隆我心錠

Lanoxin Digoxin Tablets 0.25mg B.P.

衛署藥輸字第009554號

【成分名（中文名）】Digitoxin（毛地黃毒）
【劑型、含量】
錠劑：每錠含Digitoxin 0.1mg
膠囊劑：每膠囊含Digitoxin 0.05mg
【臨床藥理】
1. 洋地黃配醣類於治療劑量下可產生以下兩種主要作用：
（1）心肌收縮力量和速度的增加，一般認為，這種增加是由於心肌細胞內鈣的流入和游離鈣離子之釋出的增加，使得心臟收縮肌纖維的活力增強所致。
（2）心臟組織的電生理學特性提高，一般認為，這種效應是由於鈉及鉀離子與三燐酸腺甘酸（Adenosine Triphosphatease）錯合而使鈉和鉀離子通過心肌細胞膜之移動受抑制所致。房室和竇房結傳導速率減低，並使心室敏感度增加，除了由於反射迷走神經興奮和包括了交感神經和副交感神經支配的直接組織效應外，也由於洋地黃之直接效應所導致。
2. Digitoxin口服吸收後，97%與蛋白質結合，由肝臟代謝，其代謝物經腎臟排泄。
3. Digitoxin之治療與中毒血清濃度如下：

藥　物	血清濃度（ng/ml）	
	治　療	中　毒
Digitoxin	13-25	>35

注意血清濃度是以ng（nanogram）而非mg（milligram）表示。
4. 給予洋地黃製劑負載劑量（Loading Dose）之前，必須確定病人在2-3星期前是否曾使用任何洋地黃製劑，因此殘餘效應，須減低劑量以避免產生毒性。
5. 洋地黃配醣類劑量應依理想體重之基礎計算（因其不能被脂性組織吸收）。
6. 推薦劑量僅為平均值，各劑量應依個別病人需要調整。
7. Digitoxin對於一些腎功能不全病人較好,因其經由尿液排泄之代謝物大多數不具活性且不影響其半衰期。
8. 不整脈之電性轉變（Electrical Conversion of Arrhythmias）須調整洋地黃配糖體之劑量。洋地黃飽和病人一般對Electric Countershock較具敏感性。
9. 透析法對於洋地黃配糖類從體內迅速移除無效。
10. 由於洋地黃配糖類引起之嚴重或完全的心傳導阻斷存在下,鉀的補充可能會有危險。
11.

