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**世界中医药学会联合会**

**World Federation of Chinese Medicine Societies**

**SCM/TR 0006-2025**

## **心血宁片临床应用专家共识**

Expert consensus on the clinical application of Xinxuening Tablets

**世界中联技术报告**

Technical report of WFCMS

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## 前 言

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本文件的起草程序遵守了世界中医药学会联合会发布的SCM 1.1-2021《标准化工作导则 第1部分：标准制修订与发布》。

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## 引 言

心血宁片由朗致集团研制，是具有独立知识产权的中成药制剂（专利号：ZL200810088937.3），已通过国家局审核获取药品注册证（国药准字Z20184011），是中国国家基本医疗保险乙类药物（化瘀宽胸剂，编号：505），收录于《中华人民共和国药典》（2020年版），研究资料见附录A。

目前，心血宁片在临床中广泛应用，相关循证医学证据不断增加，由世界中医药学会联合会介入心脏病专业委员会组织中医、西医及中西医结合心血管病专家，对心血宁片的适用范围、临床证据、适应症、安全性、理论基础及药理作用进行系统回顾与总结，结合循证医学证据与专家意见，讨论并起草了本文件，形成推荐意见和共识建议。本文件研制过程中共形成11个临床问题见附录B，推荐意见/共识建议概要表见附录C。

本文件旨在服务临床医师，为心血宁片临床应用提供参考，促进合理用药，减少用药风险，使更多患者获益。随着临床实践的深入，新的证据不断发现，本文件将不断更新和完善。

本文件的发布机构提请注意，声明符合本文件时，可能涉及到本文件与心血宁片相关的专利的使用。

本文件的发布机构对于该专利的真实性、有效性和范围无任何立场。

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# 心血宁片临床应用专家共识

## 1 范围

本文件给出了心血宁片临床应用的适应症、剂量和疗程，以及特殊人群用药、不良反应和禁忌证等内容。

本文件适用于相关专业领域各类具有所在国法律许可的执业医师使用。

## 2 规范性引用文件

下列文件中的内容通过文中的规范性引用而构成本文件必不可少的条款。其中，注日期的引用文件，仅该日期对应的版本适用于本文件；不注日期的引用文件，其最新版本（包括所有的修改单）适用于本文件。

GB/T16751.1-2021 中医临床诊疗术语 第2部分：证候

## 3 术语和定义

下列术语和定义适用于本文件。

### 3.1

#### 稳定劳力型心绞痛

由于暂时性心肌缺血引起的以胸痛为主要特征的临床综合征<sup>[1]</sup>。

注：是冠状动脉粥样硬化性心脏病的最常见表现。其中，稳定劳力型心绞痛的发作程度、频率、性质及诱发因素在数周内无明显变化。

### 3.2

#### 不稳定性心绞痛

介于稳定劳力型心绞痛和急性心肌梗死之间的临床状态<sup>[2]</sup>。

注1：包括除稳定型劳力型心绞痛以外的初发型、恶化型劳力型心绞痛和各型自发型心绞痛。

注2：是在动脉粥样硬化病变的基础上，由冠状动脉内膜下出血、斑块破裂、破损处血小板与纤维蛋白凝集形成血栓、冠状动脉痉挛以及远端小血管栓塞引起的急性或亚急性心肌供血减少所致。

### 3.3

#### 高血压

在未使用降压药物的情况下，非同日3次测量诊室血压，SBP>140 mm Hg 和（或）DBP≥90 mm Hg，SBP>140 mm Hg 和 DBP<90 mm Hg 为单纯收缩期高血压患者既往有高血压史，目前正在使用降压药物，血压虽然低于140/90 mm Hg，仍应诊断为高血压<sup>[3]</sup>。

### 3.4

#### 血脂异常

血浆中和低密度脂蛋白胆固醇、胆固醇和（或）甘油三酯水平增高，或是高密度脂蛋白胆固醇水平降低等情况，这种状态会促使动脉粥样硬化的形成<sup>[4]</sup>。

## 4 药物基本信息

### 4.1 处方来源及药物组成

心血宁片是依据中医理论，总结心脑血管疾病治疗经验，经现代药理学研究及筛选后，重新配伍科学组方而成。根据冠心病的血瘀证临床特征，选取葛根、山楂两味中药进行提取精制而成的一种纯中药制剂。

### 4.2 功效主治

心血宁片具有活血化瘀，通络止痛之效。本品用于瘀血阻络引起的胸痹，心痛，眩晕；冠心病心绞痛，高血压，血脂异常等见上述证候者。

## 5 临床应用建议

### 5.1 适应症

#### 5.1.1 胸痹心痛

心血宁片可改善瘀血阻络证或心血瘀阻证胸痹心痛患者胸闷、心前区疼痛等临床症状。（推荐意见：B 级证据，强推荐）

3 项研究<sup>[5-7]</sup>显示心血宁片可改善瘀血阻络证或心血瘀阻证胸痹心痛患者胸闷、心前区疼痛等临床症状。

#### 5.1.2 稳定劳力型心绞痛

在西医规范化治疗基础上，联合应用心血宁片可进一步改善 SAP 患者临床症状，减少患者心绞痛发作次数及持续时间，并改善心电图缺血表现。（推荐意见：B 级证据，强推荐）

6 项研究<sup>[5-10]</sup>评价心血宁胶囊（片）治疗 SAP 患者的临床疗效，结果均显示心血宁可改善 SAP 的临床症状，减少患者心绞痛发作次数及持续时间，改善心电图缺血表现。一项研究<sup>[11]</sup>对结局指标进行 Meta 分析，结果显示在西医规范治疗的基础上可进一步改善 SAP 患者的临床症状，与对照组比较差异具有统计学意义。

#### 5.1.3 不稳定性心绞痛

在西医规范化治疗基础上，联合应用心血宁片可进一步改善 UA 患者的临床症状，减少

患者心绞痛发作次数及持续时间，并改善心电图缺血表现。（推荐意见：C 级证据，强推荐）

一项纳入 80 例 UA 患者的临床研究结果显示<sup>[12]</sup>心血宁可减少 UA 患者心绞痛发作次数和持续时间，改善心电图缺血表现。

#### 5.1.4 原发性高血压

a) 单独服用心血宁片可以降低原发性高血压患者的 SBP 和 DBP 水平。（推荐意见：B 级证据，强推荐）

一项研究<sup>[13]</sup>比较心血宁与心可舒单药治疗原发性高血压患者的血压变化情况，结果显示单独使用心血宁能够降低原发性高血压患者的血压水平，其疗效与心可舒相当。

b) 在西医规范化治疗基础上，联合应用心血宁片可降低或进一步降低原发性高血压患者的 SBP 和 DBP。（推荐意见：B 级证据，强推荐）

6 项有关原发性高血压的研究<sup>[14-19]</sup>显示，观察组在对照组用药（缬沙坦分散片或卡维地洛）的基础上叠加心血宁治疗，两组患者 SBP 和 DBP 均较治疗前下降，观察组下降幅度优于对照组。

