臟得樂錠
Cordarone Tablets

病人在開始服藥前，請先詳讀本說明書。
說明書內含有您所接受之治療的重要相關資訊。
如果你有任何疑問或有不清楚之處，可以請教你的醫師或藥師。
本藥品為醫師針對您個人所開立的處方，請勿給他人服用。即使他人的症狀與您類似，但若誤食本藥，有可能對其造成傷害。
請妥善保存此說明書，以利日後查閱之需要。

1. 藥品的名稱、含量
臟得樂 200 mg，可剝半的錠劑

2. 何時應使用本藥物
臟得樂乃用以預防及治療某些心臟節律失調的疾病。

3. 警語
a) 何時不應該使用本藥物
本藥物不得使用於下列情況：
- 對碘或 amiodarone 過敏者，
- 甲狀腺功能亢進者，
- 有某種心臟節律和/或傳導功能失調者，
- 心跳過慢者，
- 懷孕超過三個月以上者，
- 正在哺育母乳者，
- 與下列藥物併用可能誘發 torsades de pointes （嚴重的心臟節律失調）：
  · 第 Ia 類抗心律不整藥物（quinidine，hydroquinidine，disopyramide…等），
  · 第 III 類抗心律不整藥物（sotalol，dofetilide，ibutilide 等），
  · sultopride（抗精神病藥），
  · 以及其他藥物（bepridil，cisapride，diphemanil，erythromycin IV，mizolastine，vincamine IV，sparfloxacin 等）。（參閱"交互作用"欄）。
  除非醫師有特別考量，否則本藥不應與 diltiazem 注射劑、某些抗感染藥物、非 sotalol 及 esmolol 的 β-阻斷劑，及某些抗精神病藥併用。

b) 特殊警語
如出現不尋常的無法呼吸、呼吸困難或乾咳，不論其是否伴隨整體健康狀況的變壞，疲倦或長期性或無法解釋的發燒、腹瀉、體重減輕或心悸的復發，都應告知醫師。
因為本藥物含有乳糖，因此禁用於有先天性半乳糖血症、葡萄糖及半乳糖吸收不良或乳糖酵素缺乏的病人（罕見的代謝性疾病）。
c) 注意事項
治療期間應作好適當的防曬，以避免"曬傷"作用的發生。
治療期間應作抽血檢驗，以監測甲狀腺或肝功能。
手術前，應該讓麻醉科醫師知道，你正在接受 amiodarone 的治療。
兒童使用 amiodarone 的安全性及有效性尚未被確立。
d) 交互作用
為了避免多種藥物之間的交互作用，特別是 diltiazem 注射劑，halofantrine，pentamidine，moxifloxacine，以及某些抗精神病藥（thioridazine，chlorpromazine，levomepromazine，trifluoperazine，cyamemazine，sulpiride，amisulpride，tiapride，pimozide，haloperidol，droperidol），及非 sotalol 和 esmolol 的 β-阻斷劑，如有服用其他任何藥物，應該告知你的醫師或藥師。
e) 懷孕與授乳
本藥物含碘，因此懷孕超過三個月以上，禁用本藥。
在本藥治療期間，禁止哺育母乳。
一般說來，懷孕或授乳期間如欲服用任何藥物，皆應先諮詢醫師或藥師。
f) 可能影響藥物使用之安全性的賦形劑
乳糖

4. 使用方法
a) 劑量
常用劑量因人而異，但大多遵循下列規則：
- 起始劑量：每日 3 錠，服用 8 至 10 日。
- 維持劑量：每日 1/2 至 2 錠。

所有病患皆應嚴格遵守醫囑用藥，切不可自行調整劑量。同樣地，在未諮詢醫師前，不可擅自停藥。
b) 服藥方式
以口服方式給藥。
c) 用藥的頻率及時間
本藥物可在餐前、用餐中或餐後吞服。錠劑咬碎不會影響藥物的性質。
d) 療程
嚴格遵守醫師指示服藥。
e) 過量的處理
當服藥過量時，應儘速通知你的醫師。
f) 單次或多次劑量忘記服用時的處理方式
偶爾一次忘記服藥並不會對您造成任何的危險。
切勿以雙份劑量去彌補忘記服用的該次劑量。

5. 不良反應
如同其他藥物，本品對某些患者也有可能造成各種不同程度的不良反應：有下列副作用發生時，應告知醫師，以決定繼續治療或停藥；
- 視覺障礙（視覺模糊或出現光暈，視力不清或視力減退則非常罕見），
- 皮膚對日光的反應；在極少數的情況有可能使皮膚呈現灰色異常，
- 甲狀腺疾病（體重增加及疲倦、或相反地，體重過度減輕及腹瀉），
- 呼吸的問題（呼吸困難、無法呼吸、發燒、乾咳），情況有可能相當嚴重，
- 心跳速率明顯減緩，
- 較罕見的案例如，良性腸胃失調、肝功能障礙、行走困難、掉髮、顫抖及作惡夢。

如有非上述所提及的任何不良反應出現，應告知你的醫師或藥師。

6. 儲存
a) 請勿服用超過外包裝標示之有效期限的藥物。
b) 30℃以下避光貯存
c) 藥品的外觀如已變質，則應予丟棄。

以下內容供專業人員參考

【成份】
每錠含有 Amiodarone Hydrochloride 200mg

【適應症】
Wolff-Parkinson-white 氏症候群，上室性及心室性心搏過速、心房撲動、心房纖維顫動、心室纖維顫動

【說明】
預防下列症狀復發：
有生命危險的心室心搏過速：藥物的給予與監測應在醫院中進行；
經證實的有症狀的及影響生活能力的心室心搏過速；
其他療法產生耐受性或無法使用其他方式治療的經過證實的上心室心搏過速；
心室纖維顫動。
可治療上心室心搏過速，減緩或降低心房纖維顫動或心房撲動。
Amiodarone 可能可用於有冠狀動脈疾病或左心室功能障礙的病人（參見"藥物藥效學特性"）。

【用法用量】
起始劑量：
一般的劑量為每日 3 錠，持續給藥 8-10 天。
維持劑量：
最低有效劑量乃因人而異，其範圍為每日 1/2 錠（可每隔一天給藥一次，每次 1 錠）至每日 2 錠。

【禁忌】
下列情況禁用 Amiodarone：
- **未放節律器的竇性心跳遲緩及竇房心臟傳導阻滯；**
- **未放節律器的竇性疾病（有竇結停止的危險）；**
- **未放節律器的高度心臟傳導障礙；**
- **Amidarone 會使甲狀腺機能亢進惡化；**
- **已知對碘或 amiodarone 過敏者；**
- **懷孕中的第二期（第 4-6 個月）及第三期（第 7-9 個月）；**
- **授乳婦；**
- **併用可能誘發 torsades de pointes 的藥物：**
  · **第 Ia 類抗心律不整藥物（quinidine，hydroquinidine，disopyramide…），**
  · **第 III 類抗心律不整藥物（sotalol，dofetilide，ibutilide…），**
  · **sultopride，**
  · **其他藥物如，bepridil，cisapride，diphemanil，erythromycin IV，mizolastine，sparfloxacin，vincamine IV…（參見"與其他藥物或其他形式的交互作用"）。**