藥　物	半衰期（hr）	作用起始（hr）	尖峰效應（hr）	作用期（approx.days）
Digitoxin	120-216	1-4	8-4	14

12. 腎功能不全、年老或使用電子心臟節律器或虛弱之病患使用本藥,在一般其它病人可以耐受之劑量或血清濃度下可能出現毒性反應,故其劑量須小心加以標定。
13. 洋地黃配糖類是我童意外中毒的一個重要原因。
14. 洋地黃配糖類用於治療肥胖症經確定不恰當且危險的,因為這些藥物會引起潛在致命性的不整脈或其它副作用。
【適應症】
心臟衰竭、心房撲動、心房纖維性顫動、陣發性心室性心搏過速。
【用法用量】
本藥須由醫師處方使用。
一般成人劑量：洋地黃飽和－口服,初劑量0.6mg,視需要每3-6小時2-0.4mg。維持劑量－口服,0.1-0.2mg,一天1次。
一般成人處方限量：洋地黃飽和－在1-2天內最高可達1.6mg。
維持劑量：視需要和耐受性而定。
〔注意〕年老、虛弱以及使用電子心臟節律器病患對洋地黃配糖類特別敏感，需加標定後給與較低劑量。
一般兒童劑量：洋地黃飽和－口服，將以下劑量分成3-數個劑量，每6小時1次。
早產兒和足月新生兒：每公斤體種0.022mg或每平方公尺體表面積0.3-0.35mg。
2星期-1歲嬰兒：每公斤體重0.045mg。
1-2歲嬰兒：每公斤體重0.04mg。
2歲和2歲以上嬰兒－每公斤體重0.03mg。
維持劑量－口服,洋地黃飽和總劑量之1/10,一天1次。
〔注意〕幼小孩童（特別是早產兒和未成熟嬰兒）病患需小心標定劑量並對血清濃度和EKG讀數加以監視。
【注意事項】
1. 對洋地黃配糖類製劑過敏反應者很少發生。若對其中某種產生過敏反應並不表示對其餘的洋地黃配糖類亦會過敏，故並不因此排除其它洋地黃製劑之使用。孕婦與授乳婦使用本藥，尚無文獻報告有何問題發生，但仍應就其危險與效益加以考慮。
2. 當下列醫療問題存在時,不可使用洋地黃配糖類：
（1）服用洋地黃製劑曾產生毒性效應。
（2）心室纖維顫動。
3. 當下列醫療問題存在，使用洋地黃配糖類須小心考慮：
肺氣腫或其它嚴重的肺部疾病、心房與心室的部份傳導阻斷、高鈣血症、下主動脈瓣肥厚性狹窄、低鉀血症、甲狀腺功能不足症、缺血性心臟疾病、急性心肌梗塞、心肌炎、腎功能不全（但Digitoxin除外）。
4. 服用洋地黃配糖類時，下列之檢測在病人之監視上特別重要，依情況某些病人做其他測試或許較為恰當：血壓、心電圖（EKG）、Apical Pulse、腎功能、血清電解質（尤其是鉀和鈣）。
5. 病人須依照指示治療並在每天同一時間服用。如有噁心、嘔吐、腹瀉、食慾減失或極度慢脈時應告知醫師。
6. 許多病人常將本類藥品與其它外形相似藥品混淆不清，而造成嚴重意外，因此，為減少此種危害,處方調劑者應做到下列各點：
（1）警告病人本藥之危害性。
（2）使用副標籤於容器上，標明“心臟用藥”。
（3）相似外觀之藥品使用不同大小或外觀之容器。
（4）建議病人勿在同一時間使用兩種容器內之錠劑。
（5）建議病人將外觀相似之藥品貯放在不同區域。
【相互作用】
1. 洋地黃配糖類與Amphotericin B或Corticosteroids或耗竭鉀之Diuretics共用時，會提高伴隨低鉀血症洋地黃毒性之可能性。
2. Antacids（特別是Magnesium Trisilicate）或Antidiarrheal Adsorbant Suspension或Cholestyramine和其它Anionic Exchange Resins或Neomycin與洋地黃配糖類併用時，會抑制洋地黃配糖類之吸收而降低其療效。
3. Antiarrhythmics（包括其他洋地黃製品）或Calcium Salts（注射給藥者）或Pancuronium或Rauwolfia Alkaloids或Succinylcholine或Sympathomimetics與洋地黃配糖類共用時，會引起加成效應，導致心律不整。
4. 伴隨有嚴重或完全的心傳導阻斷之洋地黃飽和病人，鉀鹽與洋地黃配糖類不宜共用；不過，當Thiazide利尿劑與強心配糖類共用時，鉀補充劑常被用於防止低鉀血症。
5. Propranolol與洋地黃配糖類共用時，會引起深度心動徐緩並可能使心傳導阻斷;但並不因此排除它在洋地黃引起之快速不整脈的應用。
6. Quinidine與Digitoxin共用時，會導致Digitoxin達到中毒血清濃度，因此應監視血清濃度並作劑量調整。
【副作用】
如有下列副作用產生時，須給予醫療照應：
不規則脈搏（可能為毒性反應）；食慾減失、噁心或嘔吐（可能為髓中樞刺激）；下腹部疼痛、異常疲倦或衰弱（可能為電解質不平衡）；異常慢脈（可能為房室傳導阻滯）；視線模糊或黃視似乎有黃色光圈圍繞物體（毒性症狀）；腹瀉（可能為電解質不平衡）；精神抑鬱或紊亂、欲睡、頭痛、皮膚疹或蕁麻疹可能為過敏反應）。
非心臟方面：
但可能發生於因快速吸收而產生暫時性高血漿濃度。可能也有腹瀉。以噁心作為digoxin過量之早期徵兆並不可靠。
長期給藥可能有女樣男乳症狀。
曾有無力、神氣呆滯、疲勞、身體不適、頭痛、視力障礙、抑鬱甚至精神病之中樞神經副作用報告。
口服digoxin亦曾有腸缺血及較罕見的腸壞死之作用。猩紅熱樣特色之皮膚疹是digoxin較少見的副作用，此種副作用可能伴有嗜伊紅性白血球過多。
Digoxin在極罕見的情形下會引起血小板過少。
心臟方面：
Digoxin中毒會引起各種心律不整及傳導障礙。通常早期病徵是發生心室早期收縮；此種收縮會進行成連搏脈甚至三重脈。過量時可能發生心房心跳加速，而本來心房心跳加速常以digoxin治療。心房心跳加速副作用特別伴有某種程度的心房心室阻斷，此時脈搏不一定快（參考【注意事項】）。
【保存條件】
本品應包裝於緊密容器，貯於陰涼（15-30℃）乾燥且兒童不易取得處所。

GlaxoWellcome 製　造　廠：The Wellcome Foundation Ltd.
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隆 我 心 錠
Lanoxin Digoxin Tablets 0.25mg B.P.
隆我心注射劑
Lanoxin Digoxin Injection 0.5mg B.P.

