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| **TITLE PAGE** |  |  |
| **Clinical Overview** |  |  |
|  |  |  |
|  | **Document Number:** | **c03400292-01** |
|  | **Document ID:** | **EU** |
|  |  |  |
| **Drug Substance(s):** | Piroxicam |  |
| **Dosage Form, Strength:** | Gel 5 mg piroxicam/per gram gel, 0.5% | |
|  |  |  |
| **Document Title:** | Clinical Overview |  |
|  | Finalgel CCDS No. 9012-00 |  |
|  |  |  |
| **Date of Report:** | 26 Mar 2015 | **Page 1 of 14** |
|  |  |  |
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**LIST OF ABBREVIATIONS AND DEFINITION OF TERMS**

ADR Adverse Drug Reaction

AE Adverse Event

CCDS Company Core Datasheet

DLP Data Lock Point

IBD International Birth Date

NSAID Non-Steroidal Anti-Inflammatory Drug

NNT Number Needed to Treat

OTC Over The Counter

PSUR Periodic Safety Update Report

PT Preferred Term

SCAR Severe Cutaneous Adverse Reactions

SmPC Summary of Product Characteristics

SOC System Organ Class

|  |  |
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1. **PRODUCT DEVELOPMENT RATIONALE**
2. **MEDICAL BACKGROUND AND TARGET INDICATION**

The current Clinical Overview is supportive for the Finalgel CCDS No. 9012-00.

Finalgel is a generic topical formulation of piroxicam marketed by Boehringer Ingelheim, containing 5 mg piroxicam / g (0.5%) gel, authorised for the treatment of painful inflammatory disorders of the musculoskeletal system:

* Tendonitis, tendovaginitis
* Painful frozen shoulder
* Contusions, distorsions, sprains

One common feature of the treatment for the above-mentioned painful inflammatory musculoskeletal disorders is that often they are self-managed with OTC medication and do not require a doctor visit. As seen in all treatment recommendations, the management of pain and inflammation require administration of analgesic medication (paracetamol, NSAIDs).

Piroxicam is a conventional NSAID with anti-inflammatory, analgesic, and antipyretic properties that has been used in medicine since the early 1980s. Although the mechanism of action is not completely understood, piroxicam inhibits prostaglandin synthesis and release through a reversible inhibition of the cyclo-oxygenase enzyme.

Three meta-analyses of randomised controlled clinical trials of topical non-steroidal anti-inflammatory drugs confirmed the positive benefit risk ratio of piroxicam for the registered short-term indications ranging from 1 to 3 weeks of use [ P14-03844, P10-13072, P04-09366]. Owing to the relatively low systemic exposure following topical application of piroxicam, systemic side effects are rare [U98-0265, U98-0266].

1. **DRUG PROFILE**

Finalgel is a topical medicinal product marketed by Boehringer Ingelheim with non-prescription medicine regulatory status. Finalgel is a generic to Pfizer’s Feldene gel and has received the first Marketing Authorization in Germany in 1997 as an OTC product. Currently is registered in the following countries: Azerbaijan, Belarus, Georgia, Germany, Kazakhstan, Moldova, Russia and Ukraine. The product that has been marketed for many years and it is formulated as a gel intended for topical administration containing as active ingredient piroxicam in concentration of 5mg/g (0.5%) in tubes of 35 g.

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1. **OVERVIEW OF BIOPHARMACEUTICS**

