

Surrey Heartlands Integrated Care System Area Prescribing Committee (APC)

Integrated Care Partnerships (ICPs) (Surrey Downs, Guildford & Waverley,
North West Surrey, East Surrey & associated partner organisations.

Evidence review for Surrey Area Prescribing Committee (APC)

Medicine details	
Name, brand name	Pridinol mesilate (Brand name: Myopridin® 3mg tablets)
Manufacturer	Mibe Pharma UK Limited
Proposed indication	Central and peripheral muscle spasms: lumbar pain, torticollis, general muscle pain in adults.
Requested by	<p>Dr Jan Rudiger, Consultant in Pain Medicine and Anaesthesia, Pain Lead, East Surrey Hospital</p> <p>This is a new treatment for painful muscle spasms related to acute episodes of lower back and neck pain; it is an antimuscarinic drug that works peripherally and centrally. It is also appropriate for use in painful flare-ups of acute on chronic pain, to help break the cycle of pain with the ultimate goal of reducing pain, muscle spasms and improving mobility. This will help to reduce hospital attendances, hospital admissions and facilitate the rehabilitation of pain patients.</p>

SUMMARY

Clinical Effectiveness

Pridinol's pharmacological effect develops via an atropine-like mechanism that acts on both smooth and the striated muscles. This effect is used for the treatment of skeletal muscle tension of both central and peripheral origin.⁵

Three studies described in this paper, one small double blind, placebo-controlled, multi-centre study¹, a small open label study² and a larger observational study³, reported the efficacy of pridinol very good or good.

SORT Criteria: Limited quality patient orientated evidence but with consistent findings.⁴

Improvement in quality of life and/or length of life

In patients with low back pain and associated spasm, pridinol reduced pain, reduced muscle tension and improved mobility.³

A fast and sustained reduction in pain is observed within 0.5 to 2 hours, with pain scores halving within 2 hours.³

Records of pain levels of 1253 patients (MYTOS) were documented at 3 time points. The average intensity of pain halved by 2 hours, with sustained pain observed for up to 9.4 days.³

No potential for addiction to pridinol is known. Therefore, concerns regarding addiction and dependence are negligible.^{5,6}

No monitoring is specified within the SmPC.⁵

At stated doses adverse effects are rare to uncommon and generally disappear after a dose reduction or after discontinuation of the medicinal product.⁵

Safety

Adverse effects

At the stated doses adverse effects to Myopridin are rare to uncommon and generally disappear after a dose reduction or discontinuation of the medicinal product.⁵

The following adverse effects may occur, particularly during concomitant administration with other anticholinergic medicinal products: dry mouth, thirst, transient visual disorder (mydriasis, difficulties

with accommodation, photosensitivity, and slight increase in intraocular pressure), redness and dryness of the skin, bradycardia followed by tachycardia, micturition disorders, constipation, and very rarely vomiting, dizziness and unsteady gait.⁵

Contraindications & Warnings:

Myopridin should not be prescribed to patients with: glaucoma, prostate hypertrophy, urinary retention, gastrointestinal obstructions, arrhythmia, first trimester of pregnancy, and use during breastfeeding should be avoided.⁵

Myopridin should be used in caution with: the elderly, patients with severe renal and/or hepatic insufficiency, because higher and/or longer lasting blood levels must be expected, patients who suffer from hypotension, in whom the risk of circulatory problems (fainting) may be increased.⁵

Contraindicated in: patients with rare hereditary problems of galactose intolerance, total lactose deficiency or glucose- galactose malabsorption, patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SmPC.⁵

Due to potential anticholinergic effects on eye sight, greater caution is advised whilst driving vehicles and operating machinery.⁵

Pregnancy: The medicinal product is contraindicated in the first trimester of pregnancy. In the second and third trimester Myopridin may only be used after careful medical consideration, under supervision and only if absolutely necessary.⁵

Breastfeeding: There is no data on the passage of pridinol into human milk. The use of Myopridin during breast feeding should be avoided.⁵

Risk of abuse and dependence:

Myopridin use is not limited by concerns over misuse, abuse or dependence. No potential for addiction is known.^{5,6}

Patient factors

There are no known service implications. As a tablet and as a prescription medicine, this product is available from any community pharmacy, and therefore, is available to the patient to self-administer.

Myopridin is a round white tablet with a score line on one side, enabling the patient to easily break the tablet into equal doses to take the lower dose if necessary. It is a small tablet which is approx. 9.0 mm in diameter, 2.5 mm in height. In comparison to other medications prescribed Myopridin is a small tablet which is not difficult to swallow for a patient.⁵

Safety & Tolerability: The limited side effects observed for Myopridin in comparison to the current standard of care may be of benefit to the patient.