衛署藥輸字第009554號
本藥須由醫師處方使用
衛署藥輸字第009714號
本藥限由醫師使用

給醫藥專業人員

【成　　份】
LANOXIN錠劑：白色圓形雙面凸錠劑，有刻痕並印有"WELLCOME X3A"字樣，每錠含250 μg (0.250mg)Digoxin, B.P.
LANOXIN注射劑：為一種澄清無色之滅菌水溶液，每ml含Digoxin　250 μg ，每安瓿含2ml。

【適 應 症】
心臟衰竭、心房撲動、心房纖維顫動、陣發性心室性心博過速。

【説　　明】
心臟衰竭：LANOXIN適用於治療慢性心衰竭，尤其對心室擴大病人療效特別强。
LANOXIN特別適用於伴有心房纖維顫動之心衰竭。
心室性心律不整：LANOXIN可用於治療某些上心室性心律不整，特別是心房撲動及纖維顫動，於此LANOXIN最大之益處在於降低心室速率。

【用法用量】
LANOXIN劑量需依據個人年齡，精瘦體重及腎功能而定。建議劑量只能作為初期使用原則。
每毫升含50微毫克的LANOXIN PG口服溶液附有一支有刻度滴管，應使用此滴管量所有的劑量。
成人及10歲以上兒童：

- 快速口服負荷量
一次投予750至1500微毫克(μg)(0.75～1.5毫克)。當情況較不緊急，或毒性危險性較高時，例如老年人，則口服負荷量應分次投予，間隔6小時，每再投予一次額外劑量時，皆需評估臨床反應。
- 慢速口服負荷量：
應每日投予250至750 μg (0.25至0.75毫克)，共一星期，接著投予一適當的維持劑量。一星期內應可觀察到臨床反應。
注意：慢速或快速口服負荷量之選擇應依病人臨床狀況及病情危急程度而定。
- 維持劑量：
維持劑量應依據每日經由排泄流失的尖峰體內貯存量百分比而定。下列公式臨床應用很廣泛。

$$維持劑量=尖峰體內貯存量\times\frac{\%每日流失量}{100}$$

在此處：尖峰體內貯存量＝負荷量

$$\%每日流失量=14+\frac{肌酸酐廓清率(Ccr)}{5}$$

Ccr為修正到70Kg體重或1.73m²體表面積之肌酸酐廓清率。若只有血清肌酸酐(Scr)濃度，則可用下列公式估計男性Ccr（修正至70Kg體重）：

$$Ccr=\frac{(140-年紀)}{Scr(mg/100ml)}$$

注意：此處所獲得血清肌酸酐值單位為 μ mol/L，必須用下列公式轉換成mg/100ml(mg%)：

$$Scr(mg/100ml)=\frac{Scr(\mu ml/L)\times 113.12}{10000}=\frac{Scr(\mu ml/L)}{88.4}$$

此處113.12為肌酸酐的分子量
女性方面：得到的結果應乘以0.85
注意：這些公式不適用於兒童的肌酸酐廓清率實際運用時，這表示大部分病人可投予每日0.125至0.75mg digoxin為維持劑量：但對於那些digoxin副作用敏感度較高的病人，每日62.5 μg (0.0625mg) digoxin或62.5 μg 以下digoxin之維持量即足夠。
緊急注射投藥負荷量：（對於那些前二星期內未曾投予强心配醣體之病人）
LANOXIN注射劑負荷量從500到1000 μg (0.5至1.0mg) ，依年齡、精瘦體重及腎功能而定。負荷量應分次投予，第一次約投予全部劑量的一半，其他劑量依4至8小時的間隔分次投予，每投予一次額外劑量時皆應評估臨床反應。每一次劑量應使用靜脈輸注10至20分鐘的速度（見〔稀釋〕）。
新生兒，嬰兒及10歲以下兒童（在前二星期內未曾投予强心配醣體之病人）：此群病人的靜脈負荷量應依下表投予：

小於1.5公斤之未足月新生兒	20 μg /kg24小時內
1.5至2.5公斤之未足月新生兒	30 μg /kg24小時內
足月新生兒至2歲兒童	35 μg /kg24小時內
2至5歲兒童	35 μg /kg24小時內
5至10歲兒童	25 μg /kg24小時內