#### 5.1.5 血脂异常

a) 单独服用心血宁片可以降低血脂异常患者的 TC、TG 水平。（推荐意见：C 级证据，强推荐）

一项研究<sup>[20]</sup>比较心血宁与心可舒单药治疗血脂异常患者的临床疗效，结果显示心血宁与心可舒均可降低血脂异常患者 TC、TG 水平，心血宁组下降水平大于心可舒组，两组差异具有统计学意义。

b) 在西医规范化治疗基础上，联合应用心血宁片可进一步降低血脂异常患者的 TG、TC 水平。（推荐意见：C 级证据，强推荐）

两项研究<sup>[16, 18]</sup>显示在缬沙坦的基础上联合应用心血宁治疗原发性高血压，患者血压下降的同时，TC、TG 均下降，差异具有统计学意义。

### 5.2 有临床证据的应用

有临床证据的其他使用见附录 E。

## 6 安全性

### 6.1 不良反应/不良事件

一项心血宁片治疗冠心病心绞痛患者的临床观察结果显示，310 名试验组患者在使用心血宁片期间疗程期间，1 例患者服药后出现轻度胃部不适（可自行缓解），其余病例均未发现不良反应<sup>[7]</sup>。

中国国家药物不良反应监测中心显示，2019 年-2022 年间共收到 14 例不良反应报告。少数患者服用本品后可出现腹胀、腹泻、皮疹、局部红肿等症状，停药减药后症状均可减轻或消失，未见严重不良事件/不良反应报告见附录 F。

## 6.2 禁忌证

心血宁片尚无妊娠或哺乳期、15 岁以下儿童的安全性研究，故不建议孕妇或哺乳期妇女、15 岁以下儿童服用；没有严重肝肾功能障碍患者的应用经验，体内药代动力学过程尚不清晰，故建议严重肝肾功能不全患者慎用；考虑其活血化瘀功效，有出血倾向的患者慎用；对本药物成分过敏者禁用（共识建议）。

## 6.3 联合用药

现有文献报告，心血宁片的临床应用多是西医规范化治疗基础上的叠加试验，未见联合使用增加相关不良反应及毒副作用。与其他中药或中成药联合使用时，应注意辨证施治原则，关注用药安全性。



## 附录 A

### (资料性)

#### 心血宁片研究资料

##### A.1 中医理论基础

心血宁片为葛根提取物、山楂提取物复方制剂,《神农本草经》中记载“葛根主诸痹”,此“痹”不仅指周身痹痛,“胸痹”亦当含于内。葛根一可解表通里,鼓舞胃中清阳上升,二可活血通脉,助心行血而开痹。《医学衷中参西录》中云:“山楂善入血分为化瘀血之要药……,疗心腹疼痛”,为消积化瘀之要药,且味甘性辛凉之葛根与其配伍,化瘀血而不伤正气,开郁气而不伤正气。两药合用,符合中医“气血理论”。《素问·调经论》“气血不和,百病乃变化而生……孙络水溢,则经有留血”。《灵枢·百病始生》“阳络伤则血外溢……阴络伤则血内溢”。心主血脉,心病多瘀。心血宁片功能主治为:活血化瘀、通络止痛,故临床可用于中医辨证为瘀血阻络证的冠心病心绞痛、高血压、血脂异常的治疗。

##### A.2 常用片剂工艺

《中华人民共和国药典一部》(2020 年版)示心血宁片的制作工艺为:葛根提取物 150g 山楂提取物 25g,加淀粉适量,混匀,制成颗粒,干燥,加入适量硬脂酸镁,混匀,压制成 1000 片,包糖衣或薄膜衣,即得。

##### A.3 药理研究

本品以葛根提取物为君药,葛根中的葛根素和总黄酮能够改善心绞痛及心肌梗死患者的临床症状,可降低血压<sup>[25]</sup>,可抑制索拉非尼引发的心肌铁死亡,对索拉非尼所致的心肌毒性具有良好的保护作用<sup>[26]</sup>。山楂提取物为臣药,山楂叶总黄酮为山楂叶的主要活性物质群,具有抗动脉粥样硬化、抗心肌缺血、降血压、降低 TG 与 LDL、升高 HDL、降血糖及抗炎等作用;研究提示还可拮抗乌头碱引起的心律不齐,并有持久的强心作用<sup>[27-31]</sup>。冠心宁合方的研究提示其可以降低 H 型高血压患者的血压并改善患者的高 Hcy 血症<sup>[32]</sup>。

心血宁片取药食同源之葛根、山楂,集其所长,药少而力宏效专,相辅相成,共奏活血化瘀,通络止痛之效,可以扩张冠状动脉,增加冠状动脉血流量,增强心肌收缩能力,降低血压,降低血脂,并降低 H 型高血压患者 Hcy 等作用。

##### A.4 毒理学研究

急性毒理实验:选用昆明种小鼠灌胃给予心血宁片口服最大耐受量,未达到致死剂量。

亚急性毒性测定:取小鼠 60 只,雌雄各半,体重  $19.3 \pm 0.5\text{g}$ ,每日早 8 点 (ig)  $0.2\text{g/ml}$  的心血宁片悬液  $20\text{ml/kg}$ ,连续给药 30 天,用药期间未见毒性反应,未检测出  $\text{LD}_{50}$  值。

最大耐受量测定:取小白鼠 40 只,雌雄各半,体重  $20.5 \pm 0.6\text{g}$ ,禁食给水 12h 后,灌胃 (ig) 给予  $0.2\text{g/ml}$  的心血宁片  $40\text{ml/kg}$  观察,6h 后同法再给药一次,连续观察 10 天,

小鼠的活动、摄食、饮水、毛色、粪便均无明显异常变化，亦无死亡发生，未检测出 LD<sub>50</sub> 值。因此心血宁片小鼠口服的最大耐受量大于 16g/kg，此剂量相当于临床正常用量的 400 倍。