Amiodarone 通常不建議與下列藥物併用：
- **diltiazem 注射劑，**
- **halofantrine，pentamidine，moxifloxacin，**
- **某些抗精神病藥（thioridazine，chlorpromazine，levomepromazine，trifluoperazine，cyamemazine，sulpiride，amisulpride，tiapride，pimozide，haloperidol 及 droperidol），**
- **其他非 sotalol 及 esmolol 的 β-阻斷劑（參見"交互作用"欄）。**

【警語及注意事項】
警語：
治療前應先做心電圖檢查。
- **可能加重老年人心跳減緩的症狀。**
- **Amiodarone 會誘發心電圖的改變。這種"cordarone"式的改變為再極化的延長使得 QT 間隔拉長，因而可能發展出 U 波；此乃其療效的效應而**

非毒性。
- 治療期間，如果發生第 2 或第 3 級心臟房室傳導阻滯、心臟實房傳導阻滯或雙束枝心臟傳導阻滯則應停藥。第 1 級心臟房室傳導阻滯發生時，即應加強監測。
- Amiodarone 含碘，因此會影響甲狀腺功能測試（與放射性碘鍵結，PBI）的結果；然而，甲狀腺的功能監測仍然可行（T3、T4 和極為敏感的甲狀腺刺激激素 TSH）。
- 只有在預防危及生命的心室性心律不整時，amiodarone 才得以與下列藥物併用（參見"交互作用"欄）：
  · 非 sotalol（禁止併用），亦非 esmolol（併用時應相當謹慎）的 β-阻斷劑。
  · verapamil 及 diltiazem，應只併用於預防有生命危險的心室心律不整。

Amiodarone 含有乳糖，因此禁止使用於有先天性半乳糖血症、葡萄糖和半乳糖吸收不良或乳糖酵素缺乏的病人。
如發生呼吸困難或乾咳，不論其是否伴隨整體健康狀況之惡化，都應考慮這有可能是肺部毒性的徵兆，應進一步作胸部 X 光檢查（參見"不良反應"欄）。

注意事項：
電解質失調，尤其是低血鉀症：與低血鉀相關的情況都應特別注意，因為它可能引發心律不整。
Amiodarone 給藥前應先治療低血鉀症。
下列的不良反應大多與劑量過高有關，藉由小心地調整至最低維持劑量可以避免或緩解其副作用。
治療期間病患應避免日曬。
Amiodarone 可能導致甲狀腺異常（參見"不良反應" 欄）。
在治療前，所有病患都應作甲狀腺刺激激素(TSH)之監測，之後，於治療期間應做定期監測，例如每 6 個月一次，並於停藥後數個月再監測一次。
如有任何甲狀腺功能異常的臨床徵兆，則應測量甲狀腺刺激激素的血中濃度（參見"不良反應" 欄）。
Amiodarone 在兒童的安全性及有效性上，尚未做過有對照組的臨床試驗評估。
定期肝功能評估（轉胺酵素）有助於篩檢 amiodarone 所造成的肝功能障礙（參見"不良反應" 欄）。

麻醉
手術前應告知麻醉師，病患正以 amiodarone 治療中。
長期服用 amiodarone 會增加全身或局部麻醉之血流動力方面的危險性，意即會提高副作用的發生率。特別是在心跳遲緩、低血壓、心輸出量降低及傳導方面的障礙。
此外，有少數服用 amiodarone 的病患曾在手術後發生急性的呼吸窘迫症狀。這些患者在施以人工換氣法時，應予以嚴密監測（參見"不良反應" 欄）。

【交互作用】
許多抗心律不整的藥物會壓抑心臟的自主性、傳導性與收縮性。
併用不同種類的抗心律不整藥物有可能獲得較佳的療效，但是必須高度謹慎並且嚴密監視其臨床與心電圖的表現。Amiodarone 禁止與會誘發 torsade de pointes 的抗心律不整藥物併用。
除非是特殊情況，否則同類型的抗心律不整藥物不建議併用，因為這會增加心臟方面的副作用。
Amiodarone 與造成心跳遲緩及/或降低房室傳導的減弱心肌收縮力的藥物併用時，必須相當謹慎，同時應監測其臨床與心電圖表現。

禁止併用
＋會引起 torsades de pointes 的藥物：
- 第 Ia 類抗心律不整藥物（quinidine，hydorquinidine，disopyramide），
- 第 III 類抗心律不整藥物（dofetilide，ibutilide，sotalol），
- 其他藥物如：bepridil，cisapride，dephemanil，erythromycin IV，mizolastine，vincamine IV，
- sultopride
- 會增加心室節律失調的危險性，尤其是 torsades de pointes。

＋Sparfloxacin
QT 間隔加大因而增加 torsades de pointes 之危險性（電生理學的附加效應）。

不建議併用
＋會誘發 torsades de pointes 之抗精神病藥：
某些 phenothiazine 類的抗精神病藥（chlorpromazine，cyamemazine，levomepromazine，thioridazine，trifluoperazine），benzamide 類抗精神病藥（amisulpride，sulpiride，tiapride），butyrophenone 類抗精神病藥（droperidol，haloperidol）及其他抗精神病藥（pimozide）。
會增加心室節律失調的危險性，尤其是 torsades de pointes。

＋Halofantrine，moxifloxacin，pentamidine
會增加心室節律失調的危險性，尤其是 torsades de pointes。在可能的情況下，應將可能引起 torsades de pointes 的非抗感染藥物停藥。如併用不可避免，則應事前控制 QT 間隔並監測心電圖。

＋Diltiazem 注射劑
有心跳減緩及心臟房室傳導阻滯的危險性。如果一定要併用，應嚴密觀察其臨床表現並監測其連續性心電圖。

＋非 sotalol 及 esmolol 的 β-阻斷劑
會造成收縮性、自主性及傳導方面的障礙(抑制代償性交感神經之機制)。

併用時須特別注意
＋口服抗凝血劑
會增加抗凝血作用以及出血的危險。
在 Amiodarone 治療期間以及停藥後，應調整口服抗凝血劑的劑量並更頻密的監測凝血酵素原及凝血時間。

＋Cyclosporin
Amiodarone 會減少 cyclosporin 在肝臟的代謝，因而提高 cyclosporin 的血中濃度，增加腎毒性的機率。
在 amiodarone 的治療期間或停藥後，都應測量 cyclosporin 的血中濃度，監控腎功能並調整其劑量。