At stated doses adverse effects to Myopridin are rare to uncommon and generally disappear after a dose reduction or discontinuation of the medicinal product.⁵

Myopridin use is not limited by concerns over misuse, abuse or dependence, no potential for addiction is known.⁵ Avoiding more addictive treatments, such as benzodiazepines and opiates, will benefit patient's long term.⁶

Myopridin increases the efficacy of physiotherapy and may help patients to implement other strategies such as movement and exercise. Patients may be able to resume daily activities e.g. working sooner and therefore improve overall quality of life.²

Cost implications

Treatment dose of one tablet three times a day costs less than 80p per day.

A treatment course for 10 days: £7.84 for 30 tablets.

No additional monitoring or additional health costs are associated with Myopridin.

The prevalence for back pain in England is around 17%. This means that about 17% of the population of all ages will have back pain during the year.⁷

The prevalence of low back pain in the CCGs:

- NHS Guildford and Waverley CCG: 16.5%
- NHS Surrey Downs CCG: 16.9%
- NHS North West Surrey CCG: 16.8%
- NHS East Surrey CCG: 16.5%⁷

CCG	NHS Guildford and Waverley CCG	NHS Surrey Downs CCG	NHS North West Surrey CCG	NHS East Surrey CCG
Prevalence of back pain in adults	16.5%	16.9%	16.8%	16.5%
Per 100,000 population	100,000	100,000	100,000	100,000
Population experiencing back pain	16,500	16,900	16,800	16,500
Half of these patients typically see their doctor and the remainder self-treats	8,250	8,450	8,400	8,250
Half of these patients are typically seen by their doctor and sent away with advice on exercise, mobility and over the counter non-steroidal anti-inflammatory drugs (NSAIDs)	4,125	4,225	4,200	4,125
If half of those remaining have muscle spasm associated with their back pain	2,063	2,113	2,100	2,063
If only half of those who could be treated with Myopridin actually receive it.	1,031	1,056	1,050	1,031
Total cost/100,000 based on £7.84 for 10 days	£8,083.04	£8,279.04	£8,232.00	£8,083.04

For the pharmacological management of low back pain as per NICE:

- Consider oral NSAID such as Ibuprofen or naproxen first-line, if there are no contraindications. And NSAID should be used at the lowest effective dose for the shortest possible time. Gastro-protective treatment should also be offered while an NSAID is being used
- If an NSAID is contraindicated, not tolerated, or ineffective, offer codeine with or without paracetamol, taking into account the risk of opioid dependence and adverse effects such as constipation
- Do not offer paracetamol alone, routinely offer opioids, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, gabapentinoids or antiepileptics for managing low back pain
- If the person has muscle spasm, consider offering a short course of a benzodiazepine, such as diazepam 2mg up to three times a day for 5 days, if not contraindicated.⁸

There are several medicines that are used to treat back pain, but are no longer recommended due to a perceived lack of effectiveness and a significant risk of addiction.⁶ Including Myopridin in the formulary may further reduce the likelihood of these medicines being prescribed.

In some instances, patients with acute low back pain who are fearful and want to seek immediate medical attention, will go to the Emergency Department rather than consulting the GP.¹⁰

The tariff cost for attendance at the Emergency Department is £107

If there is a requirement for admitting the patient with low back pain then the non-elective tariff ranges from £811-£1947.⁹

15% of patients get referred to hospital outpatients.¹⁰ Where most of them are to an orthopaedic surgeon, some might be to a rheumatologist or other specialities. A recent audit found that patients with low back pain appeared in 10 different clinics and two fifths of them had already been seen in a different speciality with the same complaint.¹⁰

The cost of an outpatient attendance depends on the speciality that the patient is referred to.

Speciality	First attendance
Trauma and orthopaedics	£163
Pain	£199
Rheumatology	£273

This cost would include standard blood tests, but if the patient was then referred for an investigation, for example an x-ray then an additional cost would occur as well as an additional follow up visit. It is possible that the patient would receive injection therapy with additional costs.

Avoiding a referral to a hospital specialist would save approximately £200 (£163-£273 depending on speciality)⁹

Relevant guidance / reviews

The current pharmacological treatments recommended for low back pain are via the National Institute for Health and Care Excellence in their guidance NG59 and NICE Clinical Knowledge Summaries (CKS).