NA

1. **OVERVIEW OF CLINICAL PHARMACOLOGY**

No new data have been obtained by the Marketing Authorization Holder. However, the wording of the chapters ‘Pharmacological Properties’ and ‘Pharmacokinetics’ have been reworded to align the CCDS with the Originator’s SmPC [R14-2335]:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Previous** | | **Proposed** | |  |
|  | |  | |  |
| Pharmacological properties |  | Pharmacological properties |  |  |
|  | |  | |  |
| Piroxicam, the active ingredient of | | Piroxicam, the active ingredient of Finalgel | |  |
| Finalgel®, inhibits the enzyme | | is a non-steroidal anti-inflammatory agent | |  |
| cyclooxygenase. This is a basic charisteristic | | useful in the treatment of inflammatory | |  |
| of non – steroidal anti – inflammatory drugs | | conditions. The mode of action of piroxicam | |  |
| (NSAID), which allows them to influence | | is inhibition of prostaglandin synthesis and | |  |
| many pathophysiologic processes. | | release through a reversible inhibition of the | |  |
|  |  | cyclo-oxygenase enzyme. Piroxicam has anti | |  |
| Piroxicam has anti – inflammatory, | | – inflammatory, analgesic, antipyretic, | |  |
| antithrombogenic activities after oral, rectal, | |  |
| analgesic, antipyretic, antithrombogenic | | subcutaneous, intraperitoneal routes as | |  |
| activities after systemic application by oral, | | demonstrated in animal and human models. | |  |
| rectal, subcutaneous, intraperitoneal routes. | |  |  |  |
| Ist pharmacological profile is based on the | | Data on the anti-inflammatory and analgesic | |  |
| inhibition of prostaglandin synthesis from | | effects of piroxicam 0.5%gel compared with | |  |
| arachidonic acid in vitro, of collagen – | | its vehicle and indometacin 1% Gel in rats | |  |
| induced aggregation of human and animal | | and guinea pigs are available. Using | |  |
| platelets in vitro, of the release of lysosomal | | established animal models of pain and | |  |
| enzymes, of the generation of the reactive | | inflammation, piroxicam 0.5% gel was as | |  |
| superoxide anion, of chemotaxis / migration | | effective as oral piroxicam and indomethacin | |  |
| of neutrophils, macrophages, monocytes, | | 1% Gel and significantly more effective than | |  |
| platelets, of the carrageenin – induced foot | | its vehicle. | |  |
| edema in rats, of the UV – induced erythema | |  |  |  |
| in guinea pigs, of the proliferation of cotton – | |  |  |  |
| string – induced granulomas in rats, of | |  |  |  |
| mycobacterium adjuvant – induced | |  |  |  |
| arthritis in rats, of phenylbenzochinone – | |  |  |  |
| induced writhing in mice, of E. coli – | |  |  |  |
| induced fever in rats, and of urat crystal – | |  |  |  |
| induced synovitis in dogs. | |  |  |  |
|  |  |  |  |  |

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|  |  |  |  | |
| **Previous** | | **Proposed** | |  |
|  | |  | |  |
| Pharmacokinetics | | Pharmacokinetics | |  |
|  |  |  |  |  |
| Piroxicam is a well-established therapeutic | | On the basis of various pharmacokinetic and | |  |
| substance for systemic and topical | | tissue distribution studies in animals, with | |  |
| administration belonging to the class of drugs | | piroxicam gel 0.5%, the highest | |  |
| inhibiting the enzyme cyclooxygenase, thus | | concentrations of piroxicam were achieved in | |  |
| beeing a non – steroidal antiinflammatory | | the tissues below the site of application with | |  |
| drug (NSAID). It has antipyretic, analgesic | | low concentrations being reached in the | |  |
| antirheumatic properties. Depending on the | | plasma. Piroxicam gel 0.5% was | |  |
| method of application, on the topical | | continuously and gradually released from the | |  |
| excipient base, and on the (pre)treatment of | | skin to underlying tissues, equilibrium | |  |
| the skin, between 6.7 and 62 % (animal | | between skin, and muscle or synovial fluid | |  |
| experiment) of the topically applied | | appeared to be reached rapidly, within a few | |  |
| piroxicam is percutaneously absorbed after a | | hours of application. From a pharmacokinetic | |  |
| single administration. Topical application of | | study in man, 2 g of the Gel was applied to | |  |
| 20 mg piroxicam contained in 4 g of a | | the shoulders of normal volunteers twice | |  |
| 0.5% gel under occlusion resulted in | | daily (corresponding to 20 mg | |  |
| systemic absorption with the pharmaco- | | piroxicam/day) for 14 days, plasma levels of | |  |
| kinetic criteria tmax =26,7  1,8h, | | piroxicam rose slowly, reaching steady state | |  |
| cmax=149,2  30,3 ng/ml plasma, AUC0 | | after about 11 days. The plasma levels at this | |  |
| =11447  2276 ngh/ml, t ½ Elimination = | | time were between 300 – 400 ng/ml, or one- | |  |
| 45,9 h . Repeated applications to a certain | | twentieth of those observed in subjects | |  |
| site has resulted in piroxicam concentrations | | receiving 20 mg orally. | |  |
| in the adjacent tissues fat, muscle, collagen, | | The serum half-life of piroxicam is | |  |
| synovial membrane, synovia varied between | | approximately 50 hours | |  |
| 15 and 40 ng/g or ng/ml respectively. Within | |  |  |  |
| a few days of concentrations are reached at | |  |  |  |
| sites distant from the place of topical | |  |  |  |
| administration, distant skin excepted. | |  |  |  |
|  |  |  |  |  |