＋口服 diltiazem
有心跳遲緩或心臟房室傳導阻滯的危險，老年人尤須注意。
應做心電圖及臨床監測。

＋Digitalis 藥物
會壓抑心臟的自主性（嚴重心跳遲緩）以及引起房室傳導失調。如併用 digoxin，則 digoxin 的血中濃度會因其清除率下降而上升。必要時，病人應做心電圖，並監測臨床表現、digoxin 血中濃度及調整 digoxin 之劑量。

＋Esmolol
會造成收縮性、自主性及傳導方面的障礙(抑制代償性交感神經之機制)。
應做心電圖及臨床監測。

＋造成低血鉀的藥物：低血鉀性利尿劑（單獨或合併使用），刺激性緩瀉劑，皮質類固醇（全身性用藥），tetracosactide，amphotericin B (IV 途徑)
會增加心室節律失調的危險性，尤其是 torsades de pointes。（低血鉀為其誘導因子）。
應做心電圖，實驗室檢驗以及臨床監測。

＋Phenytoin
會增加 phenytoin 的血中濃度而出現過量的徵兆，特別是神經方面的症狀（phenytoin 在肝臟的代謝降低）。
需監測病患的臨床表現、phenytoin 血漿濃度並做可能的劑量調整。

＋使心跳減緩的藥物：心跳減緩性的鈣離子阻斷劑（diltiazem，verapamil），β-阻斷劑（不包括 sotalol），clonidine，guanfacine，digitalis 藥物，mefloquine，抗膽酯酵素製劑（donezepil，galantamine，rivastigmine，tacrine，ambemonium，pyridostigmine，neostigmine）
會增加心室節律失調的危險性，尤其是 torsades de pointes。
應做心電圖及臨床監測。

＋Simvastatin
有增加不良反應的危險(和劑量相關)，如橫紋肌溶解症(降低降膽固醇藥物之肝臟代謝所導致之症狀)。
併用時 simvastatin 之日劑量不可超過 20mg。
若在此劑量下無法達成治療目標，請使用其他無此不良反應的 Statin 類藥物。

【懷孕及授乳】
懷孕：
動物實驗尚未能證明其有任何致畸性。如果對動物無致畸性，則對人類應該也沒有致畸性。
到目前為止，會使人類產生畸形的物質，都已由兩種動物的動物實驗上證實其致畸性。
目前尚無足夠的臨床資料評估 amiodarone 是否在懷孕的前三個月有致畸性的可能。
懷孕前的用藥，對胎兒的甲狀腺於發育的第 14 週開始鍵結碘分子沒有影響。然而，在懷孕期間服用 amiodarone，會使體內碘過多，造成胎兒在生物或臨床（甲狀腺腫）上的甲狀腺功能低下。
所以，自懷孕第 2 期（第 4-6 個月）開始，禁止使用 amiodarone。
授乳：
Amiodarone 及其代謝產物與碘分子，皆會以高於在母體的血漿濃度存在於乳汁中。由於其對新生兒有產生甲狀腺低下的危險，所以使用本品的母親禁止以母乳哺育嬰兒。

【不良反應】
眼科方面：
成人患者幾乎都會發生角膜微沉積（corneal microdeposit）的現象；它通常侷限於瞳孔下方，但不需因此停藥。極少數病人會伴隨有光暈的產生與視覺模糊。
角膜微沉積為脂肪複合物沉積所造成，通常在停藥後即可恢復。
有少數關於視覺模糊或視力減退的眼部神經病變（視神經炎），以及眼睛後方視乳突水腫的報告。它可能進一步惡化造成視力受損，但其與 amiodarone 的相關性尚不得而知。然而，在不確定病因前，建議最好停藥。

皮膚方面：
光敏感性。病患於治療期間應避免暴露於陽光（紫外線）下。
接受放射性治療的病人曾有紅疹的報告。
皮膚發疹，通常為非專一性的，和極少數的剝落性皮膚炎亦曾被報告過，其與 amiodarone 的關連性尚未確立。
皮膚的藍灰色色素沉積可能發生於長期服用高劑量的患者，治療停止後，色素沉積會逐漸消退（10 至 24 個月）。

甲狀腺方面：
在甲狀腺失調的臨床症狀尚未出現前，不需要因為游離甲狀腺荷爾蒙的濃度變化而停藥（T4 濃度增加，T3 濃度正常或稍微降低）。
甲狀腺功能不足的典型症狀包括：體重增加、神情呆滯及昏沈欲睡；經診斷，甲狀腺刺激激素有明顯的濃度上升。在 amiodarone 停藥後 1 至 3 個月後，甲狀腺功能會逐漸恢復正常。然而，amiodarone 停藥並非絕對必要，可根據病患的狀況評估，並根據所監測出的甲狀腺刺激激素之濃度來調整劑量，可以 amiodarone 併用 L-thyroxine 荷爾蒙作為取代性的治療方式。
甲狀腺功能亢進較容易被誤診（因為它不會出現很多徵兆）（可能的症狀包括：無法解釋的體重輕微下降，抗心絞痛及/或抗心律不整藥物的療效降低）；老年人有可能出現精神病的徵兆或甲狀腺中毒的現象。這可經由測定甲狀腺刺激激素濃度極低而確立其診斷。
在這種情況下，Amiodarone 必須停藥，通常臨床症狀在 3-4 週後可以獲得緩解。由於嚴重的甲狀腺機能亢進有可能致命，因此必須緊急給予適當的治療。其中最被受關切的為甲狀腺毒症，包括病症本身及其對心肌平衡的影響。當合成性抗甲狀腺藥物治療無效時，建議以類固醇（1mg/kg）長期（3 個月）治療之。
在 amiodarone 停藥後，甲狀腺機能亢進可能還會持續數個月之久。

肺臟方面：
瀰漫性或間質性肺炎及阻塞性細支氣管炎及肺炎（BOOP）曾被報告過。病人用力有呼吸困難及乾咳症狀時，不論其是否伴隨有整體健康狀況變壞（疲倦、體重減輕及發燒），皆應做胸部 X 光檢查，必要時 amiodarone 應停藥。這些肺部不適有可能進一步惡化，造成肺部纖維化。不論是否給予皮質類固醇治療，amiodarone 若能於早期停藥，則肺部病變一般是可復原的。臨床症狀在停藥後 3-4 週後會消失，X 光報告及肺功能則在數月後會獲得改善。
曾有少數的胸膜炎病例被報告過，它一般都伴隨著間質性肺炎。
少數病例曾發生支氣管痙攣，特別是氣喘病患者。
少數病患在手術後，曾發生立即性、可能致死的急性呼吸窘迫症狀（可能和高氧濃度產生交互作用所致）（參見"警語及注意事項"）。