参照《中药、天然药物急性毒性研究技术指导原则》，心血宁片在大于临床用药剂量 400 倍一日给药及大于临床用量 100 倍连续 30 天给药均是安全的。

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附录 B  
(资料性)  
临床问题清单

本文件研制过程中共形成 11 个临床问题（表 B.1）。

表B.1 临床问题清单

序号	临床研究
适应证及具有循证医学证据的临床应用	
1	心血宁片适用于什么证型的冠心病患者？
2	心血宁片除了治疗冠心病，还可以治疗哪些循环系统疾病？
3	心血宁片能否改善稳定劳力型性心绞痛患者临床症状（减少心绞痛发作次数，缩短心绞痛持续时间）及心电图表现？
4	心血宁片能否改善不稳定性心绞痛患者的临床症状（减少心绞痛发作次数，缩短心绞痛持续时间）及心电图表现？
5	心血宁片是否有利于降低原发性高血压患者的血压水平，改善患者头晕症状？
6	心血宁片是否能够降低血脂异常患者TC、TG、LDL-C水平？
7	心血宁片是否有利于降低血清同型半胱氨酸水平？
用法用量问题	
8	心血宁片用法、剂量及疗程
9	心血宁片是否存在明确注意事项，如用药(配伍) 禁忌、特殊人群用药及其他临床用药注意事项？
安全性问题	
10	心血宁片常见不良反应有哪些？出现不良反应时应如何应对？
11	长期服用心血宁片的安全性如何？

## 附录 C

(资料性)

### 推荐意见/共识建议概要表

本文件采用国际公认的 GRADE 系统进行证据等级评价，采用德尔菲法与名义组法相结合，对于有循证医学证据的适应症，根据证据等级，形成“推荐意见”；对于目前文献不充分，具有临床适应症的，经专家讨论，形成“共识建议”。最终专家共形成 12 条推荐意见及 8 条共识建议，具体见表 C.1、表 C.2。

表C.1 心血宁片推荐意见概要表

推荐意见	共识条目	证据等级	推荐强度
推荐意见 1	心血宁片可改善瘀血阻络证或心血瘀阻证胸痹心痛患者胸闷、心前区疼痛等临床症状。	B	强推荐
推荐意见 2.1	在西医常规治疗的基础上，加用心血宁片可以进一步改善稳定劳力型心绞痛患者心绞痛发作次数，缩短心绞痛持续时间。	B	强推荐
推荐意见 2.2	在西医常规治疗的基础上，加用心血宁片可以进一步改善稳定劳力型心绞痛患者心电图表现。	B	强推荐
推荐意见 3.1	在西医常规治疗的基础上，加用心血宁片可以进一步改善不稳定性心绞痛患者心绞痛发作次数，缩短心绞痛持续时间。	C	强推荐
推荐意见 3.2	在西医常规治疗的基础上，加用心血宁片可以进一步改善不稳定性心绞痛患者心电图表现。	C	强推荐
推荐意见 4.1	单独服用心血宁片可降低原发性高血压患者的收缩压和舒张压水平。	B	强推荐
推荐意见 4.2	在西医常规治疗的基础上，加用心血宁片可以进一步降低原发性高血压患者的收缩压和舒张压水平。	B	强推荐
推荐意见 4.3	在西医常规治疗的基础上，加用心血宁片可以进一步改善原发性高血压患者头晕、头痛症状。	B	强推荐
推荐意见 5.1	单独服用心血宁片可降低血脂异常患者的 TC、TG 水平。	C	强推荐
推荐意见 5.2	在西医常规治疗的基础上，加用心血宁片可以进一步降低血脂异常患者的 TC、TG 水平。	C	强推荐
推荐意见 6.1	单独服用心血宁片可降低高血压合并高同型半胱氨酸血症患者的血压和血清同型半胱氨酸水平。	B	强推荐
推荐意见 6.2	单独服用心血宁片可降低缺血性脑卒中合并高同型半胱氨酸血症患者的血清同型半胱氨酸水平。	C	弱推荐

表C.2 心血宁片共识建议概要表

共识建议	共识条目	建议/不建议
共识建议 1	心血宁片多用于冠心病心绞痛属于中医瘀血阻络证或心血瘀阻证者。	建议
共识建议 2	心血宁片可应用于高血压、血脂异常属于中医瘀血阻络证型者。	建议
共识建议 3.1	心血宁片临床使用时按照说明用量使用：一次 4 片（0.21g/片）一天 3 次，或遵医嘱。	建议
共识建议 3.2	通常以 4-12 周为一个疗程，在疗程范围内，治疗时间越长，疗效越佳。	建议
共识建议 4	孕妇、严重肝肾功能不全、存在出血倾向或对本药物成分过敏者禁用。	建议
共识建议 5	个别患者服药期间可能出现胃部不适，可通过减量或停药来缓解。	建议
共识建议 6	本药物性味较为温和，若无不良反应，符合适应症的患者可在医生指导下规律服用。	建议

附录 D  
(规范性)  
疾病诊断要点

#### D.1 稳定劳力型心绞痛

参照2018年中华医学会心血管病学分会《稳定性冠心病诊断与治疗指南》<sup>[1]</sup>：1) 发作部位常位于胸骨后或心前区，可以放射到颈咽部、左臂及左手指内侧等，性质常呈压迫感、紧缩感等；2) 常由劳累或情绪激动诱发，多数情况下持续3-5min，休息或用硝酸酯类药物后数分钟内缓解；3) 结合年龄和存在的冠心病危险因素，除外其他疾病所致的心绞痛；且其发作程度、频率、性质及诱发因素在数周内无明显变化。

#### D.2 不稳定性心绞痛

参照2016年中华医学会心血管病学分会《非ST段抬高型急性冠状动脉综合征诊断和治疗指南》<sup>[2]</sup>：1) 表现为典型的心绞痛症状；2) 症状发作时心电图可出现2个或更多的相邻导联ST段下移 $>0.1\text{mV}$ 及胸前导联对称的T波深倒置并呈动态改变，缓解后ST段缺血改变改善；3) 心肌肌钙蛋白(cardiac troponin, cTn)阴性，血清肌酸激酶同工酶(creatine kinase-MB, CK-MB)在2倍正常值范围内。UA是介于稳定劳力型心绞痛和急性心肌梗死之间的临床状态，包括除稳定型劳力型心绞痛以外的初发型、恶化型劳力型心绞痛和各型自发型心绞痛。

#### D.3 高血压

参照中国高血压联盟《中国高血压防治指南(2018年修订版)》<sup>[3]</sup>：在未使用降压药物的情况下，非同日3次测量诊室血压，收缩压 $\geq 140\text{ mmHg}$ 和/或舒张压 $\geq 90\text{ mmHg}$ ；SBP $\geq 140\text{ mmHg}$  和 DBP  $< 90\text{ mmHg}$  为单纯收缩期高血压。患者既往有高血压史，目前正在使用降压药物，血压虽低于140/90 mmHg，仍诊断为高血压。

#### D.4 血脂异常

参照中华医学会心血管病学分会《中国成人血脂异常防治指南(2016年修订版)》<sup>[4]</sup>：连续2次检测血清TC $\geq 6.2\text{ mmol/L}$ ，或TG $\geq 2.3\text{ mmol/L}$ ，或LDL-C $\geq 4.1\text{ mmol/L}$ ，或HDL-C $\leq 1.0\text{ mmol/L}$ 。