NICE recommends prescribing a non-steroidal anti-inflammatory drug (NSAID), for the lowest effective dose for the shortest period of time, taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity as well as patients risk factors including age.⁸

Whilst prescribing an oral NSAID for low back pain, an appropriate clinical assessment should be made with ongoing monitoring of risk factors and the use of gastro protective treatment. Thereafter a weak opioid can be considered (with or without paracetamol) for managing acute low back pain only if an NSAID is contraindicated, not tolerated, or has been ineffective.⁸

Paracetamol alone, opioids, selective serotonin reuptake inhibitors or tricyclic antidepressants, gabapentinoids or antiepileptic's should not be considered.⁸

As per the NICE CKS Guidance for non-specific low back pain (without radiculopathy), if a patient has muscle spasm, consider offering a short course of a benzodiazepine, such as diazepam 2mg up to three times a day for 5 days, if not contraindicated. (in Nov. 2020)¹⁷

No evidence was identified for paracetamol, nefopam or muscle relaxants other than benzodiazepines for the management of sciatica. (NICE, NG59 in December 2020)¹⁸

Surrey Guidance: Pharmacological management of persistent non-malignant pain in adults. Is due to be reviewed in June 2021.¹¹

Pharmacological Management of low back pain (excluding sciatica)

Consider alternative diagnosis and risk stratification (STarT Back risk assessment tool) to inform decision making.

Non-pharmacological interventions (page 7) should be considered first.

These may include self-management; group exercise programme; psychological therapy which may be combined with physical therapy (for referral see page 7)

Following consideration of non-pharmacological interventions:

- Offer **oral NSAIDs** - **Ibuprofen** up to 1200mg daily or **Naproxen** up to 1000mg daily (*diclofenac or COX-2 [celecoxib first line COX-2] may be considered as alternatives – see appendix 2*)
- **Use at the lowest effective dose for the shortest possible time.**
- Gastroprotective treatment should also be offered while an NSAID is being used.
- If an NSAID is contraindicated, not tolerated, or ineffective, offer a weak opioid (e.g. **codeine**) with or without **paracetamol**, taking into account the risk of opioid dependence and adverse effects such as constipation.
- If the person has muscle spasm, consider offering a short course of a benzodiazepine, such as diazepam 2 mg up to three times a day for up to 5 days, if not contraindicated

- NICE does not recommended SSRI, SNRI, TCA and anticonvulsants (including gabapentin and pregabalin) for managing low back pain
- Do not offer paracetamol alone for managing low back pain
- NICE does not recommend opioids for managing **chronic** low back pain

Likely place in therapy relative to current treatments

Pridinol mesilate (Myopridin®) may be used in preference to benzodiazepines as an adjunctive treatment to NSAIDs (or used alone if NSAIDs contraindicated) for adult patients with pain related muscle spasms as per the SPC.

The age range of 18-55 years is being recommended due to a potentially low level of co-morbidities and therefore associated polypharmacy. If this polypharmacy includes other anticholinergics then the anticholinergic burden would be added to by pridinol, which should be avoided – particularly in older people. Therefore, Myopridin would be considered for patients between 18-55 years of age suffering from an acute onset of back pain or neck pain.

The initiation of Myopridin 3mg tablets (pridinol mesilate) is suitable for initiation and maintenance in primary care. (Green status)

A substantial proportion of patients with back pain have muscle spasm. Evidence shows that pain may cause muscle spasm and the muscular activity can be painful.¹³ The NHS currently (as per NICE NG59) recommend NSAIDs as a treatment for lower back pain. They also recommend that a muscle relaxant can be used for patients with painful muscle spasms.

The NICE CKS Guidance states considering a short 5-day course of diazepam for individuals with non-specific low back pain with muscle spasm⁸

There are huge concerns surrounding the use of opioids and benzodiazepines such as diazepam due to addiction and dependence, and the debilitating side effect profile such as sedation.⁵

The use of benzodiazepines such as diazepam to manage low back pain and muscle spasm is primarily due to widespread clinician adoption rather than clinical evidence, as there is a paucity of clinical evidence.


Myopridin use is not limited by concerns over misuse, abuse or dependence, and no potential for addiction is known. There is no sedative effect which may be experienced with the current SOC.^{5,6}

Expected duration of therapy: 10-day course of treatment.

Recommendation to APC

Green status to allow GPs to prescribe appropriately as early as possible.