1. **OVERVIEW OF EFFICACY**

Finalgel is a topically applied formulation of piroxicam with the strength of 0.5% (5mg piroxicam per 1 g gel).

Four studies comparing the effectiveness and safety of piroxicam gel 0.5% (Finalgel) with the innovator product (i.e. Feldene gel) in the treatment of pain conditions associated with gonarthrosis, non-articular rheumatism and acute musculoskeletal injuries, demonstrated the therapeutic equivalence of the generic formulation and the innovator product. There were no statistically significant differences between the formulations in terms of reduction in pain and an improvement in mobility from baseline for both preparations [U98-0266].

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A summary of the available clinical evidences from literature is presented below: The clinical effectiveness of piroxicam gel 0.5% has been assessed in numerous randomized controlled clinical trials conducted world-wide enrolling more than 3000 patients. A recent Cochrane systematic review by Massey et all [P10-13072] for topical NSAIDs for acute pain in adults included 47 randomized, double-blind, active or placebo (inert carrier)controlled trials; most compared topical NSAIDs in the form of a gel, spray, or cream with a similar placebo, with 3455 participants in the overall analysis of efficacy. For all topical NSAIDs combined, compared with placebo, the NNT for clinical success, equivalent to 50% pain relief, was 4.5 (range: 3.95.3) for treatment periods of 6 to 14 days. Topical diclofenac, ibuprofen, ketoprofen, and piroxicam were of similar efficacy, but indomethacin and benzydamine were not significantly better than placebo.

There were very few systemic adverse events or withdrawals due to adverse events. There were insufficient data to reliably compare individual topical NSAIDs with each other or the same oral NSAID. The authors concluded that topical NSAIDs can provide good levels of pain relief in acute conditions such as sprains, strains and overuse injuries, probably similar to that provided by oral NSAIDs. Topical NSAIDs are not associated with an increased incidence of local skin reactions compared with placebo, and do not cause systemic (mainly gastrointestinal) problems commonly seen with oral NSAIDs, making them particularly useful for individuals unable to tolerate oral administration, or for whom it is contraindicated. [P10-13072].

These findings are in line with a previous systematic review by Moore et al.[P14-08344] that concluded that piroxicam gel 0.5% was significantly superior to placebo in reducing pain in patients with acute musculoskeletal disorders or injuries, while in chronic conditions, such as gonarthrosis, piroxicam gel 0.5% was also more effective than placebo in a limited number of patients. Studies comparing piroxicam gel 0.5% with other NSAIDs generally indicated that the drug is comparable in efficacy with indomethacin gel l%, diclofenac gel 1% or 1.16%, felbinac gel 3%, ketoprofen gel, and oral ibuprofen (3 times daily 400 mg).

In a systematic review from 2005 on topical analgesics [P04-09366] 26 placebo-controlled trials with 2853 patients were identified for strains and sprains treated with topical NSAIDs. The authors concluded that in 19 of the 26 trials, topical NSAIDs were significantly better than placebo and that ketoprofen had the best NNT of 2.6, significantly better than ibuprofen (4.1), felbinac (4.0), piroxicam (4.7) and indometacin (10). Local AEs, systemic AEs, or withdrawals due to an AE were rare, and no different between topical NSAIDs and placebo. The authors concluded that topical NSAIDs were effective and safe in treating acute painful conditions for one week [P04-09366].