附录 E  
(规范性)  
有临床证据的应用

### E.1 高血压合并高同型半胱氨酸血症

单独服用心血宁可降低高血压合并高同型半胱氨酸血症患者血压和血清同型半胱氨酸水平。(推荐意见: B 级证据, 强推荐)

一项研究<sup>[21]</sup>采用多中心、随机对照方法, 观察心血宁治疗一级高血压合并高同型半胱氨酸(homocysteine, Hcy)血症患者(简称“H 型高血压患者”<sup>[22]</sup>)的临床疗效, 结果显示心血宁可降低患者的血压水平, 同时能够降低血 Hcy, 其降低血 Hcy 效果与叶酸片相当。

### E.2 其他临床应用

一项研究<sup>[23]</sup>采用多中心、随机、双盲、双模拟的研究方法, 比较心血宁与叶酸片单药治疗缺血性卒中合并高 Hcy 患者的临床疗效, 结果显示单独服用心血宁对缺血性脑卒中合并高 Hcy 血症患者具有一定治疗效果。(推荐意见: C 级证据, 弱推荐)。

另有文献报道<sup>[24]</sup>心血宁片可以改善慢性心力衰竭患者的临床症状。

此类疾病非说明书适应症, 临床应用宜审慎。

### E.3 用量及疗程

片剂, 0.21g/片, 口服, 一次 4 片, 一天 3 次(共识建议)

现有的心血宁片文献报告多以 4-12 周为一个疗程。冠心病、高血压、血脂异常等为慢性长期伴随疾病, 应根据患者的临床症状和中医证候辨证使用, 不应拘泥于临床研究的疗程。在现有文献报告的疗程范围内, 其作用效果与使用时间成正相关<sup>[5]</sup>。目前尚无心血宁片长期使用相关不良反应的报告, 长期使用应予以关注。(共识建议)

附录 F  
(资料性)  
中国国家药物不良反应监测中心报告

中国国家药物不良反应监测中心出具的心血宁片报告见表 F.1。

表F.1 药物不良反应监测中心报告

序号	编号	生产批号	不良反应症状	累及系统	停药减药后 反应是否减轻或消失	年度
1	ADR-20190604-019	181001	纳差；胃部不适	胃肠疾病	是	2019
2	ADR-20200508-009	191005	腹泻	胃肠疾病	是	2020
3	ADR-20200904-027	200703	烧灼感	胃肠疾病	是	
4	ADR-20201109-039	191005	全身瘙痒	皮肤及皮肤附件疾病	是	
5	ADR-20201109-041	200203	头晕；心慌；胃部不适	神经、心血管、 胃肠系统疾病	是	
6	ADR-20201207-051	200901	多梦	精神疾病	是	
7	ADR-20200904-027	190803	双脚踝关节；局部红 肿；疼痛	全身整体性疾病	是	
8	ADR-20210509-014	200701	恶心	胃肠疾病	是	2021
9	ADR-20210614-019	200808	过敏	皮肤及皮肤附件疾病	是	
10	ADR-20211022-064	200704	红色丘疹	皮肤及皮肤附件疾病	是	
11	ADR-20211029-069	210203	腹胀	胃肠疾病	是	
12	ADR-20220129-003	210304	恶心	胃肠疾病	是	2022
13	ADR-20230110-128	210804	口干	胃肠疾病	是	
14	ADR-20221023-095	6925803301 274	皮疹；瘙痒	皮肤及皮肤附件疾病	是	



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## Forward

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## Introduction

Xin Xue Ning Tablet is developed by Lonch Group, with independent intellectual property rights of Chinese patent medicine preparations (State Food and Drug Administration approval number Z20184011). It is Class B drug of national basic medical insurance (Stasis-Removing and Chest Stiffness-Relieving Agent, No.: 505), and has been included in the Pharmacopoeia of the People's Republic of China (2020 Edition). The research materials are shown in Appendix A.

At present, Xin Xue Ning Capsule has been widely used in clinical practice, supported by increasing relevant evidence-based medicine evidence. Therefore, organized by the Specialty Committee of Interventional cardiology of the World Federation of Chinese Medicine Societies, domestic experts in cardiovascular diseases of traditional Chinese medicine, western medicine and integrative medicine systematically review and summarize the applicable scope, clinical evidence, indications, safety, theoretical basis and pharmacological effects of Xin Xue Ning Tablet. Based on both evidence-based medicine evidence and expert opinion, consensus group discussed and drafted the consensus and formed recommendations and consensus suggestions on indications in clinical application, dosage and course of treatment of Xin Xue Ning Tablet, as well as safety issues such as medication for special groups, adverse reactions and contraindications. The 11 clinical questions developed during the development of the consensus are shown in Appendix B, and a summary table of the recommendations/consensus suggestions is shown in Appendix C.

The consensus aims to serve clinicians, provide references for clinical application of Xin Xue Ning Tablet, promote rational medication use, reduce drug use risks, and benefit more patients. With the deepening of clinical practice and the discovery of new evidence, this consensus will be constantly updated and improved.

The issuer of the consensus draws attention to the fact that a declaration of conformity with this document may involve the use of patents in this document in relation to cardioplegia tablets.

The issuing organisation of the consensus takes no position on the authenticity, validity or scope of the patent.

The patent holder has undertaken to the issuing authority of the consensus that he is willing to negotiate a patent licence with any applicant on reasonable and non-discriminatory terms and conditions. The declaration of the patent

holder has been filed with the issuing authority of the consensus. Relevant information can be obtained from the contact details below:

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Please note that in addition to the patents mentioned above, some of the contents of the consensus may still be covered by patents. The issuer of the consensus assumes no responsibility for identifying patents.

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# Chinese Expert Consensus on the Clinical Application of Xin Xue Ning Tablets

## 1 Scope

The consensus reviews indications of Xin Xue Ning Tablet in clinical application, dosage and course of treatment, medication in special groups.

This consensus is suitable for use by all kinds of legally licensed medical practitioners in relevant professional fields.

## 2 Normative References

The contents of the following consensus constitute the essential provisions of this document through normative references in the text. Where a reference file with a date is noted, only the version corresponding to that date applies to this file; Undated references, the latest version of which (including all change orders) applies to the consensus.

GB/T16751.1--1997 TCM Clinical Diagnosis and Treatment Terms · part 2 · Syndrome

## 3 Terms and Definitions

Terms and definitions mentioned below apply to this document.

### 3.1

#### Stable Exertional Angina Pectoris

Angina pectoris is a clinical syndrome mainly characterized by chest pain induced by transient myocardial ischemia.