神經方面：
神經方面的副作用極為罕見：
－長期投與 amiodarone 可能造成週邊運動感覺神經病變和/或肌肉病變，這些病變可能發生在治療的數月內，有時是數年。在停藥後通常會消失。其復原可能不完全，而且非常慢，可能到停藥後的數個月。
－其他曾被報告過的神經方面失調包括：錐體外症狀或顫抖、腦性運動失調、罕見的良性顱內高血壓及睡眠障礙及作惡夢。

肝臟方面：
曾被報告的肝功能失調病例，已確定其有轉胺酵素濃度上升的情形。其報告如下：
- **轉胺酵素濃度中度上升（為正常值的 1.5 至 3 倍）。然而在 amiodarone 的劑量減低後，即可回復正常值，有些患者甚至會自行恢復正常。**
- **異常的急性肝臟疾病（少數個案）伴隨著轉胺酵素濃度升高和/或黃膽，有可能致死，此時應予以停藥。**
- **以 amiodarone 長期治療，曾罕見地引起慢性肝病。組織學上看來類似偽酒精性肝炎。臨床及生物學上的表徵（可能發生不定性的肝腫大，轉胺酵素的血中濃度升高為正常值的 1.5 至 5 倍）必須配合肝功能的定期檢查以了解病況。在持續 6 個月以上的療程後，即使轉胺酵素的血中濃度為中度提高，都應診斷為慢性肝病。一般在停藥後，臨床及生化檢驗值都會逐漸恢復正常。但仍有少數不可逆的惡化個案曾被報告過。**

心臟方面：
心跳遲緩，通常為中度性的而且與劑量有關。有些病例（竇結功能不良者、老年人）會發生明顯的心跳遲緩，甚至竇結停止。
傳導性障礙（心臟竇房阻滯、各種程度的房室阻滯）的情況較為罕見。
Amiodarone 對心臟節律的影響性不及大多數的抗心律不整藥物。它對心臟的副作用通常來自於與其他藥物的併用（參見"與其他藥物或其他形式的交互作用"）或電解質失調。

其他不良反應：
良性的腸胃失調（噁心、嘔吐、味覺異常有金屬味）通常發生於起始劑量時，隨著劑量的減低會獲得改善。有少數引起副睪丸炎的報告，然而其與本品的關連性尚未確立。另外，禿髮亦曾發生過，但罕見。
少數個案有過敏的反應，例如：血管炎、creatinine 濃度中度升高的腎功能障礙及血小板減少症。

【過量】
Amiodarone 高劑量的急性反應尚未被廣泛記載。曾有發生竇性心跳過慢，心室節律失調，尤其是 torsades de pointes，以及肝功能障礙的報告。此時，必須給予症狀性治療，並根據 Amiodarone 的藥動學特性，建議給予長時間的心臟功能監測。
Amiodarone 及其代謝產物無法以血液透析排除體外。

【藥理學特性】
藥效學特性：
抗心律不整作用，第 III 類
ATC code: C01BD01(C:心血管系統)
抗心律不整的特性
藉由降低鉀離子通透性而延長心肌細胞的動作電位第 3 期（Vaughan Williams class III）；
使竇自主性降低而致心跳變慢，此效應無法為 atropine 所拮抗；
具有非競爭性的 α-及 β-交感神經抑制作用；
使竇房、心房及結間的傳導減緩，在心跳較快時尤其明顯；
對心室內的傳導沒有影響；
使心房、竇結與心室的不反應期增長，心肌的興奮性降低；
會減緩及延長房室附加傳導路徑的不反應期。
其他特性
中度降低週邊阻力與心跳速率，因而減少耗氧量；
直接作用於心臟動脈平滑肌，因而增加心輸出量；心輸出量的維持，乃因主動脈與週邊阻力減少及不影響心肌收縮的結果。
交叉分析 13 個隨機性、前瞻性、有對照組比較的研究，總共包括 6,553 名病人，其中 78%在近期曾發生過心肌梗塞，22%有慢性心臟衰竭。
病患的平均追蹤時間為 0.4 至 2.5 年，其服用 amiodarone 的平均維持劑量為 200 至 400 mg。
這項交叉分析的結果證實，amiodarone 實驗組能有效降低 13%的總死亡率（$CI_{95\%}$ 0.78-0.99；P＝0.030），及降低 29%的心律不整死亡率（$CI_{95\%}$ 0.59-0.85；P＝0.0003）。
然而，這項結果在解讀上必須特別小心，因為必須考慮研究中的異質性（這異質性主要是指選擇的對象、追蹤時間的長短、實驗的方法及研究的結果）。研究中，amiodarone 實驗組病患退出計劃的比例（41%）高於使用安慰劑的對照組（27%）。

相對於對照組（1%），amiodarone 組有 7%的病人出現甲狀腺功能低下的情況。甲狀腺功能亢進在實驗組（服用 amiodarone）的發生機率為 1.4%，於對照組（使用安慰劑）則為 0.5%。
間質性肺炎於實驗組（服用 amiodarone）及對照組（使用安慰劑）的發生機率分別為 1.6%及 0.5%。

藥動學特性：
Amiodarone 對組織有緩慢通過及高度的親和性。
其口服的生體可用率因人而異，大約介於 30%至 80%之間（平均值為 50%）。在投與單一劑量後，其最高血中濃度約在 3 至 7 小時之後達到，療效則在平均一星期後出現（從數日到兩週）。
Amiodarone 的半衰期很長且會因人有很大的差異（從 20 天至 100 天）。在治療的最初幾日，amiodarone 會累積於身體的大部分組織內，尤其是脂肪組織。數日後，amiodarone 開始排除體外，它在體內達到分布平衡的時間因人而異，可從 1 個月到數個月之久。
由於上述的特性，因此應使用較高的起始劑量（loading dose），使組織迅速飽和以發揮療效。
部分的碘分子會自 amiodarone 中解離出來而在尿液中形成碘化物。以每日服用 200 mg amiodarone 計算，在 24 小時內約有 6 mg 的碘被排除於尿中。由此可知，有大量的碘是存在於 amiodarone 中經過肝臟而後被排除於糞便中。
Amiodarone 幾乎不由腎臟排除，因此腎功能不良的病人仍能使用本藥的正常劑量。
在治療結束後，藥物的排除會持續數個月之久。因此必須注意，其臨床療效仍會持續作用約 10 天到 1 個月。

【儲存與包裝】
本品 30℃以下避光儲存之。

製造廠：Sanofi Winthrop Industrie
地　址：(o) 9, rue de president Allende 94258
Gentilly,Cedex,France
(p)1, rue de la Vierge 33440 Ambares,France
藥　商：賽諾菲聖德拉堡股份有限公司
台北市民生東路三段 156 號 18 樓之 6

sanofi~synthelabo

CORDARONE

Amiodarone

Read all of this leaflet carefully before you start taking this medicine.
In contains important information concerning your treatment.
If you have further questions or if you are unsure about anything, please ask your doctor or your pharmacist.
This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.
Keep this leaflet. You may need to read it again.