負荷劑量應分次投予，第一次約投予全部劑量的一半，剩餘劑量依4至8小時間隔分次投予。每投予一次額外劑量時，皆應評估臨床反應。每次劑量皆應使用靜脈輸注10至20分鐘速度投予（見〔稀釋〕）。
口服負荷劑量：應依下表之劑量投藥

小於1.5公斤之未足月新生兒	每24小時每公斤25 μg
1.5至2.5公斤之未足月新生兒	每24小時每公斤30 μg
足月新生兒至2歲兒童	每24小時每公斤45 μg
2至5歲兒童	每24小時每公斤35 μg
5至10歲兒童	每24小時每公斤25 μg

負荷劑量應分次投予，第一次約投予全部劑量的一半，剩餘劑量依4至8小時間隔分次投予。每投予一次額外劑量時皆應評估臨床反應。
維持劑量
維持劑量應依下表投予：
未足月新生兒：每日劑量＝24小時負荷劑量（靜脈或口服）之20%
足月新生兒及10歲以下兒童：每日劑量＝24小時負荷劑量（靜脈或口服）之25%
這些給藥計劃僅供參考，應以仔細觀察臨床反應及監測血清digoxin濃度（見〔監測〕）作為小兒科病人調整劑量之依據。
若開始LANOXIN治療前兩星期內曾給予其他强心配醣體，則應考慮LANOXIN之最佳負荷劑量將少於上述建議劑量。
老年人：
對於老年人應使用較非老年人低的LANOXIN劑量，否則會因老年人常有之腎功能障礙及低精瘦體重而影響LANOXIN之藥品動力學而後產生高血清digoxin濃度及相關之毒性。應定期監測血清digoxin濃度及避免低血鉀。
腎障礙或同時併用利尿劑之建議劑量：
見〔注意事項／警告〕
LANOXIN注射劑稀釋法
以1比250比例將每ml250 μg 之LANOXIN注射劑稀釋後（例如：一支含500 μg 之2ml安瓿加入500ml之輸注溶液中），與下列輸注液相容且在室溫下可安定48小時（20至25℃）

　　氯化鈉靜脈輸液，B.P. 0.9%　W/V
　　氯化鈉(0.18% W/V)及葡萄糖(4% W/V)靜脈輸液，B.P.
　　葡萄糖靜脈輸液，B.P. 5% W/V

應在完全無菌狀態下稀釋或即將使用前才稀釋。未用完溶液應丟棄。
監測：
Digoxin血清濃度可用ng/ml之Conventional　Units或nmol/L之SI單位表示之。ng/ml乘以1.28就可變成nmol/L。
Digoxin血清濃度可用放射免疫測定法來測定。在LANOXIN最後一次劑量給藥後6小時或6小時以上抽血。最有效之digoxin血清濃度範圍並未有嚴格規定，但大多數病人在digoxin血中濃度自0.8ng/ml(1.02nmol/L)到2.0ng/ml(2.56nmol/L)，有效且產生中毒症狀及病徵之危險性最低。在此範圍以上常發生中毒症狀及病徵，3.0ng/ml (3.84nmol/L)濃度以上很可能已經中毒。無論如何，在判斷病人症狀是否因digoxin引起時，病人臨床狀況加上血清鉀離子濃度和甲狀腺功能皆是重要因素。
其他强心配醣體，包括digoxin代謝物在內，會干擾目前所有的測定法，在臨床狀況與測定濃度不相稱時應想到這一點。

【禁　忌】

LANOXIN禁用於間歇性完全心阻斷或二級房室阻斷，尤其是曾有stokes-Adams發作病史之病人。
LANOXIN禁用於因强心配醣體中毒引起之心律不整。
LANOXIN禁用於伴有副房室路徑之上心室性心律不整，例如Wolff-Parkinson-White徵候群，除非曾評估過該副路徑之電生理特性及digoxin對這些路徑之作用。若已知或懷疑存在副路徑而未有上心室性心律不整病史，同樣也禁用LANOXIN。
LANOXIN禁用於肥厚性阻塞心肌病變，除非在同時有心房纖維顫動及心衰竭，但即使如此若要使用LANOXIN仍要特別小心。
LANOXIN禁用於已知對digoxin或其他digitalis配醣體過敏病人。