**Note:** It is the most common manifestation of coronary atherosclerotic heart disease. The severity, frequency, nature and inducing factors of stable exertional angina pectoris (SEAP) do not change significantly within several weeks.

### 3.2

#### Unstable Angina

Unstable angina (UA) is a clinical state between stable exertional angina pectoris and acute myocardial infarction.

**Note1:** It includes primary angina, worsening angina and various spontaneous angina except for stable exertional angina pectoris.

**Note2:** Based on the pre-existing atherosclerotic, UA is caused by acute or subacute reduction of myocardial oxygen supply because of coronary artery spasm and distal small vessel embolism, beside which coronary subintimal hemorrhage, plaque rupture, platelet and fibrin agglutination in the damaged area formed thrombus

### 3.3

#### Hypertension

In the absence of antihypertensive drugs, the office blood pressure was measured three times on different days. When the systolic pressure  $\geq 140$  mmHg and/or the diastolic pressure  $\geq 90$  mmHg, it can be diagnosed with hypertension; and when SBP  $\geq 140$  mmHg and DBP  $< 90$  mmHg, it is simple systolic hypertension. When patient had a history of hypertension and is currently taking antihypertensive drugs, it is still diagnosed with hypertension despite a blood pressure of less than 140/90 mmHg.

### 3.4

#### Dyslipidemia

Dyslipidemia usually refers to elevated levels of Total cholesterol (TC) and (or), Triglyceride (TG), and Low-Density Lipoprotein Cholesterol (LDL-C) in the serum, while High density lipoprotein cholesterol (HDL-C) levels decreased, which can contribute to the development of atherosclerosis.

## 4 Basic Information of Xin Xue Ning Capsule Components

### 4.1 Prescription Source and Composition

Rooted in the traditional Chinese medicine theory, Xin Xue Ning Tablet summarizes the experience gained from treating cardiovascular and cerebrovascular diseases, and after modern pharmacological research and selection, components of Xin Xue Ning Tablet are adjusted in a scientific way. According to the clinical characteristics of blood stasis pattern of coronary heart disease, Ge Gen (radix pueraria) and hawthorn are selected to extract and refine to form Xin Xue Ning Tablet, which is a pure Chinese medicine preparation

### 4.2 Efficacy and Indications

Xin Xue Ning Tablet has the effect of promoting blood circulation to remove stasis and removing obstruction from meridians to relieve pain. This product can be used for *qi* blockage in the chest, heartache and dizziness caused by blood stasis obstructed in meridians. Xin Xue Ning Tablet also applies to syndromes



and patterns like mentioned above in patients with coronary heart disease angina pectoris, hypertension and dyslipidemia.

## **5 Suggestions for Clinical Application**

### **5.1 Indications**

#### **5.1.1 Qi blockage in the chest and heartache**

Xin Xue Ning Tablet can improve the clinical symptoms of chest tightness and pain in the precordial area in patients with heartache (blood stasis obstructed in meridians pattern or heart blood retention pattern). (Recommendation: Level B evidence, Strong recommendation)

Three studies [5-7] have shown that Xin Xue Ning Tablet can improve the clinical symptoms of chest tightness and pain in the precordial area in patients with heartache (blood stasis obstructed in meridians pattern or heart blood retention pattern).

#### **5.1.2 Stable Exertional Angina Pectoris**

Combined with standardized treatment of western medicine, Xin Xue Ning Tablet can further improve clinical symptoms in patients with SEAP, reduce the patient's attack frequency and duration of angina pectoris, and prove electrocardiograph ischemia performance. (Recommendation: Level B evidence, Strong recommendation)

A total of 6 studies [5-10] evaluated the clinical efficacy of Xin Xue Ning Tablet in the treatment of SEAP patients, and the results all showed that Xin Xue Ning Tablet can improve the clinical symptoms of SEAP, reduce the patient's attack frequency and duration of angina pectoris, and improve the electrocardiographic ischemic performance. A study [11] conducted a meta-analysis of outcomes, showing that the clinical symptoms of SEAP patients could be further improved when use Xin Xue Ning Tablet combined with standardized western medicine treatment, and the difference was statistically significant compared with the control group.

#### **5.1.3 Unstable Angina (UA)**

Combined with the standardized treatment of western medicine, Xin Xue Ning Tablet can further improve the clinical symptoms reduce the attack frequency and duration of patients with angina, and improve the electrocardiogram ischemic performance. (Recommendation: Level C evidence, Strong recommendation).

The results of a clinical study involving 80 patients with UA showed that [12] Xin Xue Ning Tablet reduced the attack frequency and duration of angina in patients with UA, and improved electrocardiographic ischemia manifestations.

#### **5.1.4 Primary Hypertension**

a) Take Xin Xue Ning Tablet individually can reduce the level of SBP and DBP of the patients with primary hypertension. (Recommendation: Level B evidence, Strong recommendation)

A study [13] compared Xin Xue Ning Tablet and Xin Ke Shu (single drug) in patients with primary hypertension and results showed that blood pressure level was lowered when Xin Xue Ning Tablet was used individually, whose effectiveness was equally with that of Xin Ke Shu.

b) Combined with standardized treatment of western medicine, Xin Xue Ning Tablet can reduce or further reduce SBP and DBP in patients with primary hypertension. (Recommendation: Level B evidence, Strong recommendation)

A total of 6 studies of essential hypertension [14-19] showed that, when Xin Xue Ning Tablet was given to the treatment group on the basis of valsartan dispersible tablet or carvedilol (medicine used in the control group), SBP and DBP decreased in both groups compared with before treatment, and the decrease in treatment group was better than that in control group.

#### **5.1.5 Dyslipidemia**

a) Taking Xin Xue Ning Tablet individually can reduce dyslipidemia of TC and TG level. (Recommendation: Level C evidence, Strong recommendation)

One study [20] compared the clinical efficacy of Xin Xue Ning Tablet and Xin Ke Shu (single drug) on dyslipidemia, and results showed both of them could reduce TC and TG level in patients with dyslipidemia. The decrease level of Xin Xue Ning group was greater than that of Xin Ke Shu group, and the difference between the two groups was statistically significant.

b) Combined with the standardized treatment of western medicine, Xin Xue Ning Tablet can further reduce TG and TC level in patients with dyslipidemia. (Recommendation: Level C evidence, Strong recommendation)

Two studies [16, 18] displayed the joint application of Xin Xue Ning Tablet and valsartan on primary hypertension. TC and TG levels of patients were both lowered, beside which their blood pressure also dropped, with statistically significant difference.

### **5.2 Application Supported by Clinical Evidence**

Other application supported by clinical evidence are in Appendix E.