- Myopridin should mostly be prescribed in primary care when patients present with moderate to severe muscle spasm associated with neck and/or back pain
- Therefore, green light status should be given
- Myopridin should be included in the local / regional guideline for the treatment of back pain

Medicine details	
Name and brand name	Pridinol Mesilate (Brand name: Myopridin® 3mg tablets)
Licensed indication, formulation and usual dosage	<p>Myopridin has been available in the UK since January 2021</p> <p>Myopridin (pridinol mesilate) is indicated for central and peripheral muscle spasm: lumbar pain, torticollis, general muscle pain in adults Myopridin 3mg tablets are round white tablets with a score line on one side containing 3.02mg pridinol (as 4mg pridinol mesilate)</p> <p>The recommended dose is half to one tablet three times a day. The tablet should be taken with sufficient fluid (e.g. a full glass of water) and not chewed. Administration can be independent of meals with the onset of effects faster taken before meals.⁵</p>
Summary of mechanism of action, and relevant pharmacokinetics	<p>Myopridin is a muscarinic receptor agonist which acts on the alpha motor neuron in the spine. Its pharmacological effect develops via an atropine like mechanism which prevents the increased excitation in the spinal cord from being transmitted to the muscle.</p> <p>Centrally active muscle relaxant. Pridinol relieves muscle tensions more readily the early the myotonolytic treatment is started.⁵ In cases where long standing muscle spasms, where anatomical changes have also occurred in the muscle fibres, ligaments and joint capsules, pridinol can only have a partial effect.⁵</p> <p>The maximum blood concentration is attained after about 1 hour and there is uniform distribution in the body. The active substance is largely excreted with 24 hours. This takes place via the kidneys, partly in unchanged form and partly as the glucuronate and the sulfate- conjugate.⁵</p>
Important drug interactions	Myopridin potentiates the effect of anticholinergics such as atropine.
Monitoring requirements	No additional monitoring or laboratory testing is required with Myopridin.
Prescribing considerations	<p>Green- Non-Specialist Drug</p> <p>(see attached guidelines)</p>  <p>Colour classification guidelines</p>
Other considerations	<ol style="list-style-type: none"> 1. Treatment is proposed for initiation in primary care by any competent prescriber, which ensures greatest equity of access for patients who may otherwise be referred to a specialist. 2. Patients attending ED with acute back pain should have treatment packs of Myopridin that they can be given to go home with. The fast onset of action of Myopridin should enable quicker discharge from ED. 3. Myopridin can also be initiated in secondary care (East Surrey Hospital & other acute trusts) either in the pain clinic and for in-patients by healthcare professionals (mainly pain physicians and orthopaedic doctors)

	<p>The size of the Myopridin 3mg tablets is such that they are easy to take by patients with a simple dosing regimen.⁵</p> <p>Surrey Guidance: Pharmacological management of persistent non-malignant pain in adults. Is due to be reviewed in June 2021.¹²</p>
--	---

Potential patient group (if appropriate to include)																															
Brief description of disease	<p>Low back pain is the leading cause of long-term disability in the UK. The lifetime incidence of low back pain is 58-84%.¹³</p> <p>11% of men and 16% of women have chronic low back pain. Back pain accounts for 7% of GP consultations and results in loss of 4.1 million working days a year.</p> <p>Neck pain is the 4th highest cause of disability in the UK.¹³</p> <p style="background-color: yellow;">Include disease severity, morbidity and mortality, prognosis</p>																														
Potential patient numbers per 100,000	<p>The prevalence for back pain in England is around 17%. This means that about 17% of the population of all ages will have back pain during the year.¹³</p> <p>The prevalence of lower back pain in the CCGs:</p> <ul style="list-style-type: none"> - NHS Guildford and Waverley CCG : 16.5% - NHS Surrey Downs CCG: 16.9% - NHS North West Surrey CCG: 16.8% - NHS East Surrey CCG: 16.5%⁷ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 25%;">CCG</th> <th style="width: 12.5%;">NHS Guildford and Waverley CCG</th> <th style="width: 12.5%;">NHS Surrey Downs CCG</th> <th style="width: 12.5%;">NHS North West Surrey CCG</th> <th style="width: 12.5%;">NHS East Surrey CCG</th> </tr> </thead> <tbody> <tr> <td>Prevalence of back pain</td> <td>16.5%</td> <td>16.9%</td> <td>16.8%</td> <td>16.5%</td> </tr> <tr> <td>Per 100,000 population</td> <td>100,000</td> <td>100,000</td> <td>100,000</td> <td>100,000</td> </tr> <tr> <td>Population experiencing back pain</td> <td>16,500</td> <td>16,900</td> <td>16,800</td> <td>16,500</td> </tr> <tr> <td>Half of these patients typically see their doctor and the remainder self-treats</td> <td>8,250</td> <td>8,450</td> <td>8,400</td> <td>8,250</td> </tr> <tr> <td>Half of these patients are typically seen by their doctor and sent away with advice on exercise, mobility and OTC NSAIDs</td> <td>4,125</td> <td>4,225</td> <td>4,200</td> <td>4,125</td> </tr> </tbody> </table>	CCG	NHS Guildford and Waverley CCG	NHS Surrey Downs CCG	NHS North West Surrey CCG	NHS East Surrey CCG	Prevalence of back pain	16.5%	16.9%	16.8%	16.5%	Per 100,000 population	100,000	100,000	100,000	100,000	Population experiencing back pain	16,500	16,900	16,800	16,500	Half of these patients typically see their doctor and the remainder self-treats	8,250	8,450	8,400	8,250	Half of these patients are typically seen by their doctor and sent away with advice on exercise, mobility and OTC NSAIDs	4,125	4,225	4,200	4,125
CCG	NHS Guildford and Waverley CCG	NHS Surrey Downs CCG	NHS North West Surrey CCG	NHS East Surrey CCG																											
Prevalence of back pain	16.5%	16.9%	16.8%	16.5%																											
Per 100,000 population	100,000	100,000	100,000	100,000																											
Population experiencing back pain	16,500	16,900	16,800	16,500																											
Half of these patients typically see their doctor and the remainder self-treats	8,250	8,450	8,400	8,250																											
Half of these patients are typically seen by their doctor and sent away with advice on exercise, mobility and OTC NSAIDs	4,125	4,225	4,200	4,125																											