【注意事項／警告】

Digoxin毒性可能產生心律不整，其中某些心律不整可能會像可用digoxin治療之心律不整。例如，伴有各種房室阻斷之心房心跳加快其節律在臨床上極像心房纖維顫動，必須特別小心。
對於某些實房障礙病人（例如病實症候群），Digoxin可能會引起或加重實性心搏過慢或引起實房阻斷。測定血清digoxin濃度對於決定是否需要增加digoxin劑量相當有用，但其他配醣體之毒性劑量可能會在測定時產生交互反應而明顯理想之測量發生錯誤建議。此時暫時停用digoxin且仔細觀察可能比較適當。
對於曾在兩星期前服用强心配醣體病人，應重新考慮其初期建議劑量。其初期及維持劑量皆應考慮減量，低血鉀會使心肌對强心配醣體作用特別敏感。
低血鎂及顯著的高血鈣會增加心肌對强心配醣體的敏感性。
快速靜脈注射可能引起血管收縮而產生高血壓及／或減少冠狀血流。因此對於高血壓性心衰竭及急性心肌梗塞病人緩慢靜脈注射十分重要。
甲狀腺病人服用LANOXIN需小心。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相當的digoxin抗藥性故需增加劑量。在甲狀腺毒症療程當中，當甲狀腺毒症已能控制時應減低劑量。吸收不良症候群或胃腸重建(reconstructions)之病人可能需要較高之digoxin劑量。
直流電心臟電擊
直流電心臟電擊引發之心律不整危險性，當digitalis毒性存在時會大幅增加，增加幅度與所使用之心臟電擊能源成比例。
對於正在服用digoxin病人選擇性使用直流電心電擊，應在電擊前暫停digoxin24小時。急救時，例如心臟停止，若用心電擊應用最低有效能量。
直流電心臟電擊不適用於治療，因强心配醣體引起之心律不整。
Digoxin治療心律不整的許多效果來自於某種程度之房室傳導阻斷。無論如何當已存在不完全房室阻斷時，可預期會有阻斷之快速進行。對於完全心阻斷病人，可能會抑制其自發性心室脫逃(idioventricular escape)節律。心肌梗塞剛發作後時期並不禁用digoxin，但須牢記心肌梗塞後可能有低血鉀病人，其心律不整可能性增高且可能有心臟病性不穩定情況。同時必須記住直流電心臟電擊後帶來的限制。
雖然許多慢性鬱血性心衰竭病人經過digoxin急性治療後獲得改善，但有一些病人未有穩定、顯著或持續的血液動力學改進。因此當長期使用LANOXIN時，依個體差異評估其反應十分重要。
肌肉注射很痛且與肌肉壞死有關。此種給藥途徑不被推薦。
嚴重呼吸疾病病人，可能會增加心肌對digitalis配醣體之敏感性。

【突變性、致癌性、致畸性】

截至目前尚無digoxin有否突變性、致癌性或致畸性之資料，但曾有孕婦投予digoxin來治療胎兒之心搏加速及鬱血性心衰竭。

【生 育 力】

尚無digoxin影響生育之資料。

【懷孕及授乳】

孕婦不禁用digoxin，但孕婦所需劑量較難預測，有些人懷孕時digoxin劑量需增加。如同其他藥物，孕婦使用digoxin必先衡量治療對孕婦之益處是否大於對胎兒可能造成的危險性。
Digoxin會分泌在乳汁中，但分泌量極少，使用digoxin期間不必停止餵奶。

【副 作 用】

非心臟方面：
主要和過量有關，但可能發生於因快速吸收而產生暫時性高血漿濃度。症狀包括食慾不振、噁心及嘔吐，通常在服藥後數小時內消失。可能也有腹瀉。以噁心作爲digoxin過量之早期徵兆並不可靠。
長期投藥可能有女樣男乳症狀。
曾有無力、神氣呆滯、疲勞、身體不適、頭痛、視力障礙、抑鬱甚至精神病之中樞神經副作用報告。
口服digoxin亦曾有腸缺血及較罕見的腸壞死之作用。蕁麻疹或猩紅熱樣特色之皮膚疹是digoxin較少見的副作用，此種副作用可能伴有嗜伊紅性白血球過多。
Digoxin在極罕見的情形下會引起血小板過少。
心臟方面：
Digoxin中毒會引起各種心律不整及傳導障礙。通常早期病徵是發生心室早期收縮；此種收縮會進行成連搏脈甚至三重脈。過量時可能發生心房心跳加速，而本來心房心跳加速常以digoxin治療。心房心跳加速副作用特別伴有某種程度的心房心室阻斷，此時脈搏不一定快（參考〔注意事項／警告〕）。