## **6 Safety**

### **6.1 Adverse Reactions/Adverse Events**

A clinical observation on the efficacy of Xin Xue Ning Tablet for patients with coronary heart disease and angina pectoris showed that one of 310 patients in treatment group developed mild stomach discomfort after taking Xin Xue Ning Tablet (self-alleviating), while the remaining cases were found no adverse reaction [7].

According to the National Center for Adverse Drug Reaction Monitoring, adverse reactions were reported in 14 cases from 2019 to 2022. A few patients may have symptoms such as abdominal distension, diarrhea, rash, local redness and swelling after taking Xin Xue Ning Tablet, and all these symptoms can be alleviated or disappeared after stopping or reducing the medication, and no serious adverse events/adverse reactions have been reported (see Appendix F for details).

### **6.2 Contraindication**

There is no safety study of Xin Xue Ning Tablet in pregnant, lactating women or children under 15 years old, so it is not recommended for these special groups. There is also no application experience in patients with severe hepatic and renal dysfunction, and the pharmacokinetic process in vivo is not clear; so it is recommended to be used with caution in patients with severe hepatic and renal dysfunction. Considering that Xin Xue Ning Tablet can promote blood circulation to remove stasis, so patients with bleeding tendency should use with caution. Xin Xue Ning Tablet should not be used by those allergic to its components. (Consensus Suggestion).

### **6.3 Drug Combination**

In the existing literature Xin Xue Ning Tablet is mostly used combined with the standardized treatment of western medicine in clinical practice, and no relative adverse reactions and toxic and side effects induced by combination use are reported. When combined with other traditional Chinese medicine or Chinese patent medicine, attention should be paid to syndrome differentiation principles and safety.

**Annex A**  
**(Informative)**  
**Research data of Xin Xue Ning Tablet**

**A.1 Theoretical Basis of Traditional Chinese Medicine**

Xin Xue Ning Tablet is the compound preparations with Ge Gen (*Puerariae*) and hawthorn extract. *Shen Nong Ben Cao Jing* recorded that “Ge Gen could treat various Bi (arthralgia)”, and “Bi” there not only refers to obstruction and pain in the whole body, but also includes “Xiong Bi” (*Qi* blockage in the chest). *Pueraria* can firstly relieve both the interior and exterior syndromes, ascending clear *yang* in stomach, and additionally, it can promote blood circulation to remove obstruction in meridians, and help the heart motivating blood to remove Bi. In *Yi Xue Zhong Zhong Can Xi Lu*, it was wrote that hawthorn is good at invading blood level, so it is an essential medicine for removing blood stasis...it can also treat pain in heart and abdomen. Acting as the essential medicine for eliminating accumulation and removing blood stasis, hawthorn combined with Ge Gen, sweet and pungent in flavor while cool in property, can remove blood stasis and relieve *qi* stagnation but not impair healthy *qi*. The combination of these two ingredients conforms to the “*qi* and blood theory” of traditional Chinese medicine. “*Su Wen · Regulating Meridians*” said that “when *qi* and blood disharmony appears, all diseases are born... when water floods in tertiary collateral, there is blood left in the meridian.” “*Ling Shu · All Diseases Start*” wrote that “*yang* collateral injury leads to blood overflow outwards..... while *yin* collateral injury causes blood overflow inwards”. The heart controls the blood and vessels, therefore blood stasis is the most common reason of the heart disorders. The function of Xin Xue Ning Tablet is promoting blood circulation to remove stasis and removing obstructions from meridians to relieve pain, so it can be used for the treatment of coronary heart disease angina pectoris, hypertension and dyslipidemia (blood stasis obstructed in meridians pattern).

**A.2 Frequently-Used Pharmaceutical Technology of Tablet**

According to *Pharmacopoeia of the People's Republic of China First Part (2020 edition)* , the pharmaceutical technology of Xin Xue Ning Tablet is: Ge Gen extract 150g, hawthorn extract 25g, with appropriate amount of starch, mixed evenly, formed into granules, dried, added appropriate amount of magnesium stearate, mixed evenly, compressed into 1000 tablets, coated with sugar or film-coated, and get the final product.

### A.3 Pharmacological Research

As the chief herb in XinXue Ning Tablet, Ge gen in Xin Xue Ning Tablet contains puerarin and total flavonoids, which can lower blood pressure and improve the clinical symptoms of patients with angina pectoris and myocardial infarction [25]. Additionally, it can inhibit the myocardial iron death induced by sorafenib, and has a good protective effect on myocardial toxicity caused by sorafenib [26]. Hawthorn extract is the deputy herb, in which total flavonoids of hawthorn leaves are the main active substance group of hawthorn leaves. This substance has the effects of anti-atherosclerosis, anti-myocardial ischemia, lowering blood pressure, lowering TG and LDL level, increasing HDL level, lowering blood sugar and anti-inflammation etc.. Studies also suggested that it can also antagonize the arrhythmia caused by aconitine and has a lasting cardiotonic effect [27-31]. Studies on Guanxin Ning Combined Formula proved that it can lower blood pressure and improve Hcy in “H” hypertension patients [32].

Xin Xue Ning Tablet is extracted from Ge Gen and hawthorn, which are herbs of the same origin as food and medicine. These two ingredients give full play to strengths and supplement each other to achieve the grand and specific efficacy though only two kind of herbs. Ge Gen and hawthorn have joint effect of promoting blood circulation to remove stasis and removing obstruction from meridians to relieve pain. Therefore, it can dilate coronary artery, increase coronary blood flow, enhance myocardial contractility, lower blood pressure, as well as reduce blood lipids and Hcy in “H” hypertension patients.

### A. 4 Toxicological Research

**Acute toxicity experiment:** Kunming mice were selected and orally administered the maximum tolerated dose of Xin Xue Ning Tablet, which did not reach the lethal dose.

**Subacute toxicity determination:** 60 mice, half male and half female, weighing  $19.3 \pm 0.5$ g, were administered a suspension of Xin Xue Ning Tablet at a concentration of 0.2g/ml at 8:00 am daily (by gavage) at a dose of 20ml/kg for 30 consecutive days. No toxic reactions were observed during the administration period, and the LD50 value was not detected.

**Maximum tolerated dose determination:** 40 Swiss mice, half male and half female, weighing  $20.5 \pm 0.6$ g, were fasted and deprived of water for 12 hours, then orally administered a suspension of Xin Xue Ning Tablet at a concentration of 0.2g/ml at a dose of 40ml/kg by gavage. Observations were made 6 hours after administration, and the same dose was repeated using the same method for 10

consecutive days. During this period, no significant abnormalities were observed in the mice's activity, food intake, water consumption, fur color, or feces, and no deaths occurred. The LD50 value was not detectable. Therefore, the maximum tolerated dose of Xin Xue Ning Tablet orally administered to mice was greater than 16g/kg, which is equivalent to 400 times the clinical normal dosage.