1. IDENTIFICATION OF THE MEDICINE
Cordarone 200mg, scored tablet

2. WHEN THIS MEDICINE SHOULD BE USED
This medicine is indicated in the prevention and treatment of some types of heart rhythm disturbances.

3. WARNING!
a) WHEN THIS MEDICINE SHOULD NOT BE USED
This medicine SHOULD NOT BE USED in the event of:
- known allergy to iodine or to amiodarone,
- hyperthyroidism,
- some types of heart rhythm and/or conduction disturbances,
- an excessively slow heart rate,
- pregnancy after the first 3 months,
- breast-feeding,
- in combination with medicines that can cause torsades de pointes (serious heart rhythm disturbances):
  . class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide, etc.),
  . class III antiarrhythmics (sotalol, dofetilide, ibutilide, etc.),
  . sultopride (neuroleptic),
  . and other medicines (bepridil, cisapride, diphemanil, erythromycin IV, mizolastine, vincamine IV, sparfloxacin, etc.). (see " Drug interactions and other interactions").

Unless otherwise recommended by your doctor, this medicine should not be prescribed in combination with injectable diltiazem, certain antibiotics, beta-blockers other than sotalol and esmolol, along with some neuroleptics.

b) SPECIAL WARNINGS
In the event of the onset of unusual breathlessness, breathing difficulties or a dry cough, alone or associated with a deterioration in general condition, fatigue or prolonged or unexplained fever, diarrhea, weight loss or in the event of the recurrence of an excessively fast heart rate, tell your doctor.
Due to the presence of lactose, this medicine must not be used in the event of congenital galactosaemia, glucose and galactose malabsorption syndrome or lactase deficiency(rare metabolic diseases).

c) PRECAUTIONS FOR USE
Protect yourself from the sun throughout the duration of treatment to avoid the onset of a "sunburn"-type reaction.
During treatment, you may be asked to undergo blood tests to monitor your thyroid or liver function.
Before surgery, inform your anaesthetist that you are being treated with amiodarone.
In children, the safety and efficacy of amiodarone are not known.

d) DRUG INTERACTIONS AND OTHER INTERACTIONS
IN ORDER TO PREVENT POSSIBLE INTERACTIONS BETWEEN SEVERAL MEDICINES and, in particular, with injectable diltiazem, halofantrine, pentamidine, moxifloxacine, some neuroleptics (thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, amisulpride, tiapride, pimozide, haloperidol, dorperidol), and beta-blockers other than sotalol and esmolol, YOU MUST SYSTEMATICALLY INFORM YOUR DOCTOR OR PHARMACIST IF YOU ARE TAKING ANY OTHER MEDICINES.

e) PREGNANCY – LACTATION
Due to the presence of iodine, the use of this medicine is contraindicated after the first 3 months of pregnancy.
Breast-feeding is contraindicated if you are being treated with this medicine.
AS A GENERAL RULE, YOU SHOULD ALWAYS ASK A DOCTOR OR PHARMACIST FOR ADVISE BEFORE TAKING ANY MEDICATION DURING PREGNANCY OR BREAST-FEEDING.

f) LIST OF EXCIPIENTS WHICH MUST BE SPECIFIED FOR THE SAFE USE OF THIS MEDICINE IN CERTAIN PATIENTS
Lactose.

4. HOW TO USE THIS MEDICINE
a) DOSAGE
The usual dose is very variable form one individual to another but is usually:
- as an initial treatment: 3 tablets per day, for 8 to 10 days,
- as a maintenance treatment: 1/2 tablet to 2 tablets per day.

You must always scrupulously follow your doctor's prescription and you must never change the dosage without seeking medical advice. Similarly, you must not stop taking your treatment without consulting your doctor.

b) METHOD AND ROUTE OF ADMINISTRATION
This medicine is administrated by the oral route.

c) FREQUENCY AND TIME OF ADMINISTRATION
The tablets may be swallowed before, during or between meals. Crushing the tablets does not affect their properties.

d) TREATMENT DURATION
Strictly comply with your doctor's prescription.

e) MANAGEMENT OF OVERDOSE
If you take too high a dose of this medicine, quickly inform your doctor.

f) MANAGEMENT IN THE EVENT OF OMISSION OF ONE OR SEVERAL DOSES
Occasionally forgetting to take a tablet does not expose you to any particular risk.
Do not take a double dose to make up for a single dose that you have forgotten to take.

5. UNWANTED AND UNPLEASANT EFFETS
LIKE ANY ACTIVE PRODUCT THIS MEDICINEMAY IN CERTAIN PERSONS GIVE RISE TO VARYING DEGREES OF UNPLEASANT EFFECTS:
These must be reported to your doctor, who will tell you whether you should continue or stop taking your treatment:
- visual disturbances (sensation of mistiness or coloured halos around objects, very exceptionally, blurred vision or reduced vision),
- skin reaction to the sun; in rare cases, grey discolouration of the skin,
- thyroid disease (weight gain and fatigue or, conversely, excessive weight loss and diarrhea),
- respiratory problems (breathing difficulties, breathlessness, fever, dry cough), which can be very serious,
- significant slowing down in heart rate,
- in exceptional cases, benign gastrointestinal disturbances, abnormal liver findings, walking difficulties, hair loss, tremor, nightmares.

PLEASE TELL YOUR DOCTOR OR PHARMACIST ABOUT ANY UNWANTED AND UNPLEASANT EFFECT NOT MENTIONED IN THIS LEAFLET.

6. STORAGE
a) DO NOT EXCEED THE EXPIRY DATE INDICATED ON THE OUTER PACKAGING.
b) STORED BELOW 30℃ AND PROTECTED FROM LIGHT.
c) WARNING IN THE EVENT OF VISIBLE SIGNS OF DETERIORATION.

SUMMARY OF PRODUCT CHARACTERISTICS

COMPOSITION
Each tablet contains amiodarone hydrochloride 200mg.
CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS
Prevention of recurrences of:
- life-threatening ventricular tachycardia: the treatment should be instigated in a hospital environment under monitoring;
- documented symptomatic and debilitating ventricular tachycardia;
- documented supraventricular tachycardia when the need for treatment has been established and in the event of resistance or contraindication to other treatments;
- ventricular fibrillation.