The topical formulation can be particularly useful for patients who cannot tolerate oral administration, as low systemic absorption (bioavailability is 5 -10% compared to the oral formulation) of topical piroxicam should reduce the likelihood of adverse reactions. In the trials reviewed here, tolerability was considered good or excellent in up to 99% of patients of patients studied [R99-0341].

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These results are in line with the current indication, which remains unchanged. Also the section dosage remains unchanged in terms of single dose, daily dose and duration of treatment, nevertheless a remark on the external use only has been added to meet current standards. In addition, some editorial changes to enhance the clarity have been made.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Previous** | | | **Proposed** | | |
|  | |  |  | |  |
| Dosage |  | | Dosage | | |
|  |  |  |  |  | |
|  |  |  | Finalgel is for external use only. | | |
| Dosage |  | | Dosage | | |
|  |  |  |  |  |  |
| Unless otherwise prescribed and depending on | | | Unless otherwise prescribed and depending on | | |
| the extent of the painful area: | | | the extent of the painful area: | | |
| 3 – 4 times daily maximally 1 g gel | | | An amount of maximally 1 g gel equivalent to | | |
| (corresponds with the size of a hazelnut) | | | 5 mg piroxicam (corresponds with the size of | | |
| should be locally applied and gently rubbed | | | a hazelnut) should be locally applied and | | |
| into the skin. | | | gently rubbed into the skin 3 – 4 times daily. | | |
| Treatment duration | | | Treatment duration | | |
|  | |  |  | |  |
| The duration of treatment depends on the | | | The duration of treatment depends on the | | |
| control of symptoms and varies between | | | control of symptoms and varies between | | |
| approximately 2 – 3 weeks in tendinitis and | | | approximately 2 – 3 weeks in tendinitis and | | |
| tendovaginitis as well as frozen shoulder, in | | | tendovaginitis as well as frozen shoulder, in | | |
| injuries 1 – 2 weeks. | | | injuries 1 – 2 weeks. | | |
|  |  |  |  |  |  |

In the section ‘pharmacological properties’ a short description of the studies comparing Finalgel with the Originator [U98-0266] has been added in reflection of the current standards:

|  |  |  |  |
| --- | --- | --- | --- |
| **Previous** |  | **Proposed** | |
|  |  |  | |
| Clinical trials |  | Clinical trials |  |
|  |  |  | |
| NA |  | Therapeutic equivalence with the | |
|  |  | corresponding original product (Felden gel) | |
|  |  | has been demonstrated for piroxicam gel 0.5% | |
|  |  | (Finalgel) in 4 randomised, double-blind, and | |
|  |  | parallel group studies with a 2-3 week | |
|  |  | duration of treatment. Finalgel was as | |
|  |  | effective and safe as the innovator product in | |
|  |  | the treatment of painful conditions associated | |
|  |  | with gonarthrosis, non-articular rheumatism | |
|  |  | and acute musculoskeletal injuries. | |
|  |  |  |  |

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1. **OVERVIEW OF SAFETY**

In the most recent PSUR (02 Apr 2011 to 01 Apr 2014) for Finalgel [s00021654-01], data on post-marketing exposure and safety are available in the cumulative and interval summary tabulation of ADRs from post-marketing sources that includes the numbers of serious and non-serious ADRs (PTs) organized by SOC and grouped by sources for the medicinal product both for the reporting interval and cumulatively, i.e. from the IBD to the DLP of the PSUR.

During the reporting interval for the recently completed PSUR, the assessment of the Boehringer Ingelheim global drug safety database did not reveal any safety issues previously unknown for piroxicam. However, the Marketing Authorization Holder noted that there is safety related information available within the Originator’s approved SmPC [R14-2335] which was missing in the product information for Finalgel.