According to the *Technical Guidelines for Acute Toxicity Research of Traditional Chinese Medicine and Natural Medicine*, it is safe to administrate Xin Xue Ning Tablet 400 times greater than the clinical dosage for one day and 100 times greater than the clinical dosage for 30 consecutive days.

**Annex B**  
**(Informative)**  
**List of Clinical Problems**

This Consensus involves in 11 clinical problems (Table B1).

**Table B.1 List of Clinical Problems**

No.	Clinical Research
Indications and Clinical Applications Supported by Evidence-based Medicine Evidence	
1	What pattern type of coronary heart disease patients is Xin Xue Ning Tablet suitable for?
2	In addition to treating coronary heart disease, what circulatory system diseases can Xin Xue Ning Tablet treat?
3	Can Xin Xue Ning Tablet improve the clinical symptoms (reduce angina attack times, shorten the duration of angina) and electrocardiogram performance in patients with stable exertional angina pectoris?
4	Can Xin Xue Ning Tablet improve the clinical symptoms (reduce angina attack times, shorten the duration of angina) and electrocardiogram performance in patients with unstable angina?
5	Is Xin Xue Ning Tablet helpful to lower the blood pressure level of patients with primary hypertension and improve the dizziness symptoms of patients?
6	Can Xin Xue Ning Tablet reduce the levels of TC, TG and LDL-C in patients with dyslipidemia?
7	Does Xin Xue Ning Tablet help to reduce serum homocysteine level?
Usage and Dosage	
8	Usage, dosage and course of treatment of Xin Xue Ning Tablet
9	Are there clear precautions for Xin Xue Ning Tablet, such as drug combination (compatibility), contraindications, medications for special groups and other clinical medication precautions?
Safety Problems	
10	What are the common adverse reactions of Xin Xue Ning Tablet? What should do to deal with adverse reactions (if appear)?
11	What is the safety of taking Xin Xue Ning Capsule Tablet for a long time?

## Annex C (Informative)

### Summary of Recommendations/Consensus Suggestions

This consensus adopts the internationally-recognized Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the evidence, and combines Delphi method with nominal group method. For those indications supported by evidence-based medicine evidence, “Recommendations” are developed according to the level of evidence; while for those clinical indications which can not be supported by sufficient studies, “Consensus Suggestions” are formed after experts discussion. Eventually, 12 Recommendations and 8 Consensus Suggestions are formed, as detailed in Table C.1 and Table C.2.

**Table C.1 Summary of Recommendations for Xin Xue Ning Tablet**

Recommendation	Recommendation Item	Evidence Level	Recommendation Strength
Recommendation 1	Xin Xue Ning Tablet can improve the clinical symptoms of chest tightness and pain in the precordial area in patients with Xiong Bi and heartache (blood stasis obstructed in meridians pattern or heart blood retention pattern).	B	Strong recommendation
Recommendation 2.1	Combined with standardized treatment of western medicine, Xin Xue Ning Tablet can further improve clinical symptoms, reduce the frequency and duration of angina pectoris attacks in patients with SEAP.	B	Strong recommendation
Recommendation 2.2	Combined with standardized treatment of western medicine, Xin Xue Ning Tablet can further improve electrocardiograph performance in patients with SEAP.	B	Strong recommendation
Recommendation 3.1	Combined with the standardized treatment of Western medicine, Xin Xue Ning Tablet can further improve the clinical symptoms, reduce the frequency and duration of angina pectoris attacks in patients with UA.	C	Strong recommendation
Recommendation	Combined with the standardized treatment of	C	Strong



3.2	Western medicine, Xin Xue Ning Tablet can further improve electrocardiograph performance in patients with UA.		recommendation
Recommendation 4.1	Taking Xin Xue Ning Tablet individually can reduce systolic and diastolic blood pressure levels in patients with primary hypertension.	B	Strong recommendation
Recommendation 4.2	Combined with the standardized treatment of Western medicine, Xin Xue Ning Tablet can further reduce systolic and diastolic blood pressure levels in patients with primary hypertension.	B	Strong recommendation
Recommendation 4.3	Combined with the standardized treatment of Western medicine, Xin Xue Ning Tablet can further improve the symptoms of dizziness and headache in patients with primary hypertension.	B	Strong recommendation
Recommendation 5.1	Taking Xin Xue Ning Tablet individually can reduce TC and TG level in patients with dyslipidemia.	C	Strong recommendation
Recommendation 5.2	Combined with the standardized treatment of Western medicine, Xin Xue Ning Tablet can further reduce the levels of TC and TG in patients with dyslipidemia.	C	Strong recommendation
Recommendation 6.1	Taking Xin Xue Ning Tablet individually can lower blood pressure and serum homocysteine level in hypertensive patients with hyperhomocysteinemia.	B	Strong recommendation
Recommendation 6.2	Taking Xin Xue Ning Tablet individually can lower the level of serum homocysteine in patients with hyperhomocysteinemia complicated with ischemic stroke.	C	Weak recommendation

**Table C.2. Summary of Consensus Suggestions for Xin Xue Ning Tablet**

Consensus Proposal	Consensus Item	Recommended or not
Consensus Suggestion 1	Xin Xue Ning Tablet is mostly used for coronary heart disease angina pectoris (blood stasis obstructed in meridians pattern or heart blood retention pattern in TCM).	Yes

Consensus Suggestion 2	Xin Xue Ning Tablet can be applied to patients with hypertension and dyslipidemia (blood stasis obstructed in meridians pattern in TCM).	Yes
Consensus Suggestion 3.1	Follow the dosage instructions of Xin Xue Ning Tablet in clinical application: 4 tablets (0.21g per tablet) once, 3 times a day, or follow the doctor's advice.	Yes
Consensus Suggestion 3.2	Usually 4-12 weeks for a course of treatment, within the course of treatment, the longer the treatment time, the better the effect.	Yes
Consensus Suggestion 4	Pregnant women, patients who have severe hepatic and renal dysfunction, bleeding tendency or allergic to drug components should not use Xin Xue Ning Tablet.	Yes
Consensus Suggestion 5	A few patients may appear stomach discomfort during the medication period, which can be relieved by reducing or stopping the medication.	Yes
Consensus Suggestion 6	The flavour and property of Xin Xue Ning Tablet is relatively mild, and if there is no adverse reaction, patients who meet the indications can take it regularly under the guidance of doctors.	Yes

**Annex D**  
**(Normative)**  
**Key points of disease diagnosis**

**D.1 Stable Exertional Angina Pectoris**

Refer to the Guidelines for diagnosis and treatment of stable coronary heart disease (2018 Edition) <sup>[1]</sup>: 1) The attack site is usually located in the retrosternal or precardiac area, which can radiate to the cervix pharynx, left arm and left inner finger, and pain is often characterized by a sense of pressure and contraction. 2) SEAP is often induced by fatigue or emotional agitation, lasting 3-5 minutes in most cases, and will be relieved after rest or within a few minutes after the use of nitrates; 3) Excluded angina caused by other disease after considering age and existing risk factors for coronary heart disease; and there were no significant changes in the severity, frequency, nature and inducing factors within a few weeks.