	If half of those remaining have muscle spasm associated with their back pain	2,063	2,113	2,100	2,063	
	(If half the eligible patients were actually treated), the potential number of patients to be treated with Myopridin	1,031	1,056	1,050	1,031	
Outcomes required	Desired outcomes: reduction in pain (VAS), reduction in muscle tension and improved mobility, allowing patients to maintain mobilisation and manage some exercises to improve their back. Ultimately, there would be a desire to prevent long-term chronic back pain.					

Summary of current treatment pathway

Surrey Guidance: Pharmacological management of persistent non-malignant pain in adults. Is due to be reviewed in June 2021.¹¹

Pharmacological Management of low back pain (excluding sciatica)

Consider alternative diagnosis and risk stratification (STarT Back risk assessment tool) to inform decision making.

Non-pharmacological interventions (page 7) should be considered first.

These may include self-management; group exercise programme; psychological therapy which may be combined with physical therapy (for referral see page 7)

Following consideration of non-pharmacological interventions:

- Offer **oral NSAIDs** - **Ibuprofen** up to 1200mg daily or **Naproxen** up to 1000mg daily (*diclofenac* or *COX-2 [celecoxib first line COX-2]* may be considered as alternatives – see appendix 2)
- **Use at the lowest effective dose for the shortest possible time.**
- Gastroprotective treatment should also be offered while an NSAID is being used.
- If an NSAID is contraindicated, not tolerated, or ineffective, offer a weak opioid (e.g. **codeine**) with or without **paracetamol**, taking into account the risk of opioid dependence and adverse effects such as constipation.
- If the person has muscle spasm, consider offering a short course of a benzodiazepine, such as diazepam 2 mg up to three times a day for up to 5 days, if not contraindicated

- **NICE does not recommended SSRI, SNRI, TCA and anticonvulsants (including gabapentin and pregabalin) for managing low back pain**
- **Do not offer paracetamol alone for managing low back pain**
- **NICE does not recommend opioids for managing chronic low back pain**

Myopridin can be considered a first-line treatment in patients with lower back and neck pain associated with muscle spasm, either alone, or in combination with, a NSAID.

Evidence review

Isobe et al¹

Study Design: Double blind, placebo-controlled, multi-centre study.

Objective: To evaluate the therapeutic effectiveness of pridinol and side effects.

Population: Enrolment of 270 patients in total. 90 with spondylosis deformans, 87 patients with periarthritis humeroscapularis and 93 patients with cervico-omo-brachial syndrome.

Intervention: Patients were randomised to pridinol 3mg three times a day or placebo (lactose) for 3 weeks. As a rule the use of other drugs were prohibited, however the use of mild analgesics in small doses were allowed if unavoidable, and a drug was used that has no influence upon the evaluation of muscle relaxant effect of pridinol.

Evaluation: Symptom evaluation of spontaneous pain, pain elicited by movement, painful area, stiffness on the shoulder, numbness, cold sensation etc.

Assessment: Clinicians and patients were asked to judge their responses to treatment as excellent, good, fair, no response or exacerbation after 3 weeks. Patients also asked to give their general impression regarding treatment as very good, good, unchanged and exacerbated.