Treatment of supraventricular tachycardia, slowing or reduction in atrial fibrillation or atrial flutter.
Amiodarone can be used in the presence of coronary artery disease and/or impaired left ventricular function (see "Pharmacodynamic properties").
POSOLOGY AND METHOD OF ADMINISTRATION
Initial treatment :
The usual dosage regimen is 3 tablets per day, for 8 to 10 days.
Maintenance treatment :
Seek the minimum effective dose, which varies depending on the patient, ranging from ½ tablet per day (1 tablet every 2 days) to 2 tablets every day.
CONTRAINDICATIONS
This medicine is contraindicated in the following situations:
- sinus bradycardia and sino-atrial block not corrected by a pacemaker;
- sinus disease not corrected by a pacemaker (risk of sinus arrest);
- high-degree conduction disorders not corrected by a pacemaker;
- hyperthyroidism due to its possible exacerbation by amiodarone;
- known hypersensitivity to iodine or amiodarone;
- the last 6 months of pregnancy;
- breast-feeding;
- combination with medicines that can induce torsades de pointes:
  . class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide, etc.),
  . class III antiarrhythmics (sotalol, dofetilide, ibutilide, etc.),
  . sultopride,
  . other medicines, such as bepridil, cisapride, diphemanil, erythromycin IV, mizolastine, sparfloxacin, etc. (see "Interactions with other medicinal products and other forms of interaction").

This medicine IS NOT GENERALLY RECOMMENDED in combination with:
- injectable diltiazem,
- halofantrine, pentamidine, moxifloxacin,
- certain neuroleptics (thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, amisulpride, tiapride, pimozide, haloperidol, droperidol),

- and with beta-blockers other than sotalol and esmolol (see “Interactions with other medicinal products and other forms of interaction”).

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

Warnings

An ECG must be performed before starting treatment.

- Slowing of heart rate may be accentuated in elderly patients.
- The electrocardiogram is modified under amiodarone. This “cordaronic” modification consists of a prolongation in QT reflecting a repolarisation prolongation, possibly with the appearance of a U wave; this is a sign of therapeutic impregnation and not of toxicity.
- The onset of 2nd or 3rd-degree atrioventricular block, sino-atrial block or bifascicular block should lead to suspension of treatment. 1st-degree atrioventricular block should lead to increased monitoring.
- The presence of iodine in the medicinal product falsifies certain thyroid tests (binding of radioactive iodine, PBI); however, thyroid function assessment is still possible (T3, T4, TSH_{US}).
- Combination (see ”Interactions with other medicinal products and other forms of interaction”) with:
  . beta-blockers other than sotalol (contraindicated combination), and esmolol (combination requiring precautions for use),
  . verapamil and diltiazem,
  should only be considered in the prevention of life-threatening ventricular arrhythmias.

Due to the presence of lactose, this medicinal product is contraindicated in the event of congenital galactosaemia, glucose and galactose malabsorption syndrome or lactase deficiency.

The onset of dyspnoea or a dry cough, alone or associated with a deterioration in general condition, should suggest the possibility of pulmonary toxicity and requires X-ray (see ”Undesirable effects”).

Precautions for use

Electrolyte balance disturbances and, in particular, hypokalaemia: it is important to take into account situations that may be associated with hypokalaemia since the latter can promote the onset of proarrhythmic effects.

Hypokalaemia should be corrected prior to administration of amiodarone.

The undesirable effects mentioned below are usually related to excessive drug levels; they can be avoided or their severity minimised by carefully seeking the minimum maintenance dosage.

Patients should be advised to avoid exposure to sun or to use sun protection during treatment.

Amiodarone can cause thyroid anomalies (see “Undesirable effects”).

Assay of TSH is recommended in all patients before treatment and then regularly throughout treatment - for example, every 6 months - and several months after its withdrawal.

TSH levels should be measured in the event of clinical suspicion of dysthyroidism (see “Undesirable effects”).

In children, the safety and efficacy of amiodarone have not been evaluated by controlled clinical trials.

Regular monitoring of liver function (transaminase levels) is useful to screen for liver damage caused by amiodarone (see “Undesirable effects”).

Anaesthesia

Before surgery, the anaesthetist must be informed that the patient is treated with amiodarone.

Chronic treatment with amiodarone may lead to exacerbation, in terms of undesirable effects, of the haemodynamic risks of general or local anaesthetics. These concern, in particular, bradycardiac and hypotensive effects, reduced cardiac output and conduction disturbances.

In addition, a few cases of acute respiratory distress have been observed immediately after surgery in patients treated with amiodarone. Consequently, close monitoring is recommended during artificial ventilation of such patients (see “Undesirable effects”).

INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

A number of antiarrhythmic drugs depress cardiac automatism, conduction and contractility.

The combination of antiarrhythmics from different classes can provide a beneficial therapeutic effect, but is usually VERY DELICATE, requiring close clinical and ECG monitoring. The combination of antiarrhythmics inducing torsades de pointes (such as amiodarone) is CONTRAINDICATED.

The combination of antiarrhythmics from the same class is NOT RECOMMENDED, apart from in exceptional cases, due to the increased risk of cardiac undesirable effects.

Combination with medicines with negative inotropic, bradycardiac and/or atrioventricular conduction slowing drugs is DELICATE and requires close clinical and ECG monitoring.

Contraindicated combinations

+ Medicinal products that can induce torsades de pointes:
  - class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide),
  - class III antiarrhythmics (dofetilide, ibutilide, sotalol),
  - other medicinal products, such as: bepridil, cisapride, diphemanil, erythromycin IV, mizolastine, vincamine IV,
  - sultopride

  Increased risk of ventricular arrhythmia and, in particular, torsades de pointes.
+ Sparfloxacin

  Risk of torsades de pointes due to a prolongation in QT interval (addition of electrophysiological effects).

Inadvisable combinations

+ Neuroleptics inducing torsades de pointes:
  some phenothiazine neuroleptics (chlorpromazine, cyamemazine, levomepromazine, thioridazine, trifluoperazine), benzamide neuroleptics (amisulpride, sulpiride, tiapride), butyrophenone neuroleptics (droperidol, haloperidol), other neuroleptics (pimozide).
  Increased risk of ventricular arrhythmia and, in particular, torsades de pointes.
+ Halofantrine, moxifloxacine, pentamidine

  Increased risk of ventricular arrhythmia and, in particular, torsades de pointes. If possible, suspend the non-antibiotic torsadogenic drug. If the combination cannot be avoided, prior control of QT and constant electrocardiographic monitoring.
+ Injectable diltiazem

  Risk of bradycardia and atrioventricular block. If this combination cannot be avoided, only administer under close clinical and constant electrocardiographic monitoring.
+ Beta-blockers (other than sotalol and esmolol)

  Contractility, automatism and conduction disturbances (suppression of compensatory sympathic mechanisms).

Combinations requiring precautions for use

+ Oral anticoagulants

  Increased anticoagulant effect and haemorrhagic risk.