**D.2 Unstable Angina**

Refer to the Guidelines for diagnosis and treatment of non-ST-segment elevation acute coronary syndrome <sup>[2]</sup> issued by Chinese Medical Association in 2016: 1) Typical angina pectoris manifestation; 2) During the onset of symptoms, two or more adjacent leads showed ST segment descending >0.1mV and symmetrical T-wave depth inversion and dynamic changes in the electrocardiograph, and the ST segment ischemia changes improved after remission. 3) Cardiac troponin (cTn) was negative, and serum creatine kinase-MB (CK-MB) was within 2 times the normal value range. Unstable angina (UA) is a clinical state between stable exertional angina pectoris and acute myocardial infarction, including primary angina, worsening angina and various spontaneous angina except for stable exertional angina peictoris

**D.3 High Blood Pressure (Hypertension)**

Refer to Chinese Guidelines for Prevention and Treatment of hypertension (Revised Edition in 2018) <sup>[3]</sup>: In the absence of antihypertensive drugs, the office blood pressure was measured three times on different days. When the systolic pressure  $\geq 140$  mmHg and/or the diastolic pressure  $\geq 90$  mmHg, it can be diagnosed with hypertension; and when SBP  $\geq 140$  mmHg and DBP < 90 mmHg, it is simple systolic hypertension. When patient had a history of hypertension and

is currently taking antihypertensive drugs, it is still diagnosed with hypertension despite a blood pressure of less than 140/90 mmHg.

#### **D.4 Dyslipidemia**

Refer to Guidelines for prevention and treatment of dyslipidemia in adults in China (Revised Edition in 2016) <sup>[4]</sup> issued by of the Chinese Society of Cardiology, Chinese Medical Association: detected for two consecutive times, when serum TC $\geq$ 6.2mmol/L, or TG $\geq$ 2.3 mmol/L, or LDL-C $\geq$ 4.1mmol/L, or HDL-C $\leq$ 1.0 mmol/L, patients can be diagnosed with dyslipidemia.

**Annex E**  
**(Informative)**  
**Application Supported by Clinical Evidence**

**E.1 Hypertension with Hyperhomocysteinemia**

Taking Xin Xue Ning Tablet individually can reduce blood pressure and serum homocysteine level in hypertensive patients with hyperhomocysteinemia (Hcy). (Recommendation: Level B evidence, Strong recommendation)

A multi-center, randomized and controlled study<sup>[21]</sup> observed the efficacy of Xin Xue Ning Tablet on primary hypertension in patients with Hcy (“H” hypertension patients<sup>[22]</sup>). The results showed that Xin Xue Ning Tablet would rather reduce the patient’s blood pressure levels and Hcy, which was equally to that of folic acid tablets.

**E.2 Other Clinical Applications**

A multi-center, randomized, double-blind and double-simulated study<sup>[23]</sup> compared clinical efficacy of Xin Xue Ning Tablet and folic acid tablets (single drug) on ischemic stroke patients with high Hcy, and the results showed that taking Xin Xue Ning Tablet individually had a certain therapeutic effect on patients with ischemic stroke complicated with high Hcy. (Recommendation: Level C evidence, Weak recommendation).

It has also been reported<sup>[24]</sup> that Xin Xue Ning Tablet could improve the clinical symptoms of patients with chronic heart failure.

Chronic heart failure is not an indication of Xin Xue Ning Tablet, clinical application, therefore, should be cautious.

**E.3 Dosage and Course of Treatment**

Tablet form, 0.21 g per piece, taken orally, and 4 pieces once, 3 times a day. (Consensus Suggestion)

Existing literature on Xin Xue Ning Tablets mostly reports 4-12 weeks as a course of treatment. Coronary heart disease, hypertension, dyslipidemia, etc. are chronic and long-term concomitant diseases, which indicates that when applied to patients in these diseases, the treatment course of Xin Xue Ning Tablet should consider clinical symptoms and TCM syndrome differentiation of patients rather than just follow the existing research result. Within the range of treatment courses reported in the existing literature, the effect of Xin Xue Ning Tablet was

positively correlated with the duration of use <sup>[5]</sup>. Up to now, no adverse reactions related to the long-term use of Xin Xue Ning Tablets has been reported, so its long-term use should be paid attention to. (Consensus Suggestion)

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**Annex F**  
**(Informative)**  
**Report from National Center for Adverse Drug Reaction Monitoring**

The report of Xin Xue Ning Tablet issued by National Center for Adverse Drug Reaction Monitoring is shown in Table F.1.

**Table F.1 Report from National Center for Adverse Drug Reaction Monitoring**

No.	Numbering	Production batch Number	Adverse reaction	Involved system	Whether the reaction is alleviated or disappeared after withdrawal or reduction	Year
1	ADR-20190604-019	181001	Poor appetite; Stomach discomfort	Gastrointestinal diseases	Yes	2019
2	ADR-20200508-009	191005	Diarrhea	Gastrointestinal diseases	Yes	2020
3	ADR-20200904-027	200703	Burning sensation	Gastrointestinal disease	Yes	
4	ADR-20201109-039	191005	Generalized pruritus	Diseases of skin and skin appendages	Yes	
5	ADR-20201109-041	200203	Dizziness; Get flustered; Stomach discomfort	Neurological diseases, Cardiovascular diseases, Gastrointestinal diseases	Yes	
6	ADR-20201207-051	200901	Dreaminess	Mental diseases	Yes	
7	ADR-20200904-027	190803	Ankle joints of both feet; Local redness and swelling; Pain	Systemic diseases	Yes	
8	ADR-20210509-014	200701	Nausea	Gastrointestinal diseases	Yes	2021

No.	Numbering	Production batch Number	Adverse reaction	Involved system	Whether the reaction is alleviated or disappeared after withdrawal or reduction	Year
9	ADR-20210614-019	200808	Allegry	Diseases of skin and skin appendages	Yes	
10	ADR-20211022-064	200704	Red papule	Diseases of skin and skin appendages	Yes	
11	ADR-20211029-069	210203	Abdominal distension	Gastrointestinal diseases	Yes	
12	ADR-20220129-003	210304	Nausea	Gastrointestinal diseases	Yes	2022
13	ADR-20230110-128	210804	Dry mouth	Gastrointestinal diseases	Yes	
14	ADR-20221023-095	6925803301274	Rash; Pruritus	Diseases of skin and skin appendages	Yes	



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