Primary Outcomes: A statistically significantly greater number of patients with spondylosis deformans and cervico-omo-brachial syndrome described their response as excellent, good or fair in the treatment group compared to placebo

Endpoints:

- 82.6% (38/46) of patients with lumbar pain given pridinol 3mg three times a day were considered to have a very good, good or fair response compared to 59.1% (26/44) given placebo (p<0.05)
- 73.9% (336/4) of patients with pain and stiffness of the cervical spine given pridinol 3mg three times a day were considered to have very good, good or fair response compared to 59.2% (24/47) given placebo (p<0.05)¹
- Side effects were reported in 13 of 140 (9.3%) of patients taking pridinol and 10 of 135 (7.4%) of patients taking placebo.

Beyeler J²

Study Design: Open label study.

Objective: To compare treatment (pridinol) with physiotherapy to treatment (pridinol) with physiotherapy combination.

Population: 120 patients with paravertebral muscle hardening as an accompanying symptom to mostly degenerative spinal conditions. 50 patients were treated with physiotherapy, 50 patients with physiotherapy and pridinol combination. A further 20 patients were treated with pridinol alone.

Intervention: Physiotherapy consisted of heat applications and loosening exercises two to three times a week. Pridinol was administered at 3mg three times a day.

Assessment: The patients were assessed 6 times throughout the study: after half a week, one week, one and a half weeks, two weeks, three weeks and four weeks. A clinical follow up examination included a static-dynamic examination of the spine and the use of mytonographs

Outcomes: Clinicians considered the response to treatment as good very good, unchanged or poor at 3 weeks. Treatment in combination of physiotherapy and pridinol was significantly more effective than with physiotherapy alone (P<0.05)

Primary Endpoints:

- 88% of the results for patients treated with pridinol and physiotherapy were good to very good
- The group receiving physiotherapy alone took longer to show an improvement objectively and subjectively than the group receiving physiotherapy and pridinol.²

MYTOS³

Study Design: Observational study

Objective: To document the efficacy and tolerability of a maximum of one week therapy with pridinol for painful muscle tension in real life conditions, in a large patient cohort.

Population: 1369 patients who had been diagnosed with painful muscle tension in the locomotor system such as lumbago, musculoskeletal pain, acute shoulder- arm syndrome, sciatica, thoracic syndrome, acute torticollis, cervical sprain and nocturnal leg cramps.

The average age of patient cohort being 48.8 years.

Lumbago being the most common diagnosis (468 patients, 34.2%), musculoskeletal pain (369 patients, 27%), and acute shoulder arm syndrome (362 patients, 26.4%)

Intervention: 1.3mg to 3mg of pridinol three times a day for one week.

Assessment: The doctors evaluated the intensity of the clinical symptoms muscle tension, pain and mobility restrictions on an 11-point analogue scale, with 0 meaning no symptoms and 10 representing extreme symptoms at the beginning and at the first review (approximately one week) Patients were also asked to evaluate the starting dose of pridinol and their pain levels after half an hour, 1 hour and 2 hours on an 11-point analogue scale.

Primary Outcomes

- Muscle tension decreased from an average of 7.2 to 3.1 points during the study, average change -4.1 points (-56.8%)
- Pain intensity decreased from an average of 7.1 to 26 points during the study, average change of -4.5 points (-61.7%)
- Mobility restriction decreased from an average of 6.4 to 2.3% points during the study, average change -4.1 points (61.7%)

Additional Endpoints

- 83.3% of doctors and 80.4% of patients reported pridinol efficacy as good or very good.
- 80.4% of patients scored the efficacy of pridinol very good or good.
- Pridinol starts to take effect within 0.5 to 2 hours helping reduce the pain.³

Adverse effects

At the stated doses adverse effects to Myopridin are rare to uncommon and generally disappear after a dose reduction or discontinuation of the medicinal product. The frequency of adverse effects in the SPC is estimated on the basis of the MYTOS study.³

The following adverse effects may occur, particularly during concomitant administration with other anticholinergic medicinal products: dry mouth, thirst, transient visual disorder (mydriasis, difficulties with accommodation, photosensitivity, and slight increase in intraocular pressure), redness and dryness of the skin, bradycardia followed by tachycardia, micturition disorders, constipation, and very rarely vomiting dizziness and unsteady gait.⁵

Assessment of adverse effects is based on the following frequencies:⁵

Very common	(≥ 1/10)
Common	(≥ 1/100, < 1/10)
Uncommon	(≥ 1/1000, < 1/100)
Rare	(≥ 1/10,000, < 1/1,000)
Very rare	(≥ 1/10,000)
Not known	(frequency cannot be estimated from the available data)

