Digoxin中毒的惟一專一治療藥且非常有效。

【主要作用】

Digoxin與Ampicillin B或Corticosteroids或非預期的Diuretics共用時，會提高伴隨低血氧血SodiumDigoxin之毒性可能性。

【副作用】

1. 頻繁嘔吐時，應減少投與，並應保持紙質便血，常見出現嘔吐、嘔吐或嘔吐。

2. 持續性嘔吐時，應減少投與，並應保持紙質便血，常見出現嘔吐、嘔吐或嘔吐。

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【貯存條件】

本品應裝於緊密容器內，避於陰涼(15-30℃)乾燥且保持於涼處。
**Lanoxin™ Formulations**

**To the Medical and Pharmaceutical Professions**

**Presentations**
- **Tablets:**
  - Lanoxin Tablets
  - White, round, bicarbon tablets, scored and impressed "WELLCOME X3A" and each containing 250 micrograms (0.25mg) Digoxin B.P.
- **Lanoxin-125 Tablets**
  - White, round, flat tablets impressed "WELLCOME Y3B" and each containing 125 micrograms (0.125mg) Digoxin B.P.
- **Lanoxin-PG Tablets**
  - Blue, round, bicarbonate tablets, impressed "WELLCOME U3A" and each containing 62.5 micrograms (0.0625mg) Digoxin B.P.
- **Oral Solutions:**
  - **Lanoxin-PG Oral Solution (Lanoxin-PG Elixir)**
    - A clear, yellow, lime-flavoured solution containing 50 micrograms (0.05mg) in each 1ml of sweetened, aqueous-alcoholic vehicle.
- **Injections:**
  - **Lanoxin Injection**
    - A clear, colourless, sterile aqueous solution containing 250 micrograms Digoxin B.P. per ml and supplied in a 2ml ampoule.

**Indications**

**Cardiac Failure**
Lanoxin is indicated in the management of chronic cardiac failure. Its therapeutic benefit is greatest in those patients with ventricular dilatation. Lanoxin is specifically indicated where cardiac failure is accompanied by atrial fibrillation.

**Supraventricular Arrhythmias**
Lanoxin is indicated in the management of certain supraventricular arrhythmias, particularly atrial flutter and fibrillation, where its major beneficial effect is reduction of the ventricular rate.

**Dosage and Administration**
The dose of Lanoxin for each patient has to be tailored individually according to age, lean body weight and renal function. Suggested doses are intended only as an initial guide. Lanoxin PG Oral Solution, 50 micrograms in 1ml, is supplied with a graduated pipette and this should be used for measurement of all doses.

**Adults and children over 10 years:**
- **Rapid Oral Loading**
  - 75 to 1500 micrograms (0.75 to 1.5mg) as a single dose.
  - Where there is less urgency, or greater risk of toxicity e.g. in the elderly, the oral loading dose should be given in divided doses 6 hours apart, assessing clinical response before giving each additional dose.
- **Slow Oral Loading**
  - 250 to 750 micrograms (0.25 to 0.75mg) should be given daily for 1 week followed by an appropriate maintenance dose. A clinical response should be seen within one week.

**Maintenance**
The maintenance dosage should be based upon the percentage of the peak body stores lost each day through elimination. The following formulae have been widely used:

**Maintenance dosage = Peak body stores x % daily loss**

\[ \text{Where} \quad \text{Peak body stores} = \text{loading dose} \times \left( \frac{100}{\text{% daily loss}} \right) \times \frac{1}{14} \times \frac{C_{cr}}{S_{cr}} \]

\[ C_{cr} = \text{creatinine clearance corrected to 70kg bodyweight or 1.73m}^2 \text{body surface area. If only serum creatinine values are available, a } C_{cr} \text{ (corrected to 70kg bodyweight) may be estimated in men as} \]

\[ C_{cr} = \left(140 - \text{age} \right) / S_{cr} \text{ (mg/100ml)} \]

**NOTE:** Where serum creatinine values are obtained in μmol/L, these may be converted to mg/100ml (mg %) as follows:

\[ S_{cr} \text{ (mg/100ml)} = \frac{100 \times S_{cr} \text{ (μmol/L)}}{88.4} \]


**Prohibitions/Warnings**
Arrhythmias may be precipitated by digoxin toxicity, some of which can resemble arrhythmias for which the drug could be advised. For example, atrial tachycardia with varying atrioventricular block requires particular care as clinically the rhythm resembles atrial fibrillation.