【藥物交互作用】

交互作用可能因腎排泄作用、組織結合、血漿蛋白結合、體內分佈、腸吸收能力及對LANOXIN敏感度而發生。
任何藥物打算和digoxin併用時，最好先考慮交互作用的可能性，當有任何疑問時應測定血漿digoxin濃度。會引發低血鉀或細胞內鉀缺少之藥物如利尿劑、鉀鹽、皮質類固醇及carbenoxolone等可能會提高LANOXIN敏感度。
同時投予下列藥物會提高digoxin血中濃度：
amiodarone、captopril、flecainide、prazosin、propafenone、quinidine、spironolactone、tetracycline、erythromycin（可能還有其他抗生素）及propantheline。
同時投予下列藥物會降低digoxin血漿濃度：
制酸劑、kaolin-pectin、某些膨脹性緩瀉劑及cholestyramine、diphenoxylate、sulphasalazine、neomycin、rifampicin、cytostatics、phenytoin、metoclopramide及penicillamine。
鈣管道阻斷劑可能會增加或不影響digoxin血漿濃度。Verapamil增加digoxin血漿濃度。Nifedipine及diltiazem可能會增加或不影響血漿digoxin血漿濃度。Isradipine不影響血漿digoxin濃度。
Milrinone不會改變穩定狀態之digoxin血漿濃度。

【中　毒】

症狀及病徵：
見〔副作用〕。
治療：
若剛服下不久，如意外或蓄意自殺，可用洗胃減少吸收的負荷量。
無心臟病成年人過量服用10至15mg digoxin及1至3歲無心臟病兒童服用6至10mg之劑量似乎是造成半數病人死亡的劑量。若無心臟病成人服用超過25mg digoxin會死亡或造成只對digoxin結合性Fab抗體段(DIGIBIND)有反應之進行性中毒。若1至3歲無心臟病兒童服用超過10mg之digoxin，若未投予Fab段治療，通常都會死亡。若發生低血鉀，必須依病情緊急性用口服或靜脈注射之鉀補充劑矯正。當服用大量LANOXIN時，可能會因骨骼肌釋出鉀離子而引起高血鉀。對digoxin中毒病人投予鉀劑之前，應確知其血漿鉀濃度。慢性心律不整可能對atropine有反應，但可能需用暫時性心臟節律器。心室性心律不整可能對lignocaine或phenytoin有效。
透析對於移走體內具潛在威脅生命之中毒濃度digoxin並不特別有效。
當其他治療皆失敗時，靜脈投予digoxin專一性(ovine)抗體段(Fab)能快速恢復因digitoxin、digoxin及相關配醣體嚴重中毒引起之併發症。
DIGIBIND是digoxin中毒之惟一專一性治療藥且非常有效。詳情請參考DIGIBIND提供之文獻。

【製劑注意事項及建議】

貯存法
錠　　劑：保存在25℃以下室溫
口服溶液：保存在25℃以下室溫
注 射 劑：保存在25℃以下室溫並避光
稀釋法
LANOXIN PG酏劑及LANOXIN口服溶液。
LANOXIN PG酏劑及LANOXIN口服溶液不可稀釋。

【包　　裝】

錠　劑：6～1000粒瓶裝
注射劑：2公撮2、5、25、100支安瓿裝

【進一步資料】

靜脈注射一次負荷劑量在5至10分鐘內產生可感覺到之藥效，此種作用在1至5小時達到高峰。
口服投藥在0.5至2小時時開始產生藥效，在2至6小時達到高峰。
正常腎功能病人digoxin末期排泄半衰期爲30至40小時。腎功能障礙及無尿病人排泄半衰期可能延長至100小時。

製造廠：The Wellcome Foundation Ltd. London
藥　商：香港商寶威股份有限公司　台灣分公司
地　址：台北市忠孝東路四段142號5樓之5
Wellcome　MAS/9202/JKMS/BQGT 90-20/91-07　92.11

A/5426

Lanoxin™
Formulations

To the Medical and Pharmaceutical Professions

Presentations

Tablets:

Lanoxin Tablets

White, round, biconvex tablets, scored and impressed "WELLCOME X3A" and each containing 250 micrograms (0.250mg) 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, biconvex 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 (0.050mg) 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

750 to 1500 micrograms (μg) (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 750μg (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.

NOTE: The choice between slow and rapid oral loading depends on the clinical state of the patient and the urgency of the condition.

Maintenance

The maintenance dosage should be based upon the percentage of the peak body stores lost each day through elimination. The following formula has had wide clinical use:-

$$\text{Maintenance dose} = \text{Peak body stores} \times \frac{\%\ \text{daily loss}}{100}$$

Where:- Peak body stores = loading dose

% daily loss = 14 + creatinine clearance (C_{cr})/5.