Thus, the Marketing Authorization Holder proposes therefore to align the safety related information with the originator SmPC [R14-2335]. The most important additions relate to SCAR (warnings and side effects) and information on fertility. All proposed alignments with the Originator are shown in the table below:

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
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|  |  |  |  |  |  |  |  |  |  |  | |  |
| **Previous** | | | | | **Proposed** | | | | | |  |  |
|  |  |  |  | |  |  |  |  | |  |  |  |
| Special Warnings and Precautions | | | |  | Special Warnings and Precautions | | | |  | |  |  |
|  |  | |  | |  |  | |  | | |  |  |
| Application of Finalgel to juveniles is not | | | | | (moved to section ‘Use in Children’) | | | | | |  |  |
| recommended due to the lack of sufficient | | | | |  |  |  |  |  |  |  |  |
| therapeutical experience. | | | | |  |  |  |  |  |  |  |  |
| Hypersensitivity | | | | | Hypersensitivity | |  |  | |  |  |  |
| Patients with asthma, allergic rhinitis, chronic | | | | | |  |  |
|  |  |  |  | |  |  |
| Patients with asthma, allergic rhinitis, chronic | | | | |  |  |
| obstructive pulmonary disease or chronic | | | | | obstructive pulmonary disease or chronic | | | | | |  |  |
| infections of the lungs are more sensitive to | | | | | infections of the lungs are more sensitive to | | | | | |  |  |
| NSAID and react more often with attacks of | | | | | NSAID and react more often with attacks of | | | | | |  |  |
| asthma, local mucocutaneous edema and | | | | | asthma, local mucocutaneous edema and | | | | | |  |  |
| urticaria. | | | | | urticaria. | | | | | |  |  |
|  |  |  |  |  | Severe cutaneous adverse reactions | | | | |  |  |  |
|  |  |  |  |  | Severe cutaneous adverse reactions (SCAR) | | | | | |  |  |
|  |  |  |  |  | have been reported with the systemic | | | | | |  |  |
|  |  |  |  |  | administration of piroxicam. These reactions | | | | | |  |  |
|  |  |  |  |  | have not been associated with topical | | | | | |  |  |
|  |  |  |  |  | piroxicam, but the possibility of SCAR | | | | | |  |  |
|  |  |  |  |  | occurring with topical piroxicam cannot be | | | | | |  |  |
|  |  |  |  |  | excluded. Patients shall be advised that in case | | | | | |  |  |
|  |  |  |  |  | any signs or symptoms of SCAR (e.g. | | | | | |  |  |
|  |  |  |  |  | progressive skin rash often with blisters or | | | | | |  |  |
|  |  |  |  |  | mucosal lesions) occur after topical | | | | | |  |  |
|  |  |  |  |  | administration of piroxicam, they must | | | | | |  |  |
|  |  |  |  |  | discontinue treatment and seek medical advice | | | | | |  |  |
|  |  |  |  |  | immediately. If the patient has developed | | | | | |  |  |
|  |  |  |  |  | SCAR with the use of piroxicam, piroxicam | | | | | |  |  |
|  |  |  |  |  | treatment must not be re-started in this patient | | | | | |  |  |
|  |  |  |  |  | at any time. | | | | | |  |  |
|  |  | | | |  |  | | | | |  |  |
| Fertility, Pregnancy and Lactation | | |  | | Fertility, Pregnancy and Lactation | | | | | |  |  |
|  | | |  | |  | | |  | | |  |  |
| Pregnancy |  | | | | Pregnancy |  | | | | |  |  |
| Strict precautions regarding the use in | | | | | Finalgel® is contraindicated during the 3rd | | | | | |  |  |
| pregnancy, especially during the 1st and 2nd | | | | | trimester of pregnancy (see section | | | | | |  |  |
| trimester, should be observed (see also 4.3.). | | | | | contraindications). | | | | | |  |  |
|  |  |  |  |  | Inhibition of prostaglandin synthesis might | | | | | |  |  |
|  |  |  |  |  | adversely affect pregnancy. Data from | | | | | |  |  |
|  |  |  |  |  | epidemiological studies suggest an increased | | | | | |  |  |
|  |  |  |  |  | risk of spontaneous abortion after use of | | | | | |  |  |
|  |  |  |  |  | prostaglandin synthesis inhibitors in early | | | | | |  |  |
|  |  |  |  |  | pregnancy. In animals, administration of | | | | | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