In some cases of sinoatrial disorder (e.g. Sick Sinus Syndrome) digoxin may cause or exacerbate sinoatrial dysrhythmia or cause sinoatrial block.

Determination of the serum digoxin concentration may be very helpful in making a decision to treat with further digoxin, but toxic doses of other glycosides may cross-react in the assay and wrongly suggest apparently satisfactory measurements.

Observations during the temporary withholding of digoxin might be more appropriate.

In cases where cardiac glycosides have been taken in the preceding two weeks the recommendations for initial dosing of a patient should be reconsidered and a reduced dose is advised.

The dosing recommendations should be reconsidered if patients are elderly or there are other reasons for the renal clearance of digoxin being reduced.

A reduction in both initial and maintenance doses should be considered.

Hypokalaemia sensitises the myocardium to the actions of cardiac glycosides.

Hyperkalaemia and marked hyperkalaemia increase myocardial sensitivity to cardiac glycosides.

Rapid intravenous injection can cause vasodepression, producing hypotension and/or reduced coronary flow. A slow intravenous injection is therefore important in hypertensive heart failure and acute myocardial infarction.

Administering Lanoxin to a patient with thyroid disease requires care.

Initial and maintenance doses of Lanoxin should be reduced when thyroid function is subnormal. In hyperthyroidism there is relative digoxin resistance and the dose may have to be increased. During the course of treatment of thyrotoxicosis, dosages should be reduced as the thyrotoxicosis comes under control.

Patients with malabsorption syndrome or gastro-intestinal resections may require larger doses of digoxin.

**Direct current cardioversion**
The risk of provoking dangerous arrhythmias with direct current cardioversion is greatly increased in the presence of digitalis toxicity and is in proportion to the cardioversion energy used.

For elective direct current cardioversion of a patient who is taking digoxin, the drug should be withheld for 24 hours before cardioversion is performed. In emergencies, such as cardiac arrest, when attempting cardioversion the lowest effective energy should be applied.

Direct current cardioversion is inappropriate in the treatment of arrhythmias thought to be caused by cardiac glycosides.

Many beneficial effects of digoxin on arrhythmias result from a degree of atrioventricular conduction block. However, in patients with left ventricular block the effects of a rapid progression in the block should be anticipated. In complete heart block the atrioventricular escape rhythm may be suppressed. The administration of digoxin in the period immediately following myocardial infarction is contra-indicated. However, the possibility of arrhythmias arising in patients who have been hypokalaemic after myocardial infarction and are likely to be cardiologically unstable must be borne in mind. The limitations imposed thereafter on direct current cardioversion must also be remembered.

Although many patients with chronic congestive cardiac failure benefit from acute administration of digoxin, there are some in whom it does not lead to consistent, marked or lasting haemodynamic improvement. It is therefore important to evaluate the response of each patient individually when Lanoxin is continued long-term.

The intramuscular route is painful and is associated with muscle necrosis. This route cannot be recommended.

Patients with severe respiratory disease may have an increased myocardial sensitivity to digitalis glycosides.

**Mutagenicity, carcinogenicity, teratogenicity**
No data are available on whether or not digoxin has mutagenic, carcinogenic or teratogenic effects; however, maternally-administered digoxin has been used to treat fetal tachycardia and congestive heart failure.

**Fertility**
There is no information available on the effect of digoxin on human fertility.

**Pregnancy and lactation**
The use of digoxin in pregnancy is not contra-indicated, although the dosage may be less predictable in pregnant than in non-pregnant women with some requiring an increased dosage of digoxin during pregnancy. With all drugs, use should be considered only when the expected clinical benefit of treatment to the mother outweighs any possible risk to the developing foetus.

Although digoxin is excreted in breast milk, the quantities are minute and breast-feeding is not contra-indicated.

**Adverse reactions**

**Noncardiac**
These are principally associated with overdosage but may occur from a temporarily high serum concentration due to rapid absorption. They include anorexia, nausea and vomiting and usually disappear within a few hours of taking the drug. Diarrhoea can also occur. It is advisable to rely on nausea as an early warning of excessive digoxin dosage.

Gynaecomastia can occur with long-term administration.

Weakness, apathy, fatigue, malaise, headache, visual disturbances, depression and even psychosis have been reported as adverse central nervous system effects.

Oral digoxin has also been associated with intestinal ischaemia and, rarely, with intestinal necrosis.