C_{cr} is creatinine clearance corrected to 70kg bodyweight or 1.73m² body surface area. If only serum creatinine (S_{cr}) concentrations are available, a C_{cr} (corrected to 70kg bodyweight) may be estimated in men as

$$C_{cr} = \frac{(140 - \text{age})}{S_{cr}\ (\text{in mg/100ml})}$$

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

$$S_{cr}\ (\text{mg/100ml}) = \frac{S_{cr}\ (\mu\text{mol/L}) \times 113.12}{10{,}000}$$

$$= \frac{S_{cr}\ (\mu\text{mol/L})}{88.4}$$

Where 113.12 is the molecular weight of creatinine.

For women, this result should be multiplied by 0.85.

NOTE: These formulae cannot be used for creatinine clearance in children.

In practice, this will mean that most patients will be maintained on 0.125 to 0.75mg digoxin daily; however in those who show increased sensitivity to the adverse effects of digoxin, a dosage of 62.5μg (0.0625mg) daily or less may suffice.

Emergency Parenteral Loading (In patients who have not been given cardiac glycosides within the preceding two weeks).

The loading dose of parenteral **Lanoxin** is 500 to 1000μg (0.5 to 1.0mg) depending on age, lean body weight and renal function. The loading dose should be administered in divided doses with approximately half the total dose given as the first dose and further fractions of the total dose given at intervals of 4 to 8 hours, assessing clinical response before giving each additional dose. Each dose should be given by intravenous infusion (see **Dilution**) over 10 to 20 minutes.

Neonates, infants and children up to 10 years of age (if cardiac glycosides have not been given in the preceding two weeks):

The intravenous loading dose in the above groups should be administered in accordance with the following schedule:-

Preterm neonates <1.5kg	20μg/kg over 24 hours
Preterm neonates 1.5kg to 2.5kg	30μg/kg over 24 hours
Term neonates to 2 years	35μg/kg over 24 hours
2 to 5 years	35μg/kg over 24 hours
5 to 10 years	25μg/kg over 24 hours.

The loading dose should be administered in divided doses with approximately half the total dose given as the first dose and further fractions of the total dose given at intervals of 4 to 8 hours, assessing clinical response before giving each additional dose. Each dose should be given by intravenous infusion (see **Dilution**) over 10 to 20 minutes.

Oral loading dose: This should be administered in accordance with the following schedule:-

Preterm neonates <1.5kg	25μg/kg over 24 hours
Preterm neonates 1.5kg to 2.5kg	30μg/kg over 24 hours

Term neonates to 2 years	45µg/kg over 24 hours
2 to 5 years	35µg/kg over 24 hours
5 to 10 years	25µg/kg over 24 hours.

The loading dose should be administered in divided doses with approximately half the total dose given as the first dose and further fractions of the total dose given at intervals of 4 to 8 hours, assessing clinical response before giving each additional dose.

Maintenance

The maintenance dose should be administered in accordance with the following schedule:-

Preterm neonates:- daily dose = 20% of 24-hour loading dose (intravenous or oral)

Term neonates and children up to 10 years:- daily dose = 25% of 24-hour loading dose (intravenous or oral).

These dosage schedules are meant as guidelines and careful clinical observation and monitoring of serum digoxin levels (see Monitoring) should be used as a basis for adjustment of dosage in these paediatric patient groups.

If cardiac glycosides have been given in the two weeks preceding commencement of Lanoxin therapy, it should be anticipated that optimum loading doses of Lanoxin will be less than those recommended above.

The elderly

The tendency to impaired renal function and low lean body mass in the elderly influences the pharmacokinetics of Lanoxin such that high serum digoxin levels and associated toxicity can occur quite readily, unless doses of Lanoxin lower than those in non-elderly patients are used. Serum digoxin levels should be checked regularly and hypokalaemia avoided.

Dose Recommendations in Renal Disorder or with Diuretic Therapy:

See Precautions/warnings.

Dilution of Lanoxin Injection

Lanoxin Injection, 250µg per ml when diluted in the ratio of 1 to 250 (i.e. One 2ml ampoule containing 500µg added to 500ml of infusion solution) is known to be compatible with the following infusion solutions and stable for up to 48 hours at room temperature (20 to 25°C):

Sodium Chloride Intravenous Infusion, B.P., 0.9% w/v

Sodium Chloride (0.18% w/v) and Glucose (4% w/v) Intravenous Infusion, B.P.

Glucose Intravenous Infusion, B.P., 5% w/v.

Dilution should be carried out either under full aseptic conditions or immediately before use. Any unused solution should be discarded.