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|  |  |  |  |  |  |  |  |  |  |  | |  |
| **Previous** | | | | | **Proposed** | | | | | |  |  |
|  |  |  |  |  |  | | |  |  |  |  |  |
|  |  |  |  |  | prostaglandin synthesis inhibitors has been | | | | | |  |  |
|  |  |  |  |  | shown to result in increased pre- and | | | | | |  |  |
|  |  |  |  |  | postimplantation loss. Therefore, the use of | | | | | |  |  |
|  |  |  |  |  | Finalgel® during the 1st and 2nd trimester | | | | | |  |  |
|  |  |  |  |  | pregnancy is not recommended. | | | | | |  |  |
| Lactation | | | | | Lactation | | | | | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Since piroxicam is excreted in breast milk in | | | | | Finalgel® is not recommended for use in | | | | | |  |  |
| small amounts Finalgel® should not be | | | | | nursing mothers as clinical safety has not been | | | | | |  |  |
| administered to a nursing woman | | | | | established. | | | | | |  |  |
| NA | | | | | Fertility |  | | | | |  |  |
|  |  |  |  |  | Based on the mechanism of action, the use of | | | | | |  |  |
|  |  |  |  |  | NSAIDs, including piroxicam may delay or | | | | | |  |  |
|  |  |  |  |  | prevent rupture of ovarian follicles, which has | | | | | |  |  |
|  |  |  |  |  | been associated with reversible infertility in | | | | | |  |  |
|  |  |  |  |  | some women. In women who have difficulties | | | | | |  |  |
|  |  |  |  |  | conceiving or who are undergoing | | | | | |  |  |
|  |  |  |  |  | investigation of infertility, withdrawal of | | | | | |  |  |
|  |  |  |  |  | NSAIDs, including piroxicam should be | | | | | |  |  |
|  |  |  |  |  | considered. | | | | | |  |  |
|  | |  |  | |  | | |  | |  |  |  |
| Use in children | | | | | Use in children | | | | | |  |  |
|  | |  |  |  |  | | |  |  |  |  |  |
| (In section Contraindications): Finalgel® is | | | | | Dosage recommendations and indications for | | | | | |  |  |
| contraindicated in children below 14 years. | | | | | the use of Finalgel® in children have not been | | | | | |  |  |
| (In section In Special Warnings and | | | | | established. Therefore Finalgel should not | | | | | |  |  |
| be applied in children below 14 years (see | | | | | |  |  |
| precautions): Application of Finalgel to | | | | |  |  |
| chapter contraindication). The application of | | | | | |  |  |
| juveniles is not recommended due to the lack | | | | |  |  |
| of sufficient therapeutic experience. | | | | | Finalgel to adolescents is not recommended | | | | | |  |  |
| due to the lack of sufficient therapeutic | | | | | |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  | experience. | | | | | |  |  |
|  | | |  | |  | | | | |  |  |  |
| Interactions | |  | | | Interactions | | |  | | |  |  |
|  | | |  | |  | | | | |  |  |  |
| If Finalgel® is used adequately to date no | | | | | None known. | | | | | |  |  |
| drug interactions have been reported. | | | | |  |  |  |  |  |  |  |  |
|  | | | | |  | | | | |  |  |  |
| Side Effects | | | | | Side Effects | | | | | |  |  |
|  |  |  |  |  |  | | | | | |  |  |
|  |  |  |  |  | Immune system disorders : | | | | |  |  |  |
| Skin reactions of hypersensitivity due to other | | | | | Hypersensitivity reactions may occur in | | | | | |  |  |
| components of the gel are possible, in such | | | | | predisposed patients. If such reactions (which | | | | | |  |  |
| cases the application should be interupted and | | | | | may take the form of skin reactions) do occur, | | | | | |  |  |
| and an adaquate treatmentment should be | | | | | use of Finalgel should be discontinued and | | | | | |  |  |
| initiated. | | | | | appropriate treatment given (see section | | | | | |  |  |
|  |  |  |  |  | Special Warnings and Precautions). | | | | | |  |  |
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|  |  |  |  |  |  |  |  | |
| **Previous** | | **Proposed** | | | | | |  |
|  |  |  |  | | | | |  |
|  |  | Respiratory, thoracic and mediastinal | | | | | |  |
|  |  |  |  |  |  |  |  |  |
|  |  | disorders and gastro-intestinal disorders: | | | | | |  |
|  |  |  |  |  | |  |  |  |
| If Finalgel® is used on large areas, systemic | | If Finalgel is applied to large areas of skin, | | | | | |  |
| side effects cannot be excluded. In single | | systemic effects cannot be excluded. Nausea, | | | | | |  |
| cases gastro – intestinal disturbances and | | gastric symptoms, cases of abdominal pain | | | | | |  |
| dyspnea have been reported. | | and gastritis have been reported as well as | | | | | |  |
|  |  | bronchospasm and dyspnoea. | | | | | |  |
|  |  | Skin and subcutaneous tissue disorders: | | | | | |  |
|  |  |  |  |  | |  | |  |
| Occasionally local reactions of the skin like | | Skin reactions with symptoms such as skin | | | | | |  |
| inflammation, redness, urticaria, pruritus, | | irritation, erythema, rash, vesiculation, flaking | | | | | |  |
| desquamation etc. can be observed. | | and pruritus may occur at the application site. | | | | | |  |
|  |  | SCARs such as Stevens-Johnson syndrome | | | | | |  |
|  |  | and toxic epidermal necrolysis have been | | | | | |  |
|  |  | reported very rarely (see section Special | | | | | |  |
|  |  | Warnings and Precautions). | | | | | |  |
|  |  | Contact dermatitis, eczema and | | | | | |  |
|  |  | photosensitivity skin reaction have been | | | | | |  |
|  |  | observed from post-marketing experience. | | | | | |  |
|  |  | Renal and urinary disorders: | | | | | |  |
|  |  |  |  |  | | | |  |
| One single case of interstitial nephropathia | | There have been isolated reports of | | | | | |  |
| with functional renal insufficiency and | | tubolointerstitial nephritis, renal failure and | | | | | |  |
| nephrotic syndrome has been reported | | nephrotic syndrome (see section Special | | | | | |  |
|  |  | Warnings and Precautions). | | | | | |  |
|  | |  | | | | | |  |
| Overdose |  | Overdose |  | | | | |  |
|  | |  | | | | | |  |
| The application of Finalgel is to be stopped | | Overdosage is unlikely to occur with this | | | | | |  |
| if undesired effects develop. In the case of | | topical preparation. In the case of intoxication | | | | | |  |
| intoxication due to inadequate use, treatment | | due to inadequate use, symptomatic treatment | | | | | |  |
| according to the symptomatology. Results of | | is recommended. | | | | | |  |
| investigations allow the conclusion that the | |  |  |  |  |  |  |  |
| application of charcoal reduces the resorption | |  |  |  |  |  |  |  |
| of piroxicam and the available amount of the | |  |  |  |  |  |  |  |
| active agent. | |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |

With these alignments, the safety information of Finalgel is adjusted to the state of medical knowledge.

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1. **BENEFITS AND RISKS CONCLUSIONS**

Piroxicam is a conventional NSAID with anti-inflammatory, analgesic, and antipyretic properties that has been used in medicine since the early 1980s. A topical generic formulation of piroxicam is marketed by Boehringer Ingelheim under the trade name Finalgel containing 5 mg piroxicam in each gram (0.5%), and is indicated for the topical treatment of painful inflammatory disorders of the musculoskeletal system.

Randomised controlled trials with more than 3000 patients enrolled worldwide demonstrated

efficacy and favorable tolerability of piroxicam gel 0.5% as well as comparable efficacy and tolerability with the innovator product, Feldene gel.

The overall assessment from the published reports suggests that Finalgel is a safe and effective drug for the treatment of painful inflammatory disorders of the musculoskeletal system such as tendonitis, tendovaginitis, painful frozen shoulder, contusions, distorsions and sprains when it is taken under recommended OTC dosage conditions [U98-0266, U98-0265] and in accordance with the updated safety information.

The marketing authorisation holder concludes that the favorable benefit-risk profile of Finalgel remains unchanged. It is a useful medication in the symptomatic treatment of various painful conditions associated with acute musculoskeletal disorders.