System organ class	Uncommon	Rare	Not known
Immune system disorders		Hypersensitivity (such as pruritus allergic, erythema, oedema mucosal, dyspnoea)	
Psychiatric disorders	Restlessness	Anxiety, depression	Hallucinations
Nervous system disorders	Dizziness, headache, speech disorder	Disturbance in attention, coordination abnormal, taste disorder	Tremor, paresthesia
Eye disorders		Accommodation disorder, visual impairment	Glaucomatocyclitic crises in angle closure glaucoma
Cardiac disorders	Tachycardia		Arrhythmia, bradycardia
Vascular disorders	Circulatory collapse, hypotension		
Gastrointestinal disorders	Nausea, abdominal pain, dry mouth	Diarrhea, vomiting	
Musculoskeletal and connective tissue disorders			Muscular weakness

Renal and urinary disorders			Micturition disorder, acute Urinary retention in benign prostate hyperplasia
General disorders and administration site conditions	Fatigue, asthenia		Feeling hot

Equity / Stakeholder views (if relevant)	
Decisions of local Trusts DTCs and neighbouring APCs	Myopridin [®] was launched on the 18 th January 2021 and to date, there are no decisions made from other UK sources.
Recommendations from national / regional decision making groups	<p>“The All Wales Therapeutics and Toxicology Centre (AWTTC,) has concluded that Myopridin[®] (pridinol mesilate), fulfils the All Wales Medicines Strategy Group (AWMSG) appraisal exclusion criterion number 7. As a result, there is no requirement for this medicine to be nationally appraised for use within NHS Wales for its licensed indication.</p> <p>https://awmsg.nhs.wales/medicines-appraisals-and-guidance/medicines-appraisals/pridinol-myopridin/</p> <p>In Europe, approvals for the originator brand of pridinol mesilate and subsequent generic versions of the API, have been in place in Italy, Germany and Poland since the 1960's. Pridinol mesilate 3mg tablets therefore met the requirements for authorisation under Article 10 of Directive 2001/83/EC.”¹⁶</p>
Stakeholder views	<ul style="list-style-type: none"> • No patient group feedback has been obtained yet. • It would be useful to conduct an audit to assess patient's experience, satisfaction and response (pain, function, opioid use) • A consultation of primary care consultants has been carried out at East Surrey Hospital: please find the responses below under references
CCG priorities	<p>Long-term NHS plan. To reduce outpatient attendances, A&E attendances and non-elective admissions.</p> <p>To reduce the prescribing of opioids and drugs of addiction that have the potential to have a negative impact on patients' lives.¹¹</p> <p>As per the Surrey Misuse Strategy, a key priority is reducing and managing Substance Misuse and Resilience.</p> <p>It has been highlighted that medicines such as benzodiazepines and opioids can lead to dependence in patients if used for extended periods of time.¹⁵</p>

Health economic considerations	
Cost per year per patient	<p>Cost per year per patient:</p> <p>Treatment dose of one tablet three times a day costs less than 80p per day.</p> <p>Pridinol for 5-10 days 3mg TDS: £4.02 - £7.84</p> <p>Pridinol for 5-10 day 1.5mg TDS: £2.14 - £4.02</p>

	CCG	NHS Guildford and Waverley CCG	NHS Surrey Downs CCG	NHS North West Surrey CCG	NHS Surrey CCG								
	Prevalence of back pain	16.5%	16.9%	16.8%	16.5%								
	Potential patient numbers as calculated in table above	1,031	1,056	1,050	1,031								
	Total cost/100,000 based on £7.84 for 10 days	£8,083.04	£8,279.04	£8,232.00	£8,083.04								
Alternative treatments cost per patient per year	<p>There are several medicines that are used to treat back pain, but are no longer recommended due to a perceived lack of effectiveness and a significant risk of addiction.⁶ Including Myopridin in the formulary may further reduce the likelihood of these medicines being prescribed.</p> <p>Diazepam 2mg PO TDS for 5 days: £0.51</p>												
Other financial considerations (if relevant)	<p>In some instances patients with acute low back pain who are fearful and want to seek immediate medical attention will go to the Emergency Department rather than consulting the GP.</p> <p>The tariff cost for attendance at the Emergency Department is £107. If there is a requirement for admitting the patient with low back pain then the non-elective tariff range from £811-£1947.⁹</p> <p>Apparently, 15% of patients get referred to hospital outpatients. Where most of them are to an orthopaedic surgeon, some might be to a rheumatologist or other specialities.¹⁰ A recent audit found that patients with low back pain appeared in 10 different clinics and two fifths of them had already been seen in a different speciality with the same complaint.⁹</p> <p>The cost of an outpatient attendance depends on the speciality that the patient is referred to.</p> <table border="1"> <thead> <tr> <th>Speciality</th> <th>First attendance</th> </tr> </thead> <tbody> <tr> <td>Trauma and orthopaedics</td> <td>£163</td> </tr> <tr> <td>Pain</td> <td>£199</td> </tr> <tr> <td>Rheumatology</td> <td>£273</td> </tr> </tbody> </table> <p>This cost would include standard blood tests, but if the patient was then referred for an investigation, for example an x-ray then an additional cost would occur as well as an additional follow up visit. It is possible that the patient would receive injection therapy with additional costs.</p> <p>Avoiding a referral to a hospital specialist would save approximately £200 (£163-£273 depending on speciality)⁹</p>					Speciality	First attendance	Trauma and orthopaedics	£163	Pain	£199	Rheumatology	£273
Speciality	First attendance												
Trauma and orthopaedics	£163												
Pain	£199												
Rheumatology	£273												
Health economic data (if available)	No health economic data available.												