Monitoring:

Serum concentrations of digoxin may be expressed in Conventional Units of ng/ml or SI Units of nmol/L. To convert ng/ml to nmol/L, multiply ng/ml by 1.28.

The serum concentration of digoxin can be determined by radioimmunoassay. Blood should be taken 6 hours or more after the last dose of **Lanoxin**. There are no rigid guidelines as to the range of serum concentrations that are most efficacious but most patients will benefit, with little risk of toxic symptoms and signs developing, with digoxin concentrations from 0.8ng/ml (1.02nmol/L) to 2.0ng/ml (2.56nmol/L). Above this range toxic symptoms and signs become more frequent and levels above 3.0ng/ml (3.84nmol/L) are quite likely to be toxic. However, in deciding whether a patient's symptoms are due to digoxin, the patient's clinical state together with the serum potassium level and thyroid function are important factors.

Other glycosides, including metabolites of digoxin, can interfere with the assays that are available and one should always be wary of values which do not seem commensurate with the clinical state of the patient.

Contra-indications

Lanoxin is contra-indicated in ventricular tachycardia or ventricular fibrillation.

Lanoxin is contra-indicated in intermittent complete heart block or second degree atrioventricular block, especially if there is a history of Stokes-Adams attacks.

Lanoxin is contra-indicated in arrhythmias caused by cardiac glycoside intoxication.

Lanoxin is contra-indicated in supraventricular arrhythmias associated with an accessory atrioventricular pathway, as in the Wolff-Parkinson-White syndrome, unless the electrophysiological characteristics of the

accessory pathway and any possible deleterious effect of digoxin on these characteristics has been evaluated.
If an accessory pathway is known or suspected to be present and there is no history of previous supraventricular arrhythmias, **Lanoxin** is similarly contra-indicated.
Lanoxin is contra-indicated in hypertrophic obstructive cardiomyopathy, unless there is concomitant atrial fibrillation and heart failure but even then caution should be exercised if **Lanoxin** is to be used.
Lanoxin is contra-indicated in patients known to be hypersensitive to digoxin or other digitalis glycosides.

Precautions/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 (i.e. Sick Sinus Syndrome) digoxin may cause or exacerbate sinus bradycardia 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.
Hypomagnesaemia and marked hypercalcaemia increase myocardial sensitivity to cardiac glycosides.
Rapid intravenous injection can cause vasoconstriction producing hypertension and/or reduced coronary flow. A slow injection rate 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, dosage should be reduced as the thyrotoxicosis comes under control.
Patients with malabsorption syndrome or gastro-intestinal reconstructions 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 blockade. However, when incomplete atrioventricular block already exists the effects of a rapid progression in the block should be anticipated. In complete heart block the idioventricular escape rhythm may be suppressed. The administration of digoxin in the period immediately following myocardial infarction is not contra-indicated. However, the possibility of arrhythmias arising in patients who may be 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 constant, 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. As 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 inadvisable 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 eosinophilia.
Very rarely, digoxin can cause thrombocytopenia.
Cardiac
Digoxin toxicity can cause various arrhythmias and conduction disturbances. Usually an early sign is the occurrence of ventricular premature contractions; they 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 hypokalaemia or intracellular potassium deficiency may cause increased sensitivity to **Lanoxin**; they include diuretics, lithium salts, corticosteroids and carbenoxolone.
Serum levels of digoxin may be **INCREASED** by concomitant administration of the following:-
amiodarone, captopril, flecainide, prazosin, propafenone, quinidine, spironolactone, tetracycline, erythromycin (and possibly other antibiotics), and propantheline.
Serum levels of digoxin may be **REDUCED** by concomitant administration of the following:-
antacids, kaolin-pectin, some bulk laxatives and cholestyramine, diphenoxylate, sulphasalazine, neomycin, rifampicin, cytostatics, phenytoin, metoclopramide, and penicillamine.
Calcium channel blocking agents may either increase or cause no change in serum digoxin levels. Verapamil increases serum digoxin levels. Nifedipine and diltiazem 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 15mg in adults without heart disease and of 6 to 10mg in children aged 1 to 3 years without heart disease appeared to be the dose resulting in death in half of the patients. If more than 25mg of digoxin was ingested by an adult without heart disease, death or progressive toxicity responsive only to digoxin-binding Fab antibody fragments (Digibind®) resulted. If more than 10mg 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.

Bradyarrhythmias 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 500µg/ml)

Lanoxin-PG Oral Solution 50µg/ml (Lanoxin PG Elixir) and Lanoxin Oral Solution 500µg/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.

GlaxoWellcome

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