  More frequent control of prothrombin rate and monitoring of INR. Adjustment of oral anticoagulant dosage during treatment with amiodarone and after its withdrawal.
+ Cyclosporin

  Increase in circulating levels of cyclosporin due to a reduction in its hepatic metabolism with a risk of nephrotoxic effects.

  Assay of blood cyclosporin concentrations, monitoring of kidney function and adjustment of dosage during combination with amiodarone and after its withdrawal.
+ Oral diltiazem

  Risk of bradycardia or atrioventricular block, particularly in the elderly.

  Clinical and electrocardiographic monitoring.
+ Digitalis drugs

  Depression of automatism (excessive bradycardia) and atrioventricular conduction disturbances. In the event of use of digoxin, increased blood digoxin levels due to reduced digoxin clearance.

  Clinical and electrocardiographic monitoring and, if necessary, monitoring of blood digoxin levels and adjustment of digoxin dosage.
+ Esmolol

  Contractility, automatism and conduction disturbances (suppression of compensatory sympathic mechanisms).

  Clinical and electrocardiographic monitoring.
+ Potassium-lowering drugs: potassium-lowering diuretics (alone or in combination), stimulant laxatives, glucocorticoids (systemic route), tetracosactide, amphotericin B (IV route)

  Increased risk of ventricular arrhythmia and, in particular, torsades de pointes (hypokalaemia is a predisposing factor).

  Clinical, laboratory and electrocardiographic monitoring.
+ Phenytoin

  Increase in plasma concentrations of phenytoin with signs of overdose and, in particular, neurological signs (reduced hepatic metabolism of phenytoin).

  Clinical monitoring, control of plasma concentrations of phenytoin and, if necessary, adjustment of the latter’s dosage.
+ Bradycardiac drugs: bradycardiac calcium antagonists (diltiazem, verapamil), beta-blockers (except sotalol), clonidine, guanfacine, digitalis drugs, mefloquine, anticholinesterase drugs (donezepil, galantamine, rivastigmine, tacrine, ambemonium, pyridostigmine, neostigmine)

  Increased risk of ventricular arrhythmia and, in particular, torsades de pointes.

  Clinical and electrocardiographic monitoring.
+ Simvastatin

  Increased risk of undesirable effects (dose-dependent), such as rhabdomyolysis (reduced hepatic metabolism of the cholesterol-lowering drug).

  Do not exceed a dosage of 20mg/d simvastatin.

  If the therapeutic goal is not achieved at this dosage, use another statin not concerned by this type of interaction.

PREGNANCY AND LACTATION

Pregnancy :

Animal studies have not revealed any teratogenic effect. In the absence of any teratogenic effect in animals, no malformative effect is expected in humans.

In fact, to date, substances responsible for malformations in humans have been revealed to be teratogenic in animals in the course of properly conducted studies in both species.

Clinically, no sufficiently relevant data are currently available to be able to assess a potential malformative effect of amiodarone when it is administered during the first three months of pregnancy.

Since the foetal thyroid begins to bind iodine from 14 weeks after the last menstrual period, no effects on the foetal thyroid are expected in the event of administration prior to this.

Iodine overload related to the use of this medicine after this time can lead to foetal hypothyroidism, which may be biological or even clinical (goitre).

Consequently, the use of this medicine is contraindicated after the first 3 months of pregnancy.

Lactation :

Amiodarone and its metabolite, along with iodine, cross into breast milk at concentrations greater than those in maternal plasma. Due to the risk of hypothyroidism in the newborn infant, breast-feeding is contraindicated in the event of treatment with this medicine.

UNDESIRABLE EFFECTS

Ocular signs:

Corneal micro-deposits, which are almost constant in adults; usually remain localized to the area under the pupil and do not contraindicate continuation of treatment. In exceptional cases these may be accompanied by perception of coloured halos in dazzling light or sensations of mistiness.

Composed of complex lipid deposits, corneal micro-deposits are always entirely reversible on discontinuation of treatment.

A few cases of optic neuropathy (optic neuritis) with blurred vision, reduced vision and papillary oedema at the fundus of the eye have been reported. The outcome may be a more or less severe reduction in visual acuity. The relationship with amiodarone does not appear to have been established at the current time. However, in the event of any other obvious cause, it is recommended that treatment be suspended.

Cutaneous signs:
Photosensitization. Subjects are advised to avoid exposure to sun (and ultraviolet rays in general) during treatment.
Cases of erythema have also been reported during radiotherapy.
Cases of skin rashes - generally not very specific - and a few cases of exfoliative dermatitis have been reported, without the relationship with the medicine having been clearly established.
Exceptional cases of lilac or slate-grey coloured pigmentation of the skin may occur at high daily dosages prescribed for a long period of time; after treatment withdrawal, this pigmentation is slow to disappear (10 to 24 months).
Thyroid signs:
In the absence of clinical signs of dysthyroidism, a "dissociated" thyroid hormone level (increase in T4, T3 normal or slightly reduced) does not warrant withdrawal of treatment.
Hypothyroidism has a classic form: weight gain, apathy, drowsiness and clear elevation in TSH signal its diagnosis. Withdrawal of the treatment leads to a gradual return to normal thyroid function within a period of 1 to 3 months; this withdrawal is not essential. If the indication so warrants, amiodarone may be continued, combining it with L-thyroxine-based substitutive opotherapy, with TSH levels acting as a guide for the dosage.
Hyperthyroidism is more misleading: with few symptoms (slight unexplained weight loss, reduction in anti-angina and/or antiarrhythmic efficacy); psychiatric forms in the elderly, or even thyrotoxicosis. A reduction in ultra-sensitive TSH levels confirms the diagnosis.
It is essential to suspend amiodarone: this is usually enough to trigger clinical recovery within a period of 3-4 weeks. Severe cases can lead to the patient's death, making it necessary to urgently instigate appropriate treatment. If the thyrotoxicosis is worrying, either in itself or due to its effects on the precarious myocardial balance, the inconstant efficacy of synthetic anti-thyroid drugs leads to straightforward corticosteroid therapy (1 mg/kg) being recommended, for a sufficiently long period of time (3 months).
Cases of hyperthyroidism have been reported as long as several months following discontinuation of amiodarone.
Pulmonary signs
Cases of diffuse interstitial or alveolar pneumopathy and bronchiolitis obliterans organizing pneumonia (BOOP) have been reported. The onset of effort dyspnoea - either isolated or associated with a deterioration in general condition (fatigue, weight loss, febricula) – requires radiological control and, if necessary, suspension of treatment. These types of pneumopathy can actually develop into pulmonary fibrosis. Early withdrawal of amiodarone – associated or not with corticosteroid therapy – leads to a regression in the disturbances. Clinical signs usually disappear in 3 or 4 weeks, Radiological and function improvement is usually slower (several months).
A few cases of pleurisy, generally associated with interstitial pneumopathies, have been reported.
A few cases of bronchospasm have been reported, particularly in asthmatic patients.
A few cases of acute respiratory distress syndrome, sometimes fatal, have been observed, sometimes immediately following surgery (a possible interaction with high doses of oxygen has been suggested) (see "Special warnings and special precautions for use").
Neurological effects
These are rare:
- the prolonged administration of amiodarone can cause sensory, motor or mixed peripheral neuropathies and myopathies. These may occur after just a few months of treatment, but sometimes after several years. They are generally reversible on treatment withdrawal. However, this recovery may be incomplete, very slow and occur only several months after treatment discontinuation.
- other disturbances reported: tremor or other extra-pyramidal symptoms, cerebellar-type ataxia, exceptional benign intra-cranial hypertension, sleep disturbances including nightmares.