References

1. Isobe *et al* Therapeutic effect of methanesulphonate pridinol upon spondylosis deformans, periarthritis humeroscapularis and cervico-omo brachial syndrome. Data on File.
2. Beyeler J Treatment of paravertebral muscle hardening with Lyseen Orthopädische Praxis 10/XI 796-799. Data on File
3. MYTOS (My Therapeutic Observational Study) with Myoson® direct 2005
4. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:549-557 Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:549-557
5. Myopridin. Summary of Product Characteristics (SmPC). Available from: <https://www.medicines.org.uk/emc/product/11957/smpc>. [Accessed 2 March 2021]
6. Gahr, M *et al*. Abuse liability of centrally acting non-opioid analgesics and muscle relaxants – a brief update based on a comparison of pharmacovigilance data and evidence from the literature *International Journal of Neuropsychopharmacology* (2014), **17**,957–959
7. Musculoskeletal calculator. Available at: <https://www.versusarthritis.org/>. [Accessed 12 March 2021]
8. National Institute for Health and Care Excellence. Low back pain and sciatica in over 16s. assessment and management NICE guideline [NG 59] United Kingdom: National Institute for Health and Care Excellence; 30 November 2016
9. The National Tariff. Available from: <https://www.england.nhs.uk/publication/national-tariff-payment-system-documents-annexes-and-supporting-documents/> [Accessed March 2021]
10. Silman A J. Hospital referrals for low back pain: more coherence needed. *Journal of the The Royal Society of Medicine*. March 2000; 93: 135-137
11. Surrey CCG. The Pharmacological Management of Persistent Non-malignant Pain in Adults. Available from: <https://surreyccg.res-systems.net/PAD/Content/Documents/2/Surrey%20PNMP%20Update%20August%202019.pdf> [Accessed 12 March 2021]
12. Roland MO. A critical review of the evidence for a pain-spasm-pain cycle in spinal disorders. *Clin Biomech (Bristol, Avon) Actions*. 1986 May;1(2):102-9
13. Safiri *et al* Global, regional, and national burden of neck pain in the general population, 1990-2017: systematic analysis of the Global Burden of Disease Study 2017. *BMJ* 2020;**368**:m791
14. Gustavo C. Can Recurrence After an Acute Episode of Low Back Pain Be Predicted? Available from: <https://academic.oup.com/ptj/article/97/9/889/3884292> [Accessed 12 March 2021]
15. Surrey Substance Misuse Strategy. Available from: https://www.healthysurrey.org.uk/_data/assets/pdf_file/0011/198839/Surrey-Substance-Misuse-Strategy-Drugs-2019-Refresh_FINAL.pdf [Accessed 12 March 2021]
16. All Wales Medicines Strategy Group. Medicine Appraisals: Pridinol (Myopridin®). Available from: <https://awmsg.nhs.wales/medicines-appraisals-and-guidance/medicines-appraisals/pridinol-myopridin/> [Accessed June 2021]
17. National Institute for Health and Care Excellence [NICE], 2020. Clinical Knowledge Summary: Back pain – low (without radiculopathy). Available from: <https://cks.nice.org.uk/topics/back-pain-low-without-radiculopathy/management/management> (Accessed August 2021)
18. National Institute for Health and Care Excellence (NICE) Reviewed in Dec. 2020. Low back pain and sciatica in over 16s: assessment and management. NG59. Available from: <https://www.nice.org.uk/guidance/ng59/resources/low-back-pain-and-sciatica-in-over-16s-assessment-and-management-pdf-1837521693637> (Accessed September 2021)

Prepared by:

Dr Jan Rudiger, Consultant in Anaesthetics and Pain Medicine, Pain Lead at East Surrey Hospital, Surrey and Sussex NHS Healthcare

Declaration of Interest: XXXX

Date: XXXX

Reviewed by: Liz Clark, APC Pharmacist, Surrey Heartlands CCG

Declaration of Interest: None

Date: 09/08/21