Skin rashes of urticarial or scarlatiniform character are rare reactions to digoxin and may be accompanied by pronounced anaphylaxis.
Cardiac Digoxin toxicity can cause various arrhythmias and conduction disturbances. Usually an early sign is the occurrence of premature ventricular contractions, which can proceed to bigeminy or even trigeminy. Atrial tachycardias, frequently an indication for digoxin, may occur with excessive dosage of the drug. Atrial tachycardia with some degree of atrioventricular block is particularly characteristic, and the pulse rate may not necessarily be fast. (See also Precautions/warnings).

Drug interactions These may arise from effects on the renal excretion, tissue binding, plasma protein binding, distribution within the body, gut absorptive capacity and sensitivity to Lanoxin. Consideration of the possibility of an interaction whenever concomitant therapy is contemplated is the best precaution and a check on serum digoxin concentration is recommended when any doubt exists. Agents causing hyperkalaemia or intracellular potassium deficiency may cause increased sensitivity to Lanoxin; they include diuretics, lithium salts, corticosteroids and carbamazepine. Serum levels of digoxin may be INCREASED by concomitant administration of the following - amiodarone, captopril, flecainide, propranolol, quinidine, spironolactone, tenofovir, etravirine, enalapril and others (possibly other antibiotics), and propranolol. Serum levels of digoxin may be REDUCED by concomitant administration of the following - antacids, kaolin-pectin, some bismuth preparations and cholestyramine, diphosphonate, sodium, cephalaxin, rifampicin, cyclosporines, fluocinolone, and penicillin.

Calcium channel blocking agents may either increase or cause no change in serum digoxin levels. Verapamil increases serum digoxin levels. Nifedipine and dilazep may increase or have no effect on serum digoxin levels. Isradipine causes no change in serum digoxin levels. Milrinone does not alter steady-state serum digoxin levels.

Overdosage Symptoms and signs See Adverse reactions: Treatment After recent ingestion, such as accidental or deliberate self-poisoning, the load available for absorption may be reduced by gastric lavage. An overdosage of digoxin of 10 to 15 mg in adults without heart disease and of 6 to 10 mg in children aged 1 to 3 years without heart disease appeared to be the dose resulting in death in heart in half the patients. If more than 25 mg of digoxin was ingested by an adult without heart disease, death or pronounced toxicity responsive to digoxin- and Fab antibody treatment (Digibind) occurred. If more than 10 mg of digoxin was ingested by a child aged 1 to 3 years without heart disease, the outcome was uniformly fatal when Fab fragment treatment was not given. If hypokalaemia is present, it should be corrected with potassium supplements either orally or intravenously depending on the urgency of the situation. In cases where a large amount of Lanoxin has been ingested hyperkalaemia may be present due to release of potassium from skeletal muscle. Before administering potassium in digoxin overdose the serum potassium level must be known. Bradycardias may respond to atropine but temporary cardiac pacing may be required. Ventricular arrhythmias may respond to lignocaine or phenytoin. Dialysis is not particularly effective in removing digoxin from the body in potentially life-threatening toxicity. Rapid reversal of the complications that are associated with serious poisoning by digoxin, digitoxin and related glycosides has followed intravenous administration of digoxin-specific (ovine) antibody fragments (Fab) when other therapies have failed. Digibind is the only specific treatment for digoxin toxicity and is very effective. For details consult the literature supplied with Digibind.

Pharmaceutical precautions and recommendations Storage recommendations Tablets: Keep at temperatures not exceeding 25°C. Oral Solutions: Keep at temperatures not exceeding 25°C. Injections: Keep at temperatures not exceeding 25°C and protect from light. Diluent Recommendations Lanoxin Injection: See Dilution. Lanoxin Oral Solutions (50µg/ml) and 100µg/ml Lanoxin-PC Oral Solution 50µg/ml (Lanoxin PC Elixir) and Lanoxin Oral Solution 100µg/ml should not be diluted. Further Information Intravenous administration of a loading dose produces an appreciable pharmacological effect within 5 to 30 minutes, this reaches a maximum in 1 to 5 hours. Using the oral route the onset of effect occurs in 0.5 to 2 hours and reaches its maximum at 2 to 6 hours. The terminal elimination half life of digoxin in patients with normal renal function is 30 to 40 hours. It will be prolonged in patients with impaired renal function, and in anuric patients will be of the order of 100 hours.

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