Hepatic signs
Cases of liver disease have been reported; these cases have been diagnosed by an elevation in serum transaminase levels. In fact, the following have been reported:
- isolated and generally moderate (1.5 to 3 times normal values) elevation in transaminase levels, regressing following a reduction in the dosage or even spontaneously.
- exceptionally (a few isolated cases), acute liver disease with hypertransaminasaemia and/or jaundice, sometimes fatal, requiring suspension of treatment.
- rare cases of chronic liver disease during prolonged treatment. The histology is that of pseudo-alcoholic hepatitis. The discretion of the clinical and laboratory picture (inconstant hepatomegaly, hypertransaminasaemia between 1.5 and 5 times normal levels) warrants regular monitoring of liver function. Hypertransaminasaemia - even moderate - occurring after treatment for more than 6 months, may suggest a diagnosis of chronic liver disease. The clinical and laboratory disturbances usually regress after treatment is withdrawn. A few cases of an irreversible outcome have been reported.

Cardiac effects
Generally moderate, dose-dependent bradycardia. In certain cases (sinus dysfunction, elderly patients), marked bradycardia and, more exceptionally, sinus arrest have been reported.
Rarely: conduction disturbances (sino-atrial block, atrioventricular block of varying degrees).
The arrhythmogenic effect of amiodarone is weak, less than that of most antiarrhythmic drugs and generally occurs in some drug combinations (see "Interaction with other medicinal products and other forms of interaction") or electrolyte balance disturbances.
Miscellaneous effects
- Benign gastrointestinal disturbances (nausea, vomiting, dysgeusia), usually occurring during initial treatment and disappearing when the dosage is reduced. A few cases of epididymitis have been reported. The relationship with the medicine does not appear to have been established. A few rare cases of alopecia have been observed.
- A few isolated cases, expressed in a variety of ways, have been observed in a context suggesting a hypersensitivity reaction: vascularitis, renal impairment with a moderate elevation in creatinine, thrombopaenia.

OVERDOSE
There is little documentation available on the acute administration of high doses of amiodarone. A few cases of sinus bradycardia, ventricular arrhythmia - in particular, torsades de pointes - and liver damage have been reported. Treatment should be symptomatic. Given the kinetics of the product, monitoring for a sufficiently long period of time – particularly cardiac monitoring - is recommended.
Amiodarone and its metabolites can not be dialysed.
PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES
CLASS III ANTIARRHYTHMIC
ATC code: C01BD01 (C: cardiovascular system)
Antiarrhythmic properties:
- Prolongation of phase 3 of the action potential of cardiac fibre essentially resulting from a reduction in the potassium channel (Vaughan Williams class III);
- Bradycardiac effect due to reduction of sinus automatism. This effect is not antagonised by atropine;
- Non-competitive alpha and beta anti-adrenergic antagonist properties;
- Slowing down of sino-atrial, atrial and nodal conduction, which is more marked the higher the rhythm;
- No modification in intraventricular conduction;
- Increase in refractory periods and reduction in myocardial excitability at the atrial, nodal and ventricular stage;
- Slowing down of conduction and prolongation of refractory periods in the atrioventricular accessory pathways;

Other properties:
- Reduction in oxygen consumption due to a moderate decrease in peripheral resistance and reduction in heart rate;
- Increase in coronary output due to a direct effect on the smooth muscles of the myocardial arteries and maintenance of cardiac output due to a reduction in pressure and peripheral resistance and absence of any negative inotropic effect.

A meta-analysis of thirteen controlled, randomised, prospective studies including 6553 patients with a recent myocardial infarction (78%) or chronic heart failure (22%) was conducted.
The average follow-up period for the patients ranged from 0.4 to 2.5 years. The daily maintenance dosage was, on average, between 200 to 400 mg.
This meta-analysis demonstrated a significant reduction in favour of amiodarone by 13% for total mortality ($CI_{95\%}$ 0.78 - 0.99; P = 0.030) and by 29% for rhythm-related mortality ($CI_{95\%}$ 0.59 - 0.85; P = 0.0003).
However, these results must be interpreted cautiously, taking into account the heterogeneity of the studies included (heterogeneity related mainly to the population selected, the duration of follow-up, methodology used and the results of the studies).
The percentage of treatment withdrawals was higher in the amiodarone group (41%) than in the placebo group (27%).
Seven percent of the patients taking amiodarone presented hypothyroidism, versus 1% in the placebo group. Hyperthyroidism was diagnosed in 1.4% of patients taking amiodarone, versus 0.5% in the placebo group.
Interstitial pneumopathy occurred in 1.6% of patients taking amiodarone, versus 0.5% in the placebo group.
PHARMACOKINETIC PROPERTIES
Amiodarone is a medicine with slow transit and a high tissue affinity.
Its bioavailability by oral route varies depending on the individual from 30 to 80% (mean value 50%). After a single dose, peak plasma concentrations are reached in 3 to 7 hours. Therapeutic activity is obtained, on average, within one week (from a few days to two weeks).
The half-life of amiodarone is long, with a high level of inter-individual variability (20 to 100 days). During the first days of treatment, the medicine accumulates in most of the body's tissues, particularly in adipose tissues. Elimination begins after a few days and the input/output ratio balances out after a period of a few months, depending on the individuals.
These characteristics explain the use of loading doses aimed at rapidly achieving the level of tissue impregnation required for therapeutic activity.
Part of the iodine becomes detached from the medicine and is found in the urine in the form of iodide; this corresponds to 6 mg/24 hours for a daily dose of 200 mg of amiodarone. The rest of the medicinal product - thus the greatest part of the iodine – is excreted in the faeces after passing through the liver.
The negligible urinary elimination means that the medicine can be used at usual dosages in patients with impaired kidney function.
After withdrawal of treatment, elimination continues for several months. The persistence of a residual activity for ten days to one month should be taken